



House of Commons
Health Committee

National Institute for Health and Clinical Excellence (NICE)

Written evidence



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*Ordered by The House of Commons
to be printed 26 April 2007*

The Health Committee

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List of written evidence

	<i>Page</i>
1 Department of Health (NICE 01)	Ev 1
2 National Institute for Health and Clinical Excellence (NICE 71)	Ev 5
3 Academy of Medical Sciences (NICE 39)	Ev 22
4 Alzheimer’s Society (NICE 70)	Ev 26
5 American Pharmaceutical Group (NICE 89)	Ev 31
6 Amgen (NICE 58)	Ev 36
7 Archimedes Pharma (NICE 68)	Ev 38
8 Arthritis and Musculoskeletal Alliance (ARMA) (NICE 97)	Ev 40
9 Association of British Healthcare Industries (NICE 85)	Ev 41
10 Association of the British Pharmaceutical Industry (NICE 72)	Ev 43
11 AstraZeneca UK (NICE 33)	Ev 50
12 Beat (NICE 06)	Ev 53
13 BioIndustry Association (NICE 93)	Ev 54
14 Bowel Cancer UK (NICE 38)	Ev 59
15 Breakthrough Breast Cancer (NICE 60)	Ev 62
16 Bristol-Myers Squibb Pharmaceuticals Limited (NICE 51)	Ev 66
17 British Association for Counselling and Psychotherapy (NICE 92)	Ev 69
18 British Medical Association (NICE 95)	Ev 72
19 British Society for Rheumatology (NICE 53)	Ev 75
20 Cancerbackup (NICE 42)	Ev 79
21 Cancer Research UK (NICE 67)	Ev 83
22 Roy Castle Lung Cancer Foundation (NICE 24)	Ev 86
23 Continence Foundation (NICE 23)	Ev 89
24 Cystic Fibrosis Trust (NICE 43)	Ev 92
25 Deltex Medical Group (NICE 87)	Ev 94
26 Diabetes UK (NICE 78)	Ev 96
27 Joint Epilepsy Council of the UK and Ireland (NICE 40)	Ev 99
28 Ethical Medicines Industry Group (NICE 79)	Ev 102
29 European Medicines Group (NICE 84)	Ev 104
30 FEmISA (NICE 49)	Ev 105
31 GlaxoSmithKline (NICE 86)	Ev 108
32 Help the Aged (NICE 11)	Ev 112
33 The Hepatitis C Trust (NICE 29)	Ev 115
34 Improving Surgical Outcomes Group (NICE 75)	Ev 116
35 Institute for Innovation & Valuation in Health Care (NICE 18)	Ev 118
36 Johnson & Johnson (NICE 74)	Ev 122
37 KCI Medical UK (NICE 14)	Ev 128
38 Kidney Cancer UK (NICE 90)	Ev 129
39 Leukaemia CARE (NICE 64)	Ev 131
40 Lifeblood: The Thrombosis Charity (NICE 35)	Ev 135
41 Lilly (NICE 94)	Ev 137

42	25% ME Group (NICE 19)	Ev 142
43	The ME Association (NICE 28)	Ev 146
44	Medical Technology Group (NICE 52)	Ev 149
45	Medtronic Ltd (NICE 15)	Ev 152
46	Merck Serono (NICE 77)	Ev 154
47	MS Society (NICE 65)	Ev 157
48	Motor Neurone Disease Association (NICE 25)	Ev 161
49	Myeloma UK (NICE 30)	Ev 162
50	UK Myeloma Forum (NICE 96)	Ev 166
51	National Childbirth Trust (NICE 27)	Ev 167
52	National Infertility Awareness Campaign (NICE 44)	Ev 171
53	National Osteoporosis Society (NICE 69)	Ev 174
54	National Rheumatoid Arthritis Society (NICE 82)	Ev 176
55	NHS Confederation (NICE 73)	Ev 180
56	Novartis Pharmaceuticals UK Limited (NICE 59)	Ev 182
57	Pfizer Limited (NICE 47)	Ev 186
58	The British Psychological Society (NICE 81)	Ev 191
59	Rarer Cancers Forum (NICE 34)	Ev 193
60	Roche (NICE 55)	Ev 195
61	Royal College of Midwives (NICE 62)	Ev 199
62	Royal College of Nursing (NICE 100)	Ev 200
63	Royal College of Physicians of Edinburgh (NICE 45)	Ev 205
64	Royal College of Paediatrics and Child Health (NICE 66)	Ev 207
65	Royal College of Psychiatrists (NICE 22)	Ev 207
66	Royal National Institute of the Blind (NICE 63)	Ev 211
67	Sanofi-aventis (NICE 57)	Ev 214
68	Schering Health Care Ltd (NICE 56)	Ev 217
69	ScotME (NICE 91)	Ev 218
70	Servier Laboratories Limited (NICE 41)	Ev 222
71	Sirtex Medical (NICE 54)	Ev 225
72	South Asian Health Foundation (NICE 12)	Ev 229
73	Specialised Healthcare Alliance (NICE 80)	Ev 234
74	Wyeth Pharmaceuticals (NICE 88)	Ev 236
75	Daphne Austin (NICE 20)	Ev 240
76	Professor Michael Barkham (NICE 83)	Ev 244
77	Dr Imogen Evans, Mrs Hazel Thornton and Sir Iain Chalmers (NICE 21)	Ev 248
78	Professor Malcolm Hooper (NICE 07)	Ev 250
79	Dr Chris Hyde (NICE 76)	Ev 254
80	Doris Jones	Ev 257
81	Gay Lee (NICE 03)	Ev 261
82	Michael Lee (NICE 13)	Ev 261
83	Professor Ragnar Lofstedt & Frederic Boudier, King's College London (NICE 31)	Ev 265
84	Dr Tom Marshall, University of Birmingham (NICE 05)	Ev 267
85	Dr Catherine Meads, University of Birmingham (NICE 08)	Ev 268
86	Sandra Simkin (NICE 50)	Ev 270

87	Dr Keith Syrett, University of Bristol (NICE 48)	Ev 271
88	Peter Telford (NICE 32)	Ev 275
89	David Thomson (NICE 16)	Ev 280
90	John Walsh (NICE 09)	Ev 282
91	Miss Rose A Woodward (NICE 98)	Ev 282
92	Pelvic Pain Support Network (NICE 04)	Ev 283

Written evidence

Evidence submitted by the Department of Health (NICE 01)

INTRODUCTION

1. Prior to the establishment of NICE in 1999, it was widely accepted that there were unacceptable levels of variation in access to specific treatments. The Department identified a number of factors that contributed to these variations, including;

- the absence of clear standards of care for the NHS;
- the lack of a coherent approach to the assessment of good practice and what works best; and
- slow and inconsistent uptake of effective new treatments.¹

2. NICE was established, as part of a wider quality improvement strategy, to help minimise inequity of access to healthcare by addressing variations in practice, to be a national source of robust clinical guidance and to speed up the uptake of cost-effective new medicines and other interventions in the NHS.

3. NICE has evolved considerably since the 2001 Health Committee inquiry. It has developed an international reputation and consolidated its position as a widely supported source of robust guidance on care pathways and the clinical and cost effectiveness of different interventions. NICE guidance has helped to secure faster and more consistent access for patients to important new treatments. The Department considers this a major achievement on which the Institute and the thousands of individuals who have contributed to its work should be congratulated.

4. NICE's remit has been expanded since the previous Health Committee and now has a number of new and developing areas of work in addition to its technology appraisals and clinical guidelines. NICE now issues guidance on the safety and efficacy of interventional procedures and, since taking on the work of the Health Development Agency in April 2005, NICE has developed a public health work programme and issued its first pieces of public health guidance.

5. NICE has a high degree of operational independence from the Department of Health and is responsible for developing its methodology and guidance independently. The Department sets NICE's budget, holds it to account for delivery of its business plan and refers topics to NICE for its work programmes.

Why NICE's Decisions are Increasingly being Challenged, Whether Public Confidence in the Institute is Waning and, If So, Why?

6. The Department does not accept the premise that NICE appraisals are increasingly being challenged and the proportion of appeals being appealed has not increased.

7. The Department is aware that a high proportion of "negative" technology appraisals are appealed against, but this should not be seen as an indictment of NICE's processes. It is not surprising that negative appraisals are challenged as considerable revenues are at stake for the pharmaceutical companies concerned and appraisals inevitably attract a high level of interest from patient representative groups. NICE's work is both complex and controversial, and the appeal process is an important guarantee of quality and objectivity in NICE's appraisal activity. We welcome the changes NICE has made since 2001 to improve the transparency of the appeal process, specifically by hearing appeals in public.

8. The number of appeals that have been made against NICE guidance should also be looked at in the context of the number of appraisals that NICE has carried out. As at the end of February 2007, NICE has published 119 technology appraisals and, of these, 39 have been the subject of an appeal. NICE has published a further 45 clinical guidelines and 4 pieces of public health guidance.

Confidence in NICE

9. The Department fully supports NICE's role in issuing independent advice based on an objective assessment of the evidence, is confident in the Institute's ability to deliver its work programme to a high standard and believes there remains a high level of respect for and confidence in NICE more broadly.

10. Media and public attention has focussed on NICE's more controversial technology appraisals. It is important to recognise, however, that much of NICE's work, whether technology appraisals, clinical guidelines or emerging public health guidance, is widely welcomed by patients, professionals and other stakeholders. NICE also has significant international standing and is widely regarded as a world leader in its field. NICE's appraisal methodology has been commended by the World Health Organisation, and its publications have a large international audience.

¹ "A first class service: quality in the new NHS", Department of Health, July 1998.

11. Given NICE's role in ensuring the clinically and cost-effective use of finite public resources, it is inevitable that it will sometimes produce guidance that is seen as unfavourable by some stakeholders, including patient groups. Clearly, in some instances, this will lead to criticism from sources with a particular interest in that treatment, but we note that where such criticisms are expressed they are often tempered with a statement of overall support for NICE and its work.

12. NICE faces a challenge in explaining decisions based on complex health economics to a wider audience. We welcome the efforts that NICE has made to ensure that the reasons for controversial decisions are properly understood, but this will continue to be an area where a sustained communication effort is required.

13. It is important that NICE's processes remain transparent to stakeholders and that the rationale for its conclusions is clear. Since 2001, NICE has taken steps to improve the openness of its appraisal process by, for example, holding appeals in public and publishing decisions and considerations on the NICE website. NICE has also significantly improved the design and accessibility of its website to make information easier to find, in particular, from a service user perspective.

14. Recent changes to the topic selection process have also been made to further increase the openness and accessibility of the process to stakeholders.

NICE's Evaluation Process—and Whether any Particular Groups are Disadvantaged by the Process

15. The Department is not aware that any particular groups are disadvantaged by NICE's methodology.

16. The appraisal process and methodology is developed with the involvement of stakeholders and, following a full consultation, revised documentation was published in 2004. NICE will be carrying out a further scheduled review of its technology appraisal methodology during 2007, and this too will be subject to a public consultation phase.

17. The Department considers it right that NICE's process and methodology is the subject of continued development and debate and welcomes the open and consultative approach NICE takes to the development of its work.

The Speed of Publishing Guidance

Single Technology Appraisal process

18. In collaboration with the Department, NICE has developed a Single Technology Appraisal (STA) process, which is designed to speed up the issuing of guidance to the NHS, without compromising the quality and robustness of NICE's guidance.

19. The STA process is used where a single product is being appraised against the standard treatment for use in a single indication, and where there is a manageable evidence base. A Multiple Technology Appraisal (MTA) process is retained for more complex appraisals where multiple treatments are being assessed together. The target timescale for publishing guidance carried out as STAs is 12 months from the date the topic was referred. This compares with 24 months for MTAs.

20. The STA process was announced in September 2005. One of the first products to be appraised under the STA process was Herceptin for early-stage HER2-positive breast cancer, for which guidance was published in August 2006.

21. Most of the appraisals referred to NICE by the Department as part of the 13th wave and all the "minded" referrals for the 14th wave are to be carried out as STAs.

Clinical guidelines and short clinical guidelines

22. NICE has reduced the timeline for the production of full clinical guidelines and, following the success of STAs, NICE and the Department of Health are also developing a Short Clinical Guidelines Programme. It is proposed that NICE will develop two short clinical guidelines a year, and the target timescale for producing a short clinical guideline will be 9 to 11 months, which compares with 24 months for a full clinical guideline.

The Appeal System

23. Since the previous Health Committee inquiry, changes have been made to NICE's appeal system to improve the transparency of the process.

24. The appeal system is an essential element of the appraisal process, and it is clearly important that appeals are carried out in an open and transparent way. To this end, NICE now conducts its appeals in public and the Appeal Panel's conclusions and considerations are published on its website. The Appeal Panel is chaired by a non-executive member of NICE, who will have had no prior involvement in the appraisal in question, and its membership includes independent industry and lay representatives.

25. The Department believes that the appeal process is fit for purpose but notes that, as with other aspects of NICE's work, it will continue to develop. We understand that there will be an opportunity for stakeholders to comment on the appeal process during NICE's methodology review and subsequently the review of its appraisal process.

26. There have been 17 occasions when aspects of appeals have been upheld and the Appraisal Committee has been asked to reconsider its advice.

Comparison With the Work of The Scottish Inter-Collegiate Guidelines Network (SIGN)

Introduction

27. The development of guidance for the NHS in Scotland is a matter for the devolved administration. It is an inevitable consequence of devolution that, in some cases, countries will have different bodies performing similar roles.

28. Whereas NICE issues guidance on both individual treatments (technology appraisals) and pathways of care (clinical guidelines), these two types of guidance are developed by two different organisations in Scotland:

- The Scottish Medicines Consortium (SMC) is responsible for issuing advice on specific drugs to the NHS in Scotland.
- SIGN is responsible for developing clinical guidelines, which provide recommendations on the management of clinical conditions.

29. The Department believes it is important to note that there are a number of important differences between the appraisal processes of the SMC and NICE. For example, the NICE process involves a more extensive consultation than that undertaken by the SMC. NICE's STA process has the potential to produce guidance to a similar timescale to the SMC.

30. There are also a number of key differences between NICE's clinical guidelines process and SIGN's. In particular, NICE consults more thoroughly with stakeholders during the development and NICE's clinical guidelines consider both clinical and cost effectiveness issues, whereas SIGN focuses on clinical effectiveness.

Status of SMC and SIGN guidance in England

31. NICE liaises with SIGN to review topics to minimise duplication of effort between the two organisations and the Department has drawn attention to the SMC as a potential source of information where guidance from NICE is not available.

32. However, the advice produced by the SMC and SIGN is not equivalent to the guidance produced by NICE. The Department does not therefore believe that there is a strong case for giving SMC or SIGN advice formal status in England.

33. The Department appreciates that there is a public expectation that there will be coordination and information-sharing between the guidance producing bodies in different parts of the UK, but the devolved nature of responsibility for NHS policy means that it is unrealistic and inappropriate to expect that such guidance should be identical in every case. We note that NICE appraisals are adopted automatically in Wales, and may supersede some SMC guidance in Scotland.

The Implementation of NICE Guidance—Both Technology Appraisals and Clinical Guidelines—Which Guidance is Acted On, Which Is Not and the Reasons for This

Statutory position of NICE guidance

34. NICE technology appraisals are covered by a three month funding direction, which means that, where NICE has recommended a treatment, PCTs are under a statutory obligation to provide funding to make the intervention normally available within three months of guidance being issued. The direction may be amended or waived where it is felt the NHS will need longer to implement the recommendations eg staff training requirements.

35. The three month funding direction does not apply to clinical guidelines and public health guidance. It is appropriate for there to be a developmental approach to the implementation of these guidance products that recognises their more complex nature and allows NHS organisations to approach implementation in the most appropriate way.

36. There are a number of other non-statutory levers and incentives which support the implementation of NICE guidance.

37. NICE guidance is included in “Standards for Better Health”² published by the Department of Health. The standards fall into two categories:

- (i) core standards—which set out the minimum level of service patients and service users have a right to expect. The core standards include adherence to NICE’s technology appraisals and interventional procedures guidance; and
- (ii) developmental standards—which signal the direction of travel and provide a framework for NHS bodies to plan the delivery of services which continue to improve in line with increasing patient expectations. The developmental standards include clinical guidelines and public health guidance.

38. It is the responsibility of local NHS organisations to ensure that they are meeting the standards. They are performance managed by the Strategic Health Authorities (SHAs) and organisations’ own assessments of compliance are independently validated by the Healthcare Commission, which publishes progress as part of the annual health check.

39. NICE liaises with the Department of Health to feed the cost implications of NICE guidance into the Payment by Results tariff, which provides an incentive for PCTs to commission the services and treatments recommended by NICE. However, coverage of NICE guidance is not universal and this area of work is still developing.

40. The Department of Health seeks to ensure that wherever possible NICE guidance underpins specific Quality and Outcomes Framework (QOF) indicators and that there is no contradiction between the QOF and NICE guidance. NICE is working with NHS Employers (who negotiate changes to the QOF with the General Practitioners Committee of the BMA) to map QOF indicators onto NICE guidance. This process aims to ensure that QOF indicators are compatible with NICE guidance and that any apparent differences arising from the different purposes of NICE guidance and QOF are explained.

41. In 2004, NICE established an Implementation Directorate and now develops and issues a range of new tools to support existing NICE guidance. These tools have been developed in collaboration with the Department and are designed to help NHS commissioners to make funding decisions. They include:

- (i) Implementation and costing templates.
- (ii) Commissioning guides.
- (iii) Evaluation and review of NICE implementation evidence (ERNIE) database.

Other aspects of support for implementation

42. NICE is also developing a range of other guidance and tools for the NHS on disinvestment and reducing ineffective procedures, which support its implementation work. This work includes:

- (i) Guidance on treatments of doubtful effectiveness, which may be inappropriate or unnecessary for some or all patients.
- (ii) Recommendation reminders, which identify and more actively promote existing NICE recommendations, many of which have the potential to deliver savings.

Improvements in implementation

43. In 2006, Professor Mike Richards, the National Clinical Director for Cancer, published a report on the “Review of NHS Usage of Cancer Drugs Approved by NICE”³ which showed significant progress in reducing variation in access to NICE approved cancer drugs across the country in the past two years. The report concluded that there has been a 47% increase in use of key cancer drugs since the last assessment in 2004, and that geographic variation in the use of these drugs has decreased.

44. Professor Richards’ earlier 2004 report⁴ on the uptake of NICE approved drugs concluded that, where uptake is slow, this could largely be attributed to factors such as the approaches of individual clinicians rather than availability of resources.

45. The Audit Commission⁵ and Healthcare Commission^{6, 7} have also published reports that have highlighted the positive impact of NICE guidance and that include recommendations that will assist the NHS in improving performance.

² “Standards for better health”, Department of Health, July 2004.

³ “Usage of cancer drugs approved by NICE”, Department of Health, September 2006.

⁴ “Variations in usage of cancer drugs approved by NICE”, Department of Health, June 2004.

⁵ “Managing the financial implications of NICE guidance”, Audit Commission, September 2005.

⁶ “The best medicine: the management of medicines in acute and specialist trusts”, Healthcare Commission, January 2007.

⁷ “Talking about medicines: the management of medicines in trusts providing mental health services”, Healthcare Commission, January 2007.

Impact on innovation

46. The Department believes that NICE is a powerful lever for encouraging the uptake of innovative and cost-effective new drugs and other interventions within the NHS, and that it contributes an additional incentive for such innovation. Measures to support the uptake of NICE guidance are an important strand of the work of the Long-Term Leadership Strategy which is being taken forward in partnership with the UK pharmaceutical industry.

CONCLUSION

47. The Department believes that NICE has achieved a tremendous amount since 1999 and that it enjoys a high degree of respect both domestically and internationally. NICE's work is controversial and inevitably attracts comments and criticism, but we need to take a balanced view of NICE's activities and acknowledge the positive difference that NICE's work has made to the care of thousands of patients and in encouraging the NHS to take up innovation. NICE will continue to develop its processes and methods. The Department believes it is right that these issues continue to be the subject of informed debate.

Department of Health

March 2007

Evidence submitted by the National Institute for Health and Clinical Excellence (NICE 71)

INTRODUCTION

1. NICE is responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health, in three areas:

- Health technologies—guidance on the use of new and existing medicines, treatments and procedures, including interventional procedures used in the NHS.
- Clinical practice—guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS.
- Public health—guidance on the promotion of good health and the prevention of ill health for those working in the NHS, local authorities and the wider public and voluntary sector.

2. The Institute and its remit have grown rapidly since its establishment in 1999 and it is now the primary source of clinical standards, based on clinical and cost effectiveness, in England, Wales and Northern Ireland. The applicability of NICE guidance in the UK, as a whole, is summarised in Table 1.

Table 1

APPLICABILITY OF NICE GUIDANCE IN THE UK

<i>Country</i>	<i>Technology appraisals</i>	<i>Clinical guidelines</i>	<i>Interventional procedures</i>	<i>Public health guidance</i>
England	Yes	Yes	Yes	Yes
Wales	Yes	Yes	Yes	No
Scotland	Yes ^a	No	Yes	No
N Ireland	Yes ^b	Yes ^b	Yes	No

^a With advice on implementation in Scotland from NHS Quality Improvement Scotland and ^b in Northern Ireland, from the DHSSPNI.

3. Established in April 1999 to set clinical standards as part of a comprehensive quality framework for the NHS, our role has since been extended. The public health white paper *Choosing Health*, published in November 2004, confirmed the Institute's new role in providing the NHS and the wider community with guidance on effective public health practice. NICE merged with the Health Development Agency in April 2005 (producing a saving of £3 million) and by the end of 2006 systems to deliver public health interventions and programme guidance were fully established and beginning to provide guidance in a wide range of areas, including physical activity, smoking cessation, sexually transmitted infection and drug misuse.

4. The implementation of NICE guidance is, for obvious reasons, of fundamental importance. In 2004, the Institute launched a series of initiatives, described in more detail later in this submission, designed to support the NHS and the wider public health community to make better, more rapid and more consistent use of our recommendations.

5. In December 2006, the Department of Health published *Safety First*, the review of patient safety arrangements commissioned by the Chief Medical Officer. The review made a number of recommendations about the future of patient safety, including the establishment of a Patient Safety Forum, which includes NICE in its membership. The report also recommended that NICE pilot the development of technical patient safety solutions commissioned by the National Patient Safety Agency (NPSA). This is now being taken forward and will be completed in the Autumn of 2007. In February 2007, the Institute co-signed the Patient Safety Charter alongside the NPSA, the Healthcare Commission and other national bodies to emphasise organisational commitment to improving patient safety.

6. In addition to its current responsibilities, the Institute believes that the responsibilities of the National Screening Committee and the Joint Committee on Vaccination and Immunisation should fall within the scope of NICE, for the following reasons. First, both screening and immunization are bulwarks of public health. Since NICE is developing other forms of public health guidance it makes sense for the Institute to become involved. Second, the distinction between immunization to prevent disease, and immunization as a treatment, has become increasingly blurred with the emergence of “therapeutic vaccines”. Third, aspects relating to screening have become an increasing part of NICE guidelines, based on the remits given to us by the Department of Health. Our ability to take on this and any other new work which it may be appropriate for us to carry out will require additional resources. Of course, before any organisation can ask for more money, it needs to be able to demonstrate that it has made the best use of what it already has. The Institute has made more than £5.5 million in efficiency savings over the last two years. It has a budget, for 2006–07, of £31 million and employs around 240 staff.

7. The House of Commons Health Select Committee undertook an Inquiry into NICE in 2002. Annex 1 describes the actions taken by the Institute in response to the Committee’s recommendations. Additional background information about the Institute is set out in Annex 2.

8. The Institute believes that it has established a reputation, both in the United Kingdom and throughout the world, for a thorough, fair, transparent and inclusive process which leads to credible and robust guidance. It is in the nature of the work that NICE does that its advice will sometimes be controversial. After all, our purpose is to help the country to decide on the best use of the resources it devotes to the health service; resources which are, although increasing, invariably limited. Such judgements will inevitably and rightly be subject to scrutiny from those who have a direct interest in them and from the media. It is why we welcome this Select Committee inquiry and the opportunity that it provides for us to explain the way we work and to record what we have achieved.

WHY NICE’S DECISIONS ARE INCREASINGLY BEING CHALLENGED

9. We do not believe that there is any objective evidence that indicates that NICE’s decisions are increasingly being challenged, although we are conscious that there has been, in recent times, an increase in the reporting of the Institute’s decisions.

9.1 The frequency of appeals against the Appraisal Committee’s draft guidance has shown no significant change over the years (Table 4).

Table 4

APPEALS IN THE TECHNOLOGY APPRAISALS PROGRAMME

<i>Year</i>	<i>Published appraisals (total)</i>	<i>Appeals submitted (total)</i>
2000	17	7
2001	14	7
2002	24	8
2003	19	3
2004	13	4
2005	6	5
2006	20	5
2007	6	1
Total	119	40

Note: This Table does not include appeals against final draft guidance which have been upheld on appeal but have yet to be published.

9.2 With few exceptions, the Institute’s published clinical guidelines have been well received by both health professionals and patient organisations.

9.3 The Institute established a “review” process in its interventional procedures programme in 2005. Since then, 24 out of 72 pieces of guidance have been the subject of requests for reviews of decisions. Ten were upheld but all required only minor changes to the wording. None was referred back to the Interventional Procedures Advisory Committee.

 WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING, AND IF SO WHY

10. NICE guidance, especially when it advises against the use of interventions on grounds of cost ineffectiveness, is sometimes uncomfortable and on occasions, controversial. Much of NICE's guidance, however, is positive and promotes the use of effective treatments which improve the quality of care that patients can expect to receive from the NHS.

11. Polling data since 2002 (Table 5) indicates that although the proportion of respondents aware of NICE has risen, those who are neutral or positive about its guidance have remained constant at between 67 and 72%. This is broadly consistent with the results of an independent media audit (covering the period April 2005 to April 2006) carried out on behalf of NICE, showing that 63% of the "overall tone" of NICE's media coverage was either neutral or positive.

Table 5
 AWARENESS AND IMAGE OF NICE¹

<i>Year</i>	<i>Awareness of NICE</i>	<i>Rating of NICE's image (neutral or positive)</i>
2002	25%	67%
2004	27%	72%
2006	36%	71%
2007	34%	71%

¹ Data from ICM Omnibus Poll with sample sizes of 1,005 (2002), 1,010 (2004), 1,002 (2006) and 1,002 (2007).

12. The extensive, and increasing, traffic on the Institute's website provides a further indication of the value placed on NICE guidance by both national and international audiences (Table 6).

Table 6

ANNUAL NICE WEBSITE TRAFFIC (2001 to 2006)

<i>Year</i>	<i>Hits</i>	<i>Visitor sessions</i>
2001	3,888,936	597,636
2002	6,595,428	745,404
2003	8,810,760	1,185,036
2004	30,845,064	2,723,568
2005	46,027,164	4,928,304
2006	74,051,952	9,041,448

13. The quality of NICE guidance has been commended in recent reports from the World Health Organization^{8,9}, the Audit Commission¹⁰, and the Office of Fair Trading¹¹; and its relevance to the NHS is confirmed in the report of the Ministerial Industry Strategy Group.¹² An editorial in the *Lancet* (2005) described the Institute in the following terms: "... NICE's hard-won and well-deserved reputation for independence and scientific rigour . . ."; and the editor of the *British Medical Journal* (2004) stated: "NICE may prove to be one of Britain's greatest cultural exports, along with Shakespeare, Newtonian physics, the Beatles, Harry Potter, and the Teletubbies".

NICE'S EVALUATION PROCESS AND WHETHER ANY PARTICULAR GROUPS ARE DISADVANTAGED BY THE PROCESS

14. When developing advice for the NHS and wider public health community, the Institute bases its conclusions on the best available evidence. The best available evidence is rarely (if ever) complete. It may be of poor quality, lack critical elements, or both. Those responsible for formulating the Institute's advice about efficacy, effectiveness, cost effectiveness and safety are therefore required to make two categories of

⁸ World Health Organisation (2003) *The Technology Appraisal Programme of the National Institute for Clinical Excellence*. Copenhagen: World Health Organisation. www.nice.org.uk/pdf/boardmeeting/brdsep03itemtabled.pdf

⁹ World Health Organisation (2006) *The Clinical Guideline Programme of the National Institute for Health and Clinical Excellence*. Copenhagen: World Health Organisation. www.nice.org.uk/page.aspx?o=399754

¹⁰ Audit Commission (2005) *Managing the Financial Implications of NICE Guidance*. London: Audit Commission. www.audit-commission.gov.uk/reports/NATIONAL-REPORT.asp?CategoryID=&ProdID=CC53DDFE-42C8-49c7-BB53-9F6485262718

¹¹ Office of Fair Trading (2007) *The Pharmaceutical Price Regulation Scheme—an OFT market study*. London: Office of Fair Trading. www.offt.gov.uk/shared_offt/reports/comp_policy/oft885.pdf

¹² Ministerial Industry Strategy Group (2007) *Long-Term Leadership Strategy* London: Department of Health; ABPI. www.dh.gov.uk/assetRoot/04/14/28/49/04142849.pdf

judgments. These are scientific value judgments, which are concerned with interpreting the significance of the available scientific, technical and clinical data and social value judgements, which take account of the ethical principles, preferences, culture and aspirations that should underpin the nature and extent of the care provided by the NHS.

Scientific value judgments

15. In the development of its guidance, the Institute is required to take account of both clinical/public health effectiveness as well as cost effectiveness. The Institute's approach to assessing clinical/public health effectiveness has rarely caused significant adverse comment or controversy. The basis of the Institute's approach to economic evaluation, however, has sometimes been misunderstood or misinterpreted.

16. Cost utility analysis is the Institute's preferred approach to evaluating cost effectiveness. This allows both the improvement in health outcome (referred to as "health gain"), and the increased costs associated with it, to be compared to current standard practice. The principle measure of value for money is the incremental cost effectiveness ratio (ICER), expressed as the cost per quality adjusted life year (cost/QALY). This approach allows the cost effectiveness of one technology for one particular condition, to be compared with the cost effectiveness of another technology in a different condition.

17. NICE is required under the terms of its Directions (Directions and Consolidating Direction to the National Institute for Health and Clinical Excellence, March 2005. Section 2) to have regard to the "effective use of resources available in the health service and other available public funds". The Institute's Framework Document, issued by the Department of Health in 2000, indicates (Annex C, paragraph 10) that NICE, in its appraisal of health technologies, should assess whether they can be recommended as "a cost-effective use of NHS and PSS resources". Finally, the Institute is required to evaluate cost effectiveness (that is, value-for-money) rather than affordability or budgetary impact.

18. Health gain is assessed by linking the increased health-related quality of life, attributable to the new treatment (compared to current standard practice), with the time for which it is enjoyed. This enables the quality adjusted life year (QALY) to be calculated. The main assumption embodied in QALYs is that health-related quality of life can be captured in terms of:

- physical mobility;
- ability to self care;
- ability to carry out the activities of daily living;
- absence of pain and discomfort; and
- absence of anxiety and depression.

19. Having established the most plausible cost per QALY the Institute's advisory bodies must then assess whether this represents value-for-money for the NHS. There is no empirical research to indicate the cost per QALY threshold that should be applied and NICE has not adopted one. Instead, it provides its advisory bodies with a framework for decision-making as follows¹³:

- Below a most plausible ICER of £20,000/QALY, judgements about the acceptability of a technology as an effective use of NHS resources are based primarily on considerations on the cost effectiveness estimate.
- Above a most plausible ICER of £20,000/QALY, judgments about the acceptability of the technology as an effective use of NHS resources are more likely to make more explicit reference to factors including the degree of uncertainty of the ICER, the innovative nature of the technology, the particular features of the condition and population receiving the technology, and (where appropriate) the wider societal costs and benefits.
- Above an ICER of £30,000/QALY the case for supporting the technology on these factors has to be increasingly strong.

20. In making these judgments NICE recognises that its advisory bodies need to take social, as well as scientific, factors into account. The Institute has therefore developed guidance—*Social Value Judgments: Principles for the Development of NICE Guidance*—for its advisory bodies to use as a point of reference (see 23–25 below). The Institute acknowledges that the cost per QALY can only inform, and not determine, NICE guidance.

21. The Institute's approach to assessing cost effectiveness has been criticised, in particular, for three reasons.

21.1 It has been suggested that the economic perspective, used by NICE, should encompass the broader economic implications of its recommendations. Irrespective of the merits of such an approach, the Institute's Directions currently preclude it.

¹³ From *Guide to the Methods of Technology Appraisal*. National Institute for Clinical Excellence (April 2004).

21.2 It has been postulated that the measurement of health-related quality of life is either unreliable or fails to capture some essential components. This is not supported by the evidence. Health-related quality of life instruments such as the EQ-5D have been validated amongst many thousands of people across Europe and North America. They have been shown to capture the major components of health gain (either directly or indirectly). And they are widely used by health technology assessment centres across Europe, Australasia and North America.

21.3 It has also been alleged that QALYs disadvantage the elderly. This is incorrect in both theory and in practice. In practice, we have found that estimates of the cost per QALY can be advantageous to older people. For example, the Institute recommends that drug treatments for flu should be made available for people over-65 as they are a vulnerable group and likely to be more seriously affected by flu than younger people. Older people would only be potentially disadvantaged by QALYs in the event of a hugely expensive, curative procedure whose benefits were lifelong. A child aged three would then be likely to enjoy more than 70 years of benefit compared to the additional five years or so that an 80-year old. To date, NICE has not been asked to look at a single procedure of this type. Importantly, the Institute has emphasised in its *Social Value Judgments* document that the “value” of a QALY should not be age-related.

22. The scientific basis for economic evaluation in healthcare is moving rapidly and there are inevitably aspects of NICE’s methodology that should be reviewed. A review of the Institute’s methodology for technology appraisals is starting in March 2007 with a view to taking a paper to the Institute’s Board in November 2007. This review will focus on areas where methods have evolved over the last three years or where NICE’s methodological approach is being questioned. These areas include: evidence synthesis; exploring uncertainty; identifying subgroups and exploring heterogeneity; health related utility measurement; equity and social value judgements; and estimation of costs.

Social value judgments

23. The Institute’s *Social Value Judgments*¹⁴ document has been produced to help NICE and its advisory bodies in developing guidance. They describe the social value judgements that should, generally, be incorporated into the methods used to develop NICE guidance. The principles are set out in summary form below.

- *Principle 1*—The fundamental principles that underpin the processes by which NICE guidance is developed should be maintained for current, and applied to future, forms of guidance.
- *Principle 2*—For both legal and bioethical reasons those undertaking technology appraisals and developing clinical guidelines must take account of economic considerations.
- *Principle 3*—NICE guidance should not support the use of interventions¹⁵ for which evidence of clinical effectiveness is either absent or too weak for reasonable conclusions to be reached.
- *Principle 4*—In the economic evaluation of particular interventions, cost–utility analysis is necessary but should not be the sole basis for decisions on cost effectiveness.
- *Principle 5*—NICE guidance should explain, explicitly, reasons for recommending—as cost effective—those interventions with an incremental cost-effectiveness ratio in excess of £20,000 to £30,000 per QALY.
- *Principle 6*—NICE clinical guidance should only recommend the use of a therapeutic or preventive intervention for a particular age group when there is clear evidence of differences in the clinical effectiveness of the measure in different age groups that cannot be identified by any other means.
- *Principle 7*—In setting priorities there is no case for the Institute or its advisory bodies to distinguish between individuals on the basis of gender or sexual orientation unless these are indicators for the benefits or risks of preventative or therapeutic interventions.
- *Principle 8*—In developing clinical guidance for the NHS, no priority should be given based on individuals’ income, social class or position in life and individuals’ social roles, at different ages, when considering cost effectiveness. Nevertheless, in developing its approach to public health guidance, NICE wishes its advisory bodies to promote preventative measures likely to reduce those health inequalities that are associated with socioeconomic status.
- *Principle 9*—NICE clinical guidance should only recommend the use of an intervention for a particular racial (ethnic) group if there is clear evidence of differences between racial (ethnic) groups in the clinical effectiveness of the intervention that cannot be identified by any other means.
- *Principle 10*—NICE and its advisory bodies should avoid denying care to patients with conditions that are, or may be, self-inflicted (in part or in whole). If, however, self-inflicted cause(s) of the condition influence the clinical or cost effectiveness of the use of an intervention, it may be appropriate to take this into account.

¹⁴ National Institute for Health and Clinical Excellence. Social Value Judgements. www.nice.org.uk/page.aspx?o=283494

¹⁵ The term “intervention” is used in these guidelines to encompass health technologies and any other measure used to influence the course of a particular condition.

- *Principle 11*—Although respect for autonomy, and individual choice, are important for the NHS and its users, they should not have the consequence of promoting the use of interventions that are not clinically and/or cost effective.
- *Principle 12*—It is incumbent on the Institute and its advisory bodies to respond appropriately to the comments of stakeholders and consultees and, where necessary, to amend the guidance. The board is aware, however, that there may be occasions when attempts are made (directly or indirectly) to influence the decisions of its advisory bodies that are not in the broad public interest. The board requires the Institute, and members of its advisory bodies, to resist such pressures.
- *Principle 13*—Priority for patients with conditions associated with social stigma should only be considered if the additional psychological burdens have not been adequately taken into account in the cost–utility analyses.

The Institute recognises, however, that there will be circumstances when, for valid reasons, departures from these general principles are appropriate. When departures from these principles are made, the reasons should be explained.

24. The Citizens Council is a formal committee of the Institute that has helped to develop the broad social values that NICE should adopt in preparing its guidance. The 30 members of the Council reflect the age, gender, socioeconomic status and ethnicity of the people of England and Wales. Councillors serve for a period of three years, with one third retiring each year. They do not represent any particular section or sector of society; rather, they bring their own personal attitudes, preferences, beliefs and prejudices. They and their families have experience of the NHS as patients, but none of the members is a healthcare professional. At each meeting, the Council is asked for its views on an issue about which the Institute seeks advice. Meetings are facilitated by an independent organisation and members have the opportunity to hear, and cross-examine, expert witnesses as well as to engage in discussion and deliberation in both plenary and small-group sessions. The Council's conclusions are contained in a report that is presented to the Institute's board.

25. *Social Value Judgments* will be formally reviewed in 2007.

THE SPEED OF PUBLISHING GUIDANCE

26. NICE guidance has not always appeared as quickly as patients or the NHS would have wished. This has sometimes been because we have not been asked to evaluate a new treatment early enough or because we have not had enough capacity to do so immediately, or as a result of a combination of both. In addition, because we offer the opportunity for an appeal, guidance can be delayed in order for such challenges to be heard and for the consequential action to be taken. It is also the case that because NICE regards its job as finding out precisely where a treatment works best, sometimes time-consuming investigation needs to be undertaken. This is, however, much better than defaulting to the easier option of simply saying no, in the face of uncertainty.

27. When presenting evidence to the Health Select Committee inquiry into NICE in 2002, the Institute put forward the view that it should be routinely commissioned to undertake reviews of technologies at an early stage in their development to enable guidance to be issued to the NHS at or shortly after they became available for use in the NHS. To increase the speed of the development and publication of its technology appraisal guidance the Institute has put in train the following measures:

27.1 In 2006 the Institute took over, from the Department of Health, the preparatory work associated with selecting topics for NICE to develop guidance. Topic selection is now centred on Consideration Panels most of which are chaired by the relevant National Clinical Director. Decisions about which topics should be formally referred still remain the responsibility of ministers. For technology appraisals, ministers consult before confirming their decision to refer to NICE.

27.2 In November 2005, the Institute established a new process for technology appraisals—the Single Technology Appraisal (STA) process, for new pharmaceuticals (or devices), or for new major indications. In this process the assessment report (including the associated economic model) is prepared by the manufacturer rather than an academic Health Technology Assessment centre. Moreover, provided the Advisory Committee recommends use in the NHS that is broadly comparable to the licensed indications, the general consultation period is omitted (although the opportunity for an appeal is retained).

27.3 Provided this process starts around the time the manufacturer requests marketing authorisation from the relevant drug regulatory authority and, subject to appeal, NICE expects to be able to advise on use in the NHS within three months of licensing. In the case of Herceptin, where all these conditions were met, the Appraisal Committee issued its final draft guidance within three weeks of the granting of a marketing authorisation by the European Commission. The STA process has been facilitated by the withdrawal of the pharmaceutical industry's longstanding opposition to early appraisals of new products.

27.4 Timelines for the Institute's clinical guidelines have been reduced by eliminating one of the three consultation steps. Most stakeholders have agreed to this because of the consequent three month reduction in development time. The Institute has also instituted a short guideline programme for those instances where the NHS seeks advice on a relatively narrow area of practice. This should not take more than 12 months to complete including two periods for consultation with stakeholders.

 THE APPEAL SYSTEM

28. Appeals against the Appraisal Committee’s final draft guidance are an integral part of the technology appraisal process. The details of the procedures are shown in Table 6 on p15. Appeals provide registered consultees (sponsors of the technology, relevant professional and patient organisations, and two representatives of Primary Care Trusts) with an opportunity to make representations against the proposed guidance.

29. The appeal process is based on the principles of English administrative law. It is not intended, or designed, to provide an opportunity for technologies to be re-appraised, or for an appraisal to be challenged on its merits, save on limited grounds. Rather, it requires the Appraisal Committee:

29.1 To demonstrate that the appraisal has been undertaken fairly and in accordance with the Institute’s published processes. (This is treated as two separate requirements so that an appraisal must both be fair and also in accordance with the Institute’s published procedures).

29.2 To show that it has not acted perversely in reaching its conclusions.

29.3 To indicate that its recommendations do not exceed the legal powers of the Institute.

These grounds of appeal mirror the administrative court’s jurisdiction on a judicial review.

30. Appeals are heard, in public, by a panel comprising three non-executive directors of the Institute (or two non-executive directors together with a clinician actively working in the National Health Service); an individual with experience in the relevant industry following consultation with the relevant trade associations; and a lay representative.

31. Over the period of NICE’s existence the Appraisal Committee’s final draft recommendations have been subject to 43 appeals. Details are shown in Table 6. All panels’ decisions have, to date, been unanimous.

Table 6

APPEALS IN THE TECHNOLOGY APPRAISAL PROGRAMME AND THEIR OUTCOMES

<i>Year</i>	<i>Published appraisals</i> <i>(total)</i>	<i>Appeals submitted</i> <i>(total)</i>	<i>Appeals allowed (withdrawn or dismissed without a hearing)</i>	<i>Appeals upheld after a hearing</i>	<i>Appeals dismissed after a hearing</i>
2000	17	8	8 (0)	2	6
2001	14	5	4 (1)	1	3
2002	24	11	10 (1)	7	3
2003	19	4	4 (0)	1	3
2004	13	5	2 (3)	1	1
2005	6	3	3 (0)	0	3
2006	20	6	6 (0)	3	3
2007	6	1	1 (0)	1	0
Total	119	43	38 (5)	16	22

32. Two particular criticisms of the Institute’s appeal system have been made: that the grounds for appeal are drawn too narrowly; and that the membership of appeal panels should be confined to individuals with no formal connection with NICE.

32.1 The grounds for appeals are provided in the Institute’s Directions and are fully compatible with English administrative law. The Board does not seek to enlarge their scope and, in particular, considers it would be inappropriate for an appeal panel to attempt to re-appraise the clinical and cost effectiveness technologies under consideration.

32.2 The membership of appeal panels appropriately includes non-executive directors of the Institute. It is important to emphasise that appeals in the technology appraisals programme relate to the Appraisal Committee’s, not the Institute’s, final draft guidance. This distinction is important: the Appraisal Committee’s final draft guidance only becomes formal “NICE Guidance” once it has been accepted by the Institute’s Guidance Executive (acting, with delegated powers, on behalf of the Board). As members of appeal panels, non-executive directors are fulfilling their role as custodians of the quality and probity of NICE guidance.

32.3 The data in Table 6 shows that half of all allowed appeals have been upheld on one or more grounds. The notion that appeal panels might be inherently prejudiced in favour of the Appraisal Committee is not born out by the evidence.

 COMPARISON WITH THE WORK OF THE SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK

33. Scotland has two organisations with responsibilities that are similar to some of those of NICE. The Scottish Intercollegiate Guideline Network (SIGN) develops clinical guidelines; and the Scottish Medicines Consortium (SMC) appraises pharmaceuticals for their clinical and cost effectiveness.

34. SIGN, now part of NHS Quality Improvement Scotland, has published 96 clinical guidelines since its formation by the late Professor James Petrie in 1993. Like NICE, its guidelines are developed by multi-disciplinary groups including both health professionals and representative service users after a review of the relevant literature. Its guideline development time is normally between 24 and 30 months.

35. There are several differences between the status and methodological development of SIGN and NICE guidelines.

- NICE clinical guidelines form part of the performance management process of the English NHS and are developmental standards. SIGN guidelines do not have such status within the Scottish NHS.
- NICE guidelines are based on considerations of both clinical and cost effectiveness. SIGN guidelines have historically focused solely on clinical effectiveness.
- NICE's guideline development groups include (or have ready access to the skills of) guideline methodologists, statisticians, meta-analysts and health economists.

36. The SMC provides Scottish Health Boards solely with advice on the clinical and cost effectiveness of new pharmaceutical products. There are, however, important differences between NICE's technology appraisals programme and that of the SMC. Many of these relate to the Institute's core principles for developing robust guidance.

- NICE technology appraisals evaluate all categories of health technologies as directed by the Secretary of State for Health. The SMC only considers pharmaceutical products.
- NICE's technology appraisals follow published processes and methods that have been subject to public consultation. There are no equivalent documents governing the work of the SMC.
- NICE includes a comprehensive scoping phase designed to identify the basis, and appropriate boundaries, for each appraisal and is the subject of early consultation. This is pivotal as it ensures an appropriate focus for a robust appraisal. SMC has no equivalent process.
- Stakeholders (relevant patients and professional organisations, as well as healthcare industries) interact with every stage of the NICE appraisal process and have several opportunities to make their case. By contrast, the SMC's engagement and consultation processes are limited in both scope and breadth.
- All NICE's technology appraisals are subject to public consultation where preliminary recommendations are restrictive or at variance with the product's marketing authorisation. The SMC does not engage in public consultation for any of its recommendations and recommendations emerging from its New Drugs Sub-Committee are only sent to the sponsor of the technology for comment.
- NICE has a formal appeal, held in public, as part of its technology appraisal process. The SMC has no formal appeal process although it does have a mechanism for reviewing its decisions when these are challenged.

THE IMPLEMENTATION OF NICE GUIDANCE, BOTH TECHNOLOGY APPRAISALS AND CLINICAL GUIDELINES (WHICH GUIDANCE IS ACTED ON, WHICH IS NOT, AND THE REASONS FOR THIS)

37. NICE guidance is developed for the NHS in England. Some forms are also applicable in the other UK countries through Service Level Agreements (see Table 1).

38. When the Institute was first established NICE was not expected (as indicated in *A First Class Service*) to play any part in the implementation of its guidance. In 2003, however, the board agreed to commit some of the Institute's resources to the establishment of an Implementation Directorate which was launched in 2004.

39. NICE's implementation strategy has three main elements: encouraging change by working through other organisations/mechanisms to generate "leverage"; providing practical support; and monitoring the uptake of recommendations.

39.1 Other organisations or programmes with whom the Institute is actively working, to secure the implementation of its guidance include the Healthcare Commission; the Quality and Outcomes Framework; the National Tariff; Connecting for Health and the National Knowledge Service; the Royal Medical, Nursing and Midwifery Colleges; the Litigation Authority; the National Institute for Improvement and Innovation; and the Audit Commission.

39.2 Providing practical support includes the provision of a guide entitled *How to Implement NICE Guidance*; a forward planner on the NICE website; cost impact tools to help local NHS organisations estimate likely costs and savings; other practical tools (for example, audit criteria, slide sets and practical implementation advice); commissioning guides in an interactive web-based format; a small team of implementation consultants to provide practical support and advice to NHS trusts; and a shared learning database on the NICE website (ERNIE).

39.3 To monitor the uptake of its guidance NICE collects, analyses and collates published and unpublished reports to build up a comprehensive overview. This is available on the NICE website in a dedicated database (Evaluation of Reviews of NICE Implementation Effectiveness, ERNIE). Examples of the information held on ERNIE are set out in Annex 2.

40. The most comprehensive assessment of the uptake of NICE guidance, by the NHS as a whole, is provided in the Healthcare Commission's 2005–06 annual health check. This was confined to an assessment of institutions' compliance with "core" standards in the Department of Health's *Standards for Better Health*. NICE's technology appraisals and interventional procedures were included in this and the results are shown in Table 7.

Table 7

SELF-ASSESSMENT OF COMPLIANCE WITH NICE INTERVENTIONAL PROCEDURE (IP)
AND TECHNOLOGY APPRAISAL (TA) GUIDANCE

<i>Core Standard</i>	<i>Total</i>	<i>Compliant (%)</i>	<i>Insufficient assurance</i>	<i>Not met (%)</i>
CO3 (IPs)				
Acute trusts	171	153 (89)	13 (8)	5 (3)
Mental Health Trusts	61	61 (100)	0 (100)	0 (100)
PCTs	302	266 (88)	27 (9)	9 (3)
CO5 (TAs)				
Acute trusts	171	142 (83)	17 (10)	12 (7)
Mental Health Trusts	61	57 (93)	2 (3)	2 (3)
PCTs	302	248 (82)	43 (14)	11 (4)

Note: It should be emphasized that these returns represent Institutions' own evaluation of their compliance and the results of a deeper inquiry, on a sample of trusts, has yet to be published. The Healthcare Commission plans to include an assessment of compliance with NICE clinical guidelines in its next annual health check (2006–07).

41. The main barriers to implementing NICE guidance identified by the Institute are: lack of resources; disagreement with the recommendations; and lack of a clear organisational process.

41.1 The issue of lack of resources can, to a considerable extent, be mitigated by careful financial planning as described in the Audit Commission's report *Financial Planning for NICE Guidance*.

41.2 To avoid clinical disagreement with its recommendations NICE engages with clinicians at all stages of the guidance development process. As NICE's national and international reputation has increased, however, such disagreements appear to have considerably reduced.

41.3 The lack of organisational support for the implementation of NICE guidance (including board support) has improved since the publication of the *How to Implement NICE Guidance* but recent financial pressures mean that some trusts lack the capacity to manage change, particularly in areas such as clinical audit.

National Institute for Health and Clinical Excellence

March 2007

Annex 1

RESPONSES TO THE HEALTH COMMITTEE'S 2002 REPORT

1. In its 2002 report, the Committee directed a number of recommendations to both NICE and the government. Those recommendations relevant to the Institute (in italics below) are reproduced together with NICE's subsequent actions.

2. *To neglect the input of respected bodies such as the Drug and Therapeutics Bulletin and the British National formulary is to miss a key opportunity for quality assuring NICE's work, and risks serious damage to the credibility of its guidance. We recommend that NICE puts in place robust mechanisms to ensure closer and more constructive collaborative working with BNF, DTB, and other similar bodies. Although we recognise*

that such bodies may not have the capacity to contribute to every piece of guidance that NICE issues, they should be allowed a formal opportunity to contribute to work where they have relevant expertise, and there should be an established mechanism for discussing and resolving technical differences (paragraph 26).

The Institute recognised the potential contributions from collaboration with bodies undertaking comparable work and entered into formal arrangements with the editors of the British National Formulary, the Drug and Therapeutics Bulletin, and the MeReC Bulletin to seek comments on draft appraisals of pharmaceutical technologies.

3. Involving such a broad sweep of stakeholders is a complex and time-consuming task, and we welcome NICE's efforts in this area to date. We recommend that NICE should take steps to improve its stakeholder identification methods, to ensure that relevant bodies and individuals are systematically identified for inclusion. If NICE is to gain the full respect of the medical profession, it is essential that it involves clinicians with relevant clinical experience, alongside those capable of taking a broad overview. NICE should consider the possibility of inviting stakeholders in the technology appraisal process to "self nominate" in the same way as they are permitted to in the clinical guidelines process.

From the outset, the Institute had in place arrangements for relevant professional organisations to act as full consultees in appraisals. Arrangements were also in place for stakeholders to self nominate at any point in the appraisal process up to the ACD stage. However, following the Committee's Report, the Institute extended the remit of its Public and Patient Involvement Unit (PPIU) to include appraisals as well as guidelines (and, now, interventional procedures and public health). The Unit has well-developed developed strategies for ensuring that appropriate patient and carer organisations are invited to act as stakeholders/consultees in all NICE's guidance programmes.

The Institute now has a database of over 2,000 clinical, patient and industrial organisations. No request to act as a stakeholder is refused provided the body falls within the Institute's definition of a national body with a relevant interest.

4. We recommend that NICE takes steps to improve current methods of involving the NHS in the development of technical appraisals and clinical guidelines, including arrangements for the NHS to be involved in a timely appeal process. Measures to achieve this might include the extension of membership of the Appraisal Committee to more than two NHS representatives; and the establishment of a network of designated individuals within NHS Trusts and strategic health authorities, through whom NICE can maintain open dialogue with working clinicians and commissioners of care throughout the guidance development process. These individuals would be able to act as intermediary facilitators between NICE and the wider NHS, acting as a local source of reference about NICE's processes and promoting the implementation of its guidance, as well as ensuring the systematic inclusion of NHS representatives in NICE decision-making.

NHS staff have, since the Institute's inception, formed a majority of the membership of the Appraisal Committee. Since 2002 two PCTs (different for each topic) have also been designated as appellate consultees in the appraisal process to allow additional NHS input. One PCT has used this position to appeal against the Appraisal Committee's final draft guidance (in the case of Herceptin for early stage breast cancer). The Institute welcomed the suggestion to creating a network of NICE clinicians and commissioners to act as a conduit for information and to assist in the implementation of its guidance. It continues to pursue the development of such networks.

5. We welcome NICE's attempts to achieve better relationships and open channels of communication with stakeholders—particularly the professional and patient groups. The future credibility of NICE rests on its being responsible to criticisms, and to its being willing to study them, and if necessary, learn from them. Wherever possible any resulting press statements about the resolution of disagreements should be agreed with the other parties involved before release.

We agreed that it was in the interests of patients that disagreements between the Institute and its stakeholders be resolved cordially and we always work to achieve a satisfactory resolution. It is important when doing so, however, to ensure that accurate information about our guidance is placed in the public domain. Moreover, where the Institute is subject to unwarranted criticism by stakeholders NICE must reserve the right to respond in the interests of patients and the wider public.

6. We recommend that all information which NICE uses in its decision-making process is made available for public scrutiny. If industry or others have previously unpublished data which they want to use to support their case then this should no longer be presented to NICE subject to confidentiality.

NICE endorsed this proposal and the position has generally improved. It has not, however, been possible to implement the proposal in practice. NICE and the Association of the British Pharmaceutical Industry agreed an approach to the release of unpublished data but some restrictions remain. Nevertheless, where the sponsors of manufactured technologies have claimed data to be "commercial-in-confidence" or "academic-in-confidence" we have been able to obtain their agreement to allow reproduction of critical elements.

7. We recommend that NICE should improve the transparency of its processes by striving to make information on how and why its decisions are taken, and on members' declarations of interests as readily and clearly available to lay stakeholders as possible. For the sake of clarity, members should declare all interests at the beginning of each appraisal. The decision-making audit trail could be improved if the NICE website

supplemented its sections on individual technology appraisals with links to the minutes of all relevant meetings. It would also be helpful if, instead of listing the full membership of the Appraisal Committee, each guidance document listed those specific members who had taken part in decision-making on that particular treatment, and those who had withdrawn due to competing interests.

The Institute has always been fully committed to the full disclosure of potential conflicting interests of the members of its advisory bodies. Members of the appraisal committee have always been required to disclose any interests at the start of each agenda item; and those with clearly conflicting interests play no part. The Institute instituted three further measures to improve the transparency and clarity with which decision-making audit trails could be made. First, it has ensured that its website facilitates searches between its technology appraisal guidance and the relevant appraisal committee minutes. Second, the unconfirmed minutes of the appraisal committee meetings are posted on the NICE website as soon as they have been agreed by its chair. These are replaced by the confirmed minutes, when they are available. Third, technology appraisal guidance documents record only those members of the appraisal committee actually involved (rather than the full membership).

8. Improvement in the inclusiveness and transparency of NICE's processes are needed to ensure that the appeals process is not the only means for stakeholders to enter into constructive dialogue with NICE (Paragraph 45).

The appeal process has never been the sole means through which stakeholders can engage with us. Consultees in the technology appraisal process attend "scoping meetings" at the start of an appraisal, and they have opportunities to comment on the evidence used as well as the initial and final draft recommendations. Comparable opportunities are provided to stakeholders in the Institute's other programmes.

9. The current role of the Chair in the appeals system seems to be as flawed. We recommend that the government gives careful consideration to reforming the appeals system as it has at least the appearance of lacking impartiality. We are also concerned that the distance this creates between the chair and the everyday business of NICE may be to the detriment of the organisation as a whole.

Although the board disagreed with the implication that its appeal system lacked impartiality it nevertheless agreed, in 2002, that the chair of the Appeals Committee should be occupied by one of the non executive directors; and that decisions about the validity of appeals should be taken (with legal advice) by the chair of this committee. The Institute did not, however, accept that the chair of the Institute should be disqualified from either chairing, or sitting as a member of, an appeal panel.

In this context it is important to emphasise that appeals in the technology appraisals programme relate to the Appraisal Committee's, not the Institute's, final draft guidance. This distinction is important: the Appraisal Committee's final draft guidance only becomes "NICE Guidance" once it has been formally accepted by the Institute's Guidance Executive or the Board.

10. We recommend that for all new technologies, NICE's work programme is arranged to facilitate publication of guidance at the time of launch. When this is not possible, NICE should conduct rapid "interim" appraisals of clinical and cost-effectiveness to be published at the time of a treatment's launch, as was the case with zanamivir. The funding of these interim appraisals should not be mandatory. Although the amount and type of information available at time of launch may be less than ideal, an "interim" appraisal will provide useful guidance until a more detailed appraisal of the treatment is conducted as part of NICE's expanding main function of developing clinical guidelines. While issuing revised guidance does have the potential to cause confusion, we trust that NICE will learn from the experience of its zanamivir appraisal and be very explicit about the reasons for any changes in the new guidance. Appraisals on existing treatments or interventions should also be conducted as part of NICE's clinical guidelines programme (paragraph 67).

NICE also strongly endorsed (and continues to endorse) the proposal that all new relevant technologies should have completed their appraisal around the time of their launch. The Institute's new single technology appraisal process, as discussed elsewhere in its evidence to the present Inquiry, is intended to facilitate this. Updates (reviews) of guidance are essential in maintaining the value and credibility of our guidance and are always triggered by material new evidence.

11. We recommend that the Government and NICE should clarify the legal status of NICE guidance in relation to the other legal duties incumbent upon clinicians and commissioners of health care (paragraph 68).

The status of our guidance (as advice that should be fully taken into account by clinicians and NHS organisations) is clearly set out in all our documents. However, we recognise the importance of absolute clarity on this to NHS organisations (and to patients) and the status of all NICE guidance is now codified in *Standards for Better Health*. The status of NICE guidance in the devolved administrations is described, further, in our Evidence to this Inquiry.

12. We recommend that the Government ensures the systematic monitoring of the implementation of NICE guidance. The Government should ensure that CHI (and later, CHAI) is encouraged to undertake specific national reviews of NICE guidance in priority areas, and that strategic health authorities include the implementation of NICE guidance as part of their regular monitoring of PCTs and acute trusts. Monitoring data should then be used to review and improve systems for dissemination and the implementation.

NICE strongly endorsed this proposal. The Healthcare Commission has, since 2005–06, included compliance with NICE guidance as part of its annual health check. This too is discussed further in the Institute’s Evidence to the present Inquiry.

13. *We recommend that the Government should consider what practical systems and structures could be put in place to improve the NHS’s capacity to implement NICE guidance, including the possibility of designated individuals within NHS trusts and strategic health authorities liaising with NICE to facilitate implementation.*

Following the publication of the Committee’s 2002 Report the Institute established an Implementation Systems Directorate headed by an executive director. The work of this Directorate is discussed elsewhere in the Institute’s evidence to the present Inquiry.

14. *Improved regulation of submission of information to NICE should be supplemented by closer working relationships between the MCA and NICE, including the sharing of appropriate summary information prepared for the CSM, in order to prevent duplication and strengthen the quality of NICE’s output.*

Whilst sharing summary information, prepared for the CHM, may be of some assistance to NICE and its Appraisal Committee the increasing use of the centralised EU procedure for granting marketing authorisations means that the scope will be limited. Nevertheless, NICE and the MHRA work closely together in both the appraisals and guidelines programmes particularly in relation to safety.

15. *We accept that there are limitations on the information that can be gained prior to the launch of a treatment, and that there is a tension between the difficulties in assessing clinical effectiveness at an early stage, and the NHS’s evident need for guidance at the time of launch to help it manage the introduction (or restriction) of new treatments in the NHS. The system of appraisals at the time of launch that we have recommended does not preclude the possibility of conducting fuller appraisals of treatment’s effectiveness when more information has been collected. Indeed, we recommend this should take place, but within the broader context of NICE’s main work on clinical guidelines (paragraph 91).*

The Institute’s continues its commitment to review its guidance as new information becomes. Of the 119 published appraisals 12 have been reviews of previous guidance. Our clinical guidelines are now also starting to be reviewed. In some instances, technology appraisal updates have been transferred to the clinical guidelines programme where this is clearly the most appropriate way of developing and presenting guidance to patients and the NHS.

16. *We recommend that the Government institutes independent detailed peer review of a random selection of guidance prepared by NICE. This could be carried out by CHI/CHAI on a three-yearly basis (paragraph 99).*

NICE welcomed this proposal for an independent review of a selection of its guidance. In 2003 we invited the European Regional Office of the World Health Organisation to review the appraisals programme; and in 2006 the Regional Office undertook a review of the clinical guidelines programme. Both reports, whilst making many helpful suggestions to improving our processes, strongly endorsed the overall quality of both programmes’ guidance.

17. *Whether or not Quality Adjusted Life Years are used, we recommend that NICE should consider the wider societal costs and advantages of particular treatments and in particular the wider costs and benefits to the public purse of reduced benefit dependency and improved ability to work both for patients and their carers (paragraph 102).*

The economic perspective the Institute is required to adopt is mandated in its Statutory Instruments and is limited to that of the National Health Service. The issue is discussed further in the Institute’s evidence to the Committee’s present Inquiry.

18. *We note NICE’s plans to establish a Citizens Council composed of “ordinary men and women around the country” to advise on these value judgements. We agree with the many witnesses who argued for a review of NICE’s appraisal methodology, and the publication of clear criteria. We therefore recommend that NICE, aided by the Department of health, should conduct a review of its methodologies for assessing clinical and cost-effectiveness, which should result in the publication of a set of clear and consistent criteria for the assessment of both aspects. This should include a description of the weighting given to different types of evidence, a detailed argument for its use of Quality Adjusted Life Years, and the impact of both cost and clinical effectiveness on the final determination, including any cost-effectiveness “thresholds”. In tandem with this, NICE should work to strengthen its cost-effectiveness evidence based by encouraging pharmaceutical companies to collect this type of data routinely.*

At the time of the publication of the Committee’s report, in 2002, the Institute had already embarked on a full review of its technology appraisal processes and methods. A revised manual was published in 2004, which contains a full explanation of our approach to assessing and interpreting evidence, including the use of quality adjusted life years. A further revision, with full public consultation, is now being undertaken (see our evidence to the current Inquiry).

The work of the Citizens Council has been embodied in “Social Value Judgments: Principles for the Development of NICE Guidance” that provides our advisory bodies with advice on the social values that should normally underpin their work. This, too, will undergo revision, with full public consultation, during 2007.

19. We welcome in principle the idea of a web-based topic proposal system suggested in the Government's consultation, but this needs to be supported by a clear and transparent selection process for the assessment of proposed topics. We feel that current government proposals for widening the membership of the Technology Advisory Group (TAG) still leaves the NHS, and in particular patients, under-represented. We therefore recommend that the skills mix of the TAG is further weighted towards these groups, and that the deliberations and decisions of TAG meetings are put into the public domain.

There have been considerable changes to the topic selection process since the Committee's 2002 Inquiry. Although topics are still formally referred to the Institute by ministers, their development is now undertaken with NICE and centres around 7 subject-specific "Consideration Panels" which are mainly chaired by the relevant National Clinical Director. The web-based topic proposal system is one of the streams of suggestions feeding into these panels.

Annex 2

ADDITIONAL BACKGROUND INFORMATION ON NICE

1. In July 2004, the Department of Health published *Standards for Better Health*. These standards (which were updated in 2006) provide a common set of requirements applying across all health care organisations and a framework for continuous improvement in the quality of care people receive. Health care organisations are expected to comply with the core standards identified in the document, and to make progress in achieving its developmental standards. Compliance with NICE technology appraisals and interventional procedures guidance are core standards; and implementation of clinical guidelines and public health guidance is a developmental standard.

2. In December 2005, the Department of Health published *Health Reform in England*, which describes the framework for reform of the NHS in England. The Institute can play an important role in supporting many aspects of these reforms to secure better care, better patient experience and better value for money. The new field-force team of NICE Implementation Consultants is developing active relationships with the new Primary Care Trusts and Strategic Health Authorities; and the Institute will continue to develop tailored approaches for implementation, working with the Department of Health to incorporate the costs of compliance with all NICE guidance into the payment by results system. The NICE Patient and Public Involvement Programme (PPIP) is fostering relationships with patient groups, voluntary organisations and statutory patient and public involvement structures to harness their support in publicising and disseminating NICE guidance to patients and the public at local levels.

3. The 2006 white paper on community health services, *Our health, our care, our say*, shifts the focus of the NHS away from the acute sector and towards primary care and community services, and gives a higher priority to self-management of care, disease prevention and the public health goal of tackling health inequalities. These changes will have a significant impact on the environment within which NICE operates. Like the programme of change arising from *Every Child Matters*, they reinforce the importance of joint commissioning by PCTs and local authorities for health and well-being. This should support implementation of NICE guidance that cuts across services or sectors including not only public health guidance, but also guidance relating to long-term conditions and to groups such as children and older people.

4. The creation of a single outcomes framework covering health, adult social care, and children's services, along with the alignment or integration of planning and budgetary cycles, and performance management and inspection regimes, should enable NICE better to link guidance to local priorities, particularly those of local authorities. The 2006 local government white paper, *Strong and prosperous communities*, reinforces these changes, for example, by promising a new framework for strategic leadership in local communities, with local area agreements becoming a statutory requirement as the focus of joint local planning and delivery.

5. NICE must meet a variety of legal requirements to promote equality and eliminate discrimination in the way it carries out its functions and in its employment policies and practices; this includes the way guidance is developed and the contractual arrangements established by the Institute. From 2007, we will take account of new requirements arising from the Equality Act 2006 to promote equality between men and women, as well as continuing to implement commitments in our equality scheme in relation to race equality, disability equality, tackling age discrimination, and discrimination on other grounds.

8. The Institute's work programme is determined by Department of Health ministers. Once it has been agreed, the development of the guidance is entirely the responsibility of NICE and the Institute issues its guidance directly to the NHS and patients.

9. The Institute's guidance is developed by independent advisory groups composed of relevant experts (including those who speak on behalf of patients). These groups scrutinize the evidence with the utmost care to formulate guidance that is in the best interests of patients. Although the Institute seeks the views of the relevant professions, patient/carer organisations, manufacturers and government, the work of its advisory groups is independent of any vested interests.

10. Individual clinicians, NHS and patient bodies, professional organisations, manufacturers and public health bodies contribute to the development of each piece of guidance through a process that is transparent, objective, inclusive and offers appropriate opportunity for consultation. This includes the submission of evidence from all stakeholder groups and the publication of preliminary versions of guidance on the Institute's public website.

11. To date, the Institute has issued the following guidance to the NHS and wider public health audiences as set out in Table 1:

Table 1

PUBLISHED NICE GUIDANCE

<i>Year</i>	<i>Technology appraisals</i>	<i>Clinical guidelines</i>	<i>Interventional procedures</i>	<i>Public health interventions</i>
2000	17	0	n/a**	n/a
2001	14	4	n/a	n/a
2002	24	5	n/a	n/a
2003	19	7	29	n/a
2004	13	13	70	n/a
2005	6	8	46	0
2006	20	12	47	2
2007*	6	2	9	1

* As of end of February 2007

** No NICE programmes

TECHNOLOGY APPRAISALS

12. Technology appraisals offer guidance on the use of new and existing medicines and treatments within the NHS. When developing this guidance, NICE is required by its Statutory Instruments to take into account both clinical and cost effectiveness. NICE has issued 119 technology appraisals to date, including guidance on statins for cardiovascular disease and computerized cognitive behavioural therapy for depression. The Institute currently has 57 technology appraisals in development.

13. In the technology appraisals programme it has been very unusual for NICE to recommend "no use" in the NHS for a technology (Table 2).

Table 2

SUMMARY CONCLUSIONS OF TECHNOLOGY APPRAISALS GUIDANCE

<i>Technology</i>	<i>Routine use</i>	<i>Selective use</i>	<i>Research only</i>	<i>Not recommended</i>
Pharmaceuticals	29	51*	2	4**
Devices	5	11	2	0
Diagnostics	1	1	1	0
Procedures	1	6	3	0
Health promotion	2	0	0	0
Total	38	69	8	4

* Includes 2 multi-product appraisals one technology, in each, was not recommended for NHS use.

** Single or multi-product appraisals where no technology was recommended for NHS use.

14. In November 2005 NICE launched the single technology appraisal process to produce faster guidance on life-saving drugs that have already been licensed and guidance on new medicines close to when they first become available. NICE consulted with organisations representing patients, healthcare professionals and healthcare industries on its details.

CLINICAL GUIDELINES

15. Clinical guidelines provide advice on the appropriate care of people with specific diseases or conditions. When developing these guidelines, NICE is again required by its Statutory Instruments to take into account both clinical and cost effectiveness. NICE has issued 45 clinical guidelines, to date, including prevention of malnutrition in the NHS, the care of pressure ulcers and the use of long-acting reversible contraception. The Institute currently has 41 clinical guidelines in development (including six reviews) and a full list can be found at <http://guidance.nice.org.uk/type>.

16. NICE continues to endorse the proposal set out in the *Report of the Public Inquiry into Children's Heart Surgery at the Bristol Royal Infirmary 1984–95* (Kennedy Report) that NICE should give given the task of extending its programmes to cover the major areas of morbidity and mortality. A comprehensive suite of clinical guidelines will secure the quality of care that NHS patients deserve.

INTERVENTIONAL PROCEDURES

17. Since 2003 NICE has offered advice to the NHS on whether interventional procedures are safe enough and whether they work well enough for routine use in the diagnosis and treatment of NHS patients or whether special arrangements are needed for patient consent. When developing this guidance NICE considers evidence on efficacy and safety. To date NICE has issued advice on 211 interventional procedures, including laser eye surgery and managing the risk of transmitting spongiform encephalopathies (CJD, vCJD) during invasive procedures.

18. Topics are notified to NICE directly—usually by clinicians working in the NHS—rather than referred by a health minister. Guidance on interventional procedures protects patients' safety and supports people in the NHS during the introduction of new ones. Many of the procedures that NICE investigates are new, but we also look at more established procedures if there is uncertainty about their safety or how well they work.

PUBLIC HEALTH INTERVENTIONS AND PROGRAMMES

19. In April 2005 the functions of the Health Development Agency were absorbed into NICE. The Institute now develops guidance for the NHS and the wider public health community, on the effectiveness and cost effectiveness, of measures that sustain good health and prevent ill-health at both an individual and a population level. To date, NICE has issued guidance on four public health topics including physical activity, smoking cessation, underage conception and sexually transmitted infections, and drug misuse. The Institute currently has nine public health interventions and eight public health programmes in development.

ADVICE ON OPTIMAL PRACTICE

20. In September 2006 the Department of Health asked NICE to develop a new set of products to help the NHS make better use of its resources by reducing spending on treatments being used in a way which does not improve patient care or does not represent good value for money. NICE will work in partnership with healthcare professionals working in the NHS to identify topics about which that it would be useful to develop guidance. NICE is developing three new forms of advice in this area:

- Technology appraisals and clinical guidelines aimed at identifying optimal practice where there is longstanding uncertainty about the best approach to care. For example, in January 2007 NICE issued guidance on the diagnosis, treatment and management of heavy menstrual bleeding that makes recommendations on a range of effective treatments that should be discussed with women prior to considering surgical options such as hysterectomy.
- Commissioning guides offering practical web-based advice for NHS commissioners on how to commission routine services in line with NICE recommendations. The first commissioning guide on upper gastrointestinal endoscopy services was published in October 2006, underpinned by NICE guidelines on dyspepsia and referral for suspected cancer. Four further guides have been published on anticoagulation therapy services, pulmonary rehabilitation for chronic obstructive pulmonary disease (COPD), assisted-discharge scheme for COPD, and diabetes foot care services.
- Reminders highlighting recommendations from existing NICE guidance that advise the NHS to re-position or stop the use of treatments, based on the evidence of their clinical and cost effectiveness. NICE has, to date, issued online reminders about drugs for eczema, long-acting reversible contraception, and treatments for post-traumatic stress disorder to date.

Annex 3

EVALUATION AND REVIEW OF NICE IMPLEMENTATION EVIDENCE (ERNIE)

1. The ERNIE database is a source of information on the implementation and uptake of NICE guidance. One of its main purposes is to ensure implementers can see national reports and other data that help to set the context of implementation. ERNIE provides:

- a data-base of in house reports on the implementation of specific forms of NICE guidance; and
- references to external studies on the implementation of NICE guidance.

2. The external references include studies published in journals and any further reports published by any organizations which come to the attention of NICE. These studies vary greatly and range from local audits with small samples to national investigations undertaken by, for example, the Department of Health and

Healthcare Commission. To complement this external data, NICE has worked in partnership with the NHS Information Centre to secure access to national data to enable the production of NICE implementation uptake reports.

ERNIE: TECHNOLOGY APPRAISALS

3. An overview of the number of studies relating to technology appraisals is presented below.

Number of external references entered in the databases	71
Number of in-house implementation uptake reports entered in the database (as at 1 March 2007)	6
Number and % of “current” technology appraisals covered by at least one external or in-house study	66 (67%)

NB some external reports have assessed the uptake of several technology appraisals within one study. The 71 references therefore contain 171 assessments of uptake.

4. Examples of the information contained within the ERNIE database in relation to a number of technology appraisals is presented below. Examples have been selected as they represent those topics where national data is available rather than smaller local studies.

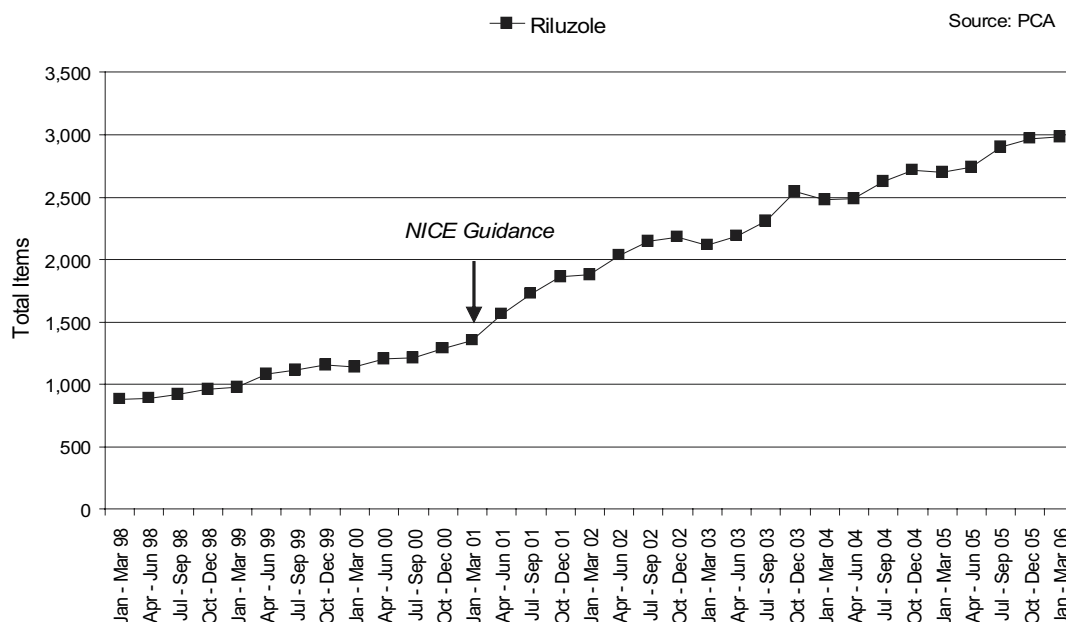
USAGE OF CANCER DRUGS

5. NICE has published a large number of pieces of guidance in relation to the use of cancer drugs. In 2004 the National Cancer Director conducted a large investigation into the prescribing of these drugs. This study was repeated and published in September 2006 to provide a further overview of the usage of these drugs. The report found that following a positive appraisal by NICE the median increase in usage of 14 cancer drugs was 47%. The report also measured variation in the use of drugs between cancer networks which had been raised as a concern by the pharmaceutical industry. The report found that there had been a reduction in variation in the usage of all 15 NICE approved drugs.

TA020 MOTOR NEURONE DISEASE (MND)—RILUZOLE

6. A NICE implementation uptake report showed a marked increase in uptake of riluzole around the time of publication of the guidance (graph 1). The guidance estimated that around 2,000 individuals are living with MND at any one time. This estimate is based on a range of assumptions and does not represent an absolute figure. The expenditure for riluzole in England for 2005 was £3.8 million. This is the equivalent of around 1,400 12-month treatment courses based on 100mg/day (British National Formulary 51). The actual number of people receiving treatment during this period will be higher given the uncertainty about the proportion of patients who either take up or complete therapy.

Graph 1 Riluzole dispensed in the community in primary care in England

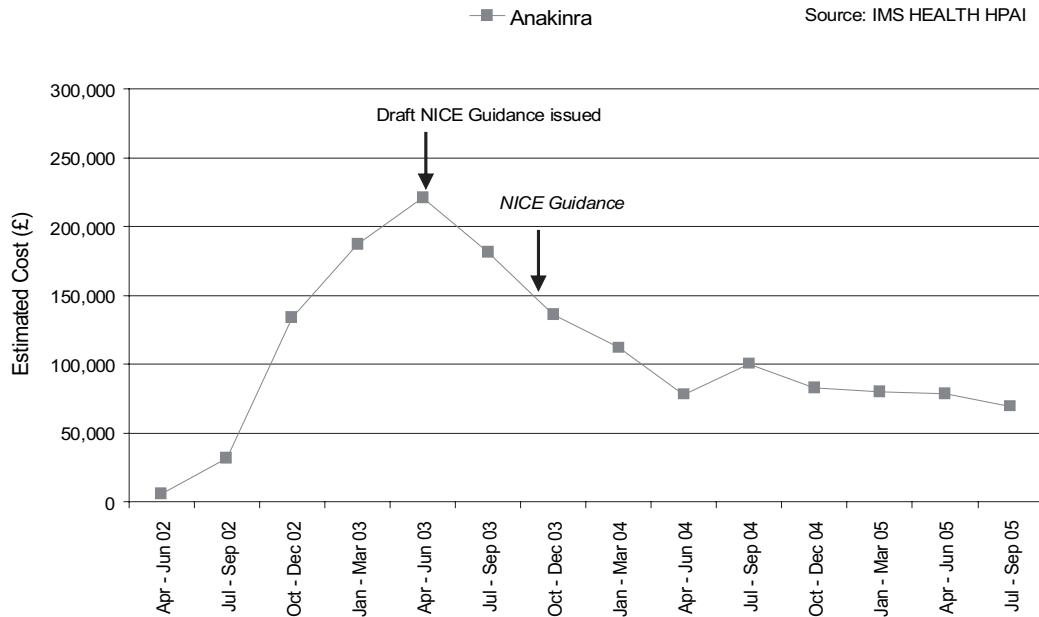


These findings mirror the results of a study completed by Abacus International in 2005. This study concluded that “NICE guidance has been fully implemented in secondary care and well implemented in primary care”.

TA072 RHEUMATOID ARTHRITIS—ANAKINRA

7. NICE recommended that Anakinra should not normally be used as a treatment for rheumatoid arthritis. It should only be given to people who are taking part in a study on how well it works in the long term. A NICE implementation uptake report showed that there was a dramatic fall in the prescribing of anakinra in July 2003 (date of publication of the draft NICE guidance). The estimated cost for the latest available quarter (July–September 2005) was around £70,000 having been over £200,000 at the point of publication of the draft guidance (graph 3).

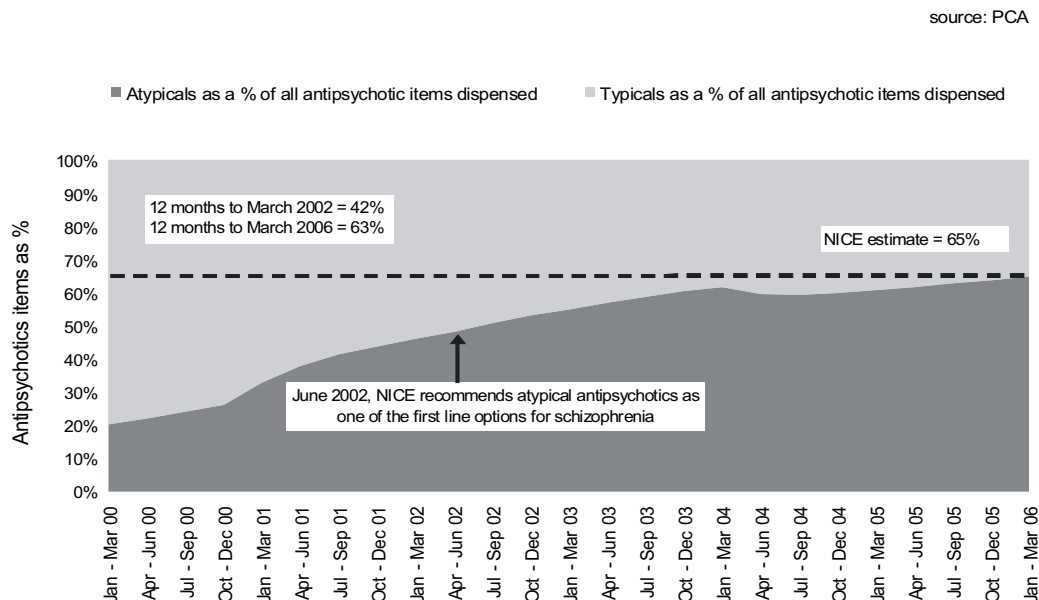
Graph 3—Anakinra issued in hospitals in England



TA043 SCHIZOPHRENIA—ATYPICAL ANTIPSYCHOTICS

8. NICE recommended the use of atypical (newer) oral antipsychotic drugs for a person who has been newly diagnosed with schizophrenia and for people who are currently taking typical (older) antipsychotic drugs that are controlling their symptoms of schizophrenia but are causing side effects. A NICE implementation uptake report showed that in the 12 months to March 2006, atypicals accounted for 63% of all antipsychotic items dispensed in primary care. This is consistent with the original NICE guidance that estimated around 65% antipsychotics prescribed ought to be atypicals (graph 4).

Graph 4—Atypical antipsychotics as a proportion of all antipsychotics dispensed in the community in England (total items)



9. A study by Abacus International in 2004 found that a similar picture is seen in secondary care where atypical prescribing has grown from 40% of antipsychotic use in 1999 to 66% in 2003.

ERNIE: CLINICAL GUIDELINES

10. An overview of the number of studies relating to clinical guidelines is presented below.

Number of external report entered in the database	31
Number of in-house implementation uptake reports entered in the database (as at 1 March 2007)	0
Total number and % of “current” clinical guidelines covered by at least one external or in-house study	16 (40% excl inherited guidelines)

NB the external references have not sought to assess the uptake of several clinical guidelines within one study. The 31 references therefore contain 31 assessments of uptake.

11. The assessment of uptake and implementation of clinical guidelines is more challenging than for technology appraisals due to the lack of routinely collected data and the large number of recommendations in each guideline. Less than a third of the above studies have looked at practice at a national level, and have instead a local focus. Furthermore, several of these have not looked specifically at the uptake of NICE guidance but may have included one or two NICE recommendations as part of a larger study.

12. In future we anticipate receiving data from studies by the Healthcare Commission regarding the implementation of NICE clinical guidelines. NICE is currently working with the HCC to identify indicators of uptake from their programmes of work and agree how this data may be published. The topics covered by Healthcare Commission work programmes are outlined in a joint statement that has been developed highlighting the different pieces of NICE guidance and how they fit into the HCC work streams www.nice.org.uk/page.aspx?o=402286. The NICE guidance covered in this work includes lung cancer, head & neck cancer, bowel cancer, cardiac rhythm management, diabetes, stroke, violence in mental health, falls, chronic heart failure, type 1 diabetes, schizophrenia, violence, induction of labour, antenatal care, caesarean section, postnatal care, self-harm and COPD.

SHARED LEARNING DATABASE

13. NICE has also developed an online shared learning database which contains examples of local implementation projects and aims to share learning across the NHS and beyond. The database, launched in December, already contains 32 examples of implementation initiatives. Examples range from the implementation of specific pieces of NICE guidance by specialist services to organisation-wide implementation systems that ensure all NICE guidance is assessed and appropriate implementation plans are put in place.

ENTRIES IN THE SHARED LEARNING DATABASE (AS AT 1 MARCH 2007)

<i>Type of example</i>	<i>Number</i>
Generic systems/processes to ensure the implementation of NICE guidance	18
Case studies relating to clinical guidelines	13
Case studies relating to technology appraisals	1

Evidence submitted by the Academy of Medical Sciences (NICE 39)

Introduction

1. The Academy of Medical Sciences welcomes the opportunity to respond to the above consultation. This response was prepared following consultation with a number of Academy Fellows¹⁶ and will focus on the following issues:

- Why NICE’s decisions are increasingly being challenged and public confidence in the Institute.
- NICE’s evaluation process and whether any groups are disadvantaged by the process.
- The speed of publishing guidance.
- Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN).
- The implementation of NICE guidance.
- Improvements in gathering evidence.

¹⁶ See Annex.

— Areas of guidance.

2. The Academy fully supports the role of NICE in providing guidance for the promotion of good health and the prevention and treatment of ill health. We consider that NICE is based on a sound principle, since it is crucial that an effective body is available to consider the efficacy and cost of innovations in healthcare. It should be recognised that this is a challenging role, and that it is almost inevitable that some of the decisions taken by NICE will be controversial. Nevertheless, NHS funds are limited and it is essential that the balance between the cost and benefit of new treatments be scrutinised carefully.

Challenge of NICE Guidance and Public Confidence in the Institute

3. Recent responses to NICE guidance for expensive new drugs such as Herceptin¹⁷ and Aricept¹⁸ indicate the growing public disquiet regarding decisions made by NICE. The perception by patients that they are being denied effective treatments is clearly an emotive issue and extensive press coverage of specific decisions further influences public confidence in the Institute. Patient advocacy groups are a growing feature of democratic health care systems. Thus, provided that such groups fairly represent the interests of patients and are not unduly influenced by commercial lobbyists, they should have an opportunity to put forward their views for a considerate hearing. However, whilst these views should be taken into account, a consistent approach based on the best available evidence should be maintained by NICE, combined with a fair appeal process. Greater public engagement during NICE appraisals may be necessary to improve understanding of the evidence-based process, restore confidence in the Institute and reduce future protests over the availability of new drugs.

NICE's Evaluation Process and Whether any Particular Groups are Disadvantaged by the Process

4. The Academy highlights that it is essential that the basic assumptions and models used during NICE's evaluation process are transparent and open to external scrutiny. We also consider it important that during evaluations of cost-effectiveness, NICE takes the overall burden of disease into account, to include societal costs to patient carers, unemployment costs or the expenditure of social services, for example. Quality of life assessments should also factor in the effect on carers or family members of those with a severe illness and relative enhancements in quality of life. The comparative benefit of a modest extension of life for an individual for whom the overall life expectancy is short is quite different from a modest extension of life for an individual for whom life expectancy is much longer. Such distinctions are important considerations during the evaluation process.

5. A further consideration is that a minority of patients may respond well to a medicine that is seen to offer unacceptably low efficacy for the majority. It would be useful if the sponsors of such medicines and independent patient advocacy groups could help to develop the means of identifying the patients most likely to respond to a treatment and to provide evidence of efficacy to NICE.

The Speed of Publishing Guidance

6. Any delay in assessment is undesirable and the referral of some drugs for licensing in the USA before Europe may contribute to the perception that the UK process is slower than necessary. Final decisions may occur between 18 months and five years after a new drug is licensed, a delay often referred to as "NICE blight".¹⁹ In order to reduce the delay between a drug being licensed and its referral for appraisal by NICE, we consider that potential drugs should be referred to NICE as they are identified, rather than via "waves" of recommendation from the Department of Health. This would reduce the time period required for the treatment to be approved.

7. Furthermore, whilst it is apparent that a detailed assessment of evidence is a necessary and time-intensive process, there is a clear need for a faster appraisal system. We welcome the introduction of the Single Technology Assessment (STA) process to "fast-track" the publication of guidance for certain new medicines referred to NICE.²⁰ Indeed, this model is based largely on the process used by the Scottish Medicines Consortium (SMC), the introduction of which greatly reduced the occurrence of problematic delays in decision-making. However, it is not yet clear whether the STA model adopted by NICE will deliver the early decisions necessary and we are concerned that the appraisal of other useful drugs may be subject to delay whilst resources are focused on drugs in the STA process. This issue is especially problematic since doctors may prescribe treatments before they have been approved by NICE when Primary Care Trusts (PCTs) are not required to fund them. Inevitably, this leads to variable availability, public disagreements and confusion amongst patients, indirectly affecting confidence in NICE.

¹⁷ Herceptin is a monoclonal antibody treatment that targets HER2+ breast cancer cells. HER2+ cells are present in approximately 15–25% of breast cancer patients.

¹⁸ Aricept is an acetylcholinesterase inhibitor, which is approved for use in people with mild to moderate Alzheimer's disease. There has been anger over NICE's decision not to license the drug for use in early and late stage patients.

¹⁹ As referred to in BMJ news (*BMJ* 2002; 324:191, *BMJ* 2000; 321:980).

²⁰ http://www.dh.gov.uk/en/Publicationsandstatistics/Pressreleases/DH_4122650

8. The scenario would be improved by the provision of NICE guidance at an early stage following referral of new medicines and the formulation of an agreed programme of ongoing (and rigorous) evaluation thereafter. All drugs could effectively be evaluated using the STA while still being subject to rigorous and specific “hurdles” before they are finally approved. Suitable evidence is not always available at the time of drug licensing for NICE to be able to carry out a full appraisal and data regarding efficacy of any drug (or the safety of drug combinations) accumulate over time. Indeed, advances in therapeutics may progress in small increments and successive steps taken over time may transform the efficacy and acceptability of a given treatment for a serious disease. The early uptake system would regulate and reward such advances according to the scale of improvement, rather than delaying progress by maintaining an “all or nothing” approach. Furthermore, it would facilitate appraisals of multiple technologies for any one disease following their introduction. This would enable a comprehensive review of treatment options and comparative benefit at a stage when clinical and cost-efficacy may be more evident.

9. Whilst appraisal decisions would still be subject to appeal, an early evaluation process might also reduce the delay in approving treatments by avoiding a lengthy appeal process. In the current system, an inclusive and transparent appeal process is crucial. However, early uptake of drugs may avoid appeals of NICE’s decisions by encouraging ongoing evaluation. The early adoption method has the added benefit of rewarding innovation and translational research by incentivising drug development whilst ensuring that only drugs that offer clear benefit to health are approved. The NHS Connecting for Health programme would have an important role to play in enabling and supporting such evaluations. It is therefore important that the requirements of NICE are considered in the development of Connecting for Health.

10. The Academy notes that although a faster appraisal system could accelerate the uptake of new treatments, care will need to be taken if, during the subsequent evaluation, drugs that are beneficial for some patients are deemed not to be cost-effective and are withdrawn. In the absence of an alternative treatment, this might lead to further pressure on NICE from pressure groups, the public and via the appeal system.

11. We emphasise that improvements in the speed of publishing guidance are dependent upon resources. It is vital that NICE is supported by sufficient resources from the Department of Health to carry out all necessary evaluations swiftly and to ensure that new guidance is implemented rapidly into clinical practice.

Comparison with SIGN

12. NICE clinical guidelines may have an advantage over SIGN guidelines in that they include an assessment of both clinical and cost effectiveness, as well as identifying treatments that provide good value for money. For example, the NICE clinical guidelines on hypertension, prepared with the British Hypertension Society, give a clear view on the clinical and cost effectiveness of different treatments and the order in which they should be introduced for the best value for money.²¹

13. In contrast, the extent of the delays in publishing NICE guidance is far greater compared to guidance from the Scottish Medicines Consortium (SMC). Decisions on new drugs taken by NICE may be finalised anywhere between 18 months and five years after decisions made by the SMC for similar drugs. The introduction of the STA, largely modelled on the SMC approach, may reduce such delay. Ongoing evaluations of the new system utilised by NICE will be important in providing further information.

The Implementation of NICE Guidance

14. The Academy supports the introduction of a programme to support and evaluate the implementation of NICE guidance. Such measures ensure that guidance is disseminated and evaluated and that the appropriate tools are provided for successful implementation. Reports on the uptake of guidance provided by the “Evaluation and Review of NICE Implementation Evidence” (ERNIE) database are a useful resource, which can inform the development of improved implementation strategies. Regular audits of implementation and compliance with guidance are essential to fully understand the effectiveness of both clinical guidelines and technology appraisal and how these have influenced NHS activity in England and Wales. Furthermore, evaluation of evidence regarding nationwide implementation may improve the consistency of provision between PCTs.

15. We recommend close communication between NICE and PCTs so that Trusts are financially prepared for the provision of new treatments. Information needs to be readily accessible for healthcare professionals so that doctors are aware of the complete range of treatments that may be prescribed and funded by the PCT. Advance preparation of all PCTs would reduce inconsistencies between those that provide a treatment and those that do not. The NICE costing template, forward planner and horizon scanning information should also be broadly disseminated and advertised to encourage timely implementation.

²¹ <http://guidance.nice.org.uk/CG34/guidance/pdf/English>

Improvements in Gathering of Evidence

16. The Academy considers that investment in clinical trial capacity in the NHS is highly desirable so that a greater number of large drug trials are carried out in the UK. The possibility that clinical trials of relevance to the NHS could be carried out using the research capacity and infrastructure provided by the UK clinical research network (UKCRN) should be explored. This would enable medicines to be available as part of a clinical drug trial at no additional drug cost and would ensure the collation of information of direct relevance to the NHS. Indeed, specific end points and outcomes required for NICE approval could be defined before commencement of the trial.

17. We also note the recommendations detailed in the Cooksey Review of Health Research Funding²² for an expansion of the Health Technology Assessment (HTA) programme. As above, this would improve clinical trial infrastructure and may facilitate a greater level of research and/or assessment of technologies for use in NICE appraisals.

18. We are concerned by potential conflicts of interest of experts. Clearly, it is essential that experts provide evidence during the appraisal of novel drugs. However, for the process to remain transparent, all potential conflicts of interest should be declared when evidence is provided for the Institute. This would reduce the risk that a perceived conflict of interest could damage the Institute's standing.

Areas of Guidance

19. In light of the recommendations made in the report "*Pandemic Influenza: Science to Policy*" published by the Academy of Medical Sciences and Royal Society (2006), we consider that NICE guidance on antiviral drugs likely to be used during an influenza pandemic should be updated as soon as possible. It is crucial that appropriate appraisal of such drugs is carried out in advance as part of the Government's pandemic preparedness strategy.

20. The Academy further considers that NICE could play a role in the appraisal of complementary and alternative medicines (CAM). Studies show that up to 50% of General Practitioners provide some access to CAM²³ and it is important that patients are assured of the safety and efficacy of such treatments. Moreover, CAM treatments or interventions provided by the NHS should be evaluated using robust scientific evidence prior to use in routine practice and consistent nationwide provision ensured.

The Academy of Medical Sciences

March 2007

Annex

The Following Academy Fellows Contributed to this Response

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The Academy of Medical Sciences

²² A Review of UK Health Research Funding, Sir David Cooksey, December 2006.

²³ Thomas K J, Coleman P, Nicholl J P (2003). Trends in access to complementary or alternative medicines via primary care in England: 1995–2001 results from a follow-up national survey. *Family Practice* 20(5): 575–7.

Evidence submitted by the Alzheimer's Society (NICE 70)

EXECUTIVE SUMMARY

The Alzheimer's Society welcomed the establishment of NICE and supports its role of ensuring fair access to clinically effective treatment. We have been extensively involved in the development of two technology appraisals as well as the dementia clinical guideline.

There are four drug treatments licensed for the treatment of Alzheimer's disease. Their clinical efficacy has been confirmed by gold-standard Cochrane systematic reviews. Benefits extend well beyond outcomes commonly captured in clinical trials such as stabilisation of illness and improvements in function and cognition; and include other key benefits such as being more aware and more active, calmer, taking more interest in things, improved conversation, better quality of life and restored confidence.

Why NICE's Decisions are Increasingly Being Challenged

NICE are challenged when it is felt their decisions are poor because they are a very powerful body and their decisions have a huge impact on people's lives. Two key reasons for challenges are:

NICE do not give sufficient weight to patient/professional evidence

Health economic analysis must be placed in the context of people's lives and real life clinical practice. In the experience of the Alzheimer's Society, little weight is given to evidence submitted by people with experience of the drugs. NICE failed to consider that the evidence from patients and carers might be considered on its own merits rather than as pointers for the committee to consider further published research. In addition, the knowledge and experience of clinicians with expertise in the disease area has also been ignored, resulting in guidance that does not translate easily to clinical practice. Methods for incorporating patient evidence into the appraisal process should be developed.

Issues with transparency of decision-making

Challenges are likely where there is inadequate explanation as to how the appraisal committee arrived at a decision. During the appraisal of Alzheimer's drugs it has been impossible to understand how a number of decisions have been reached.

Whether Public Confidence in the Institute is Waning and If So Why

Frequent, high profile challenges to NICE will undermine the Institute's authority and reputation. Given the important role of NICE, we believe the Institute must respond to this by seriously addressing the criticisms raised by stakeholders. The failure of guidance to reflect the views of people with experience of treatments and clinicians with expertise in the area damages public confidence in the Institute.

NICE's Evaluation Process and Whether any Particular Groups are Disadvantaged by the Process

There are specific methodological challenges in using QALYs in dementia. These include:

- Difficulties in measuring quality of life in dementia
- Capturing benefits to carers
- Complexities of funding in dementia care
- Capturing the benefits of the drug treatments.

Unless the wider benefits of the technology are given more weight and the QALY estimates less in cases where QALY estimates are not robust, we believe people with dementia and their carers will be strongly disadvantaged. There is precedent for this—in the 2001 appraisal of Alzheimer's drugs QALY estimates were considered unreliable by the appraisal committee and given little weight.

Appeal Process

The Alzheimer's Society recommends an independent appeals process is developed and more detail on how the appeal panel reach decisions is provided to appellants.

1. INTRODUCTION

The comments we make in this memorandum are chiefly concerned with the technology appraisal process. The memo addresses:

- Background to the drug treatments and our involvement with NICE.
- Why NICE's decisions have been increasingly challenged.
- Whether public confidence in the Institute is waning and why.
- NICE's evaluation process and whether any particular groups are disadvantaged by the process.
- The appeal process.

2. BACKGROUND

2.1 The impact of dementia is vast and as our population ages the numbers of people with dementia will rise rapidly from 700,000 today to over 1 million by 2025.²⁴ Alzheimer's disease is the most common cause of dementia. There is no known cure, however drug treatments have been developed that significantly improve symptoms in some people. Donepezil (Aricept), rivastigmine (Exelon) and galantamine (Reminyl) all work in a similar way and are known as acetylcholinesterase inhibitors. Another drug, memantine (Ebixa), works in a different way and is the only drug licensed for the severe stages of Alzheimer's disease.

2.2. The clinical effectiveness of all four drugs has been confirmed by over 30 clinical trials and Cochrane systematic reviews of the trials.^{25, 26} People with experience of the treatments report benefits in terms of happiness, awareness and confidence, as well as effects on memory and activities of daily living. NICE agrees that the acetylcholinesterase inhibitors are clinically effective for a significant proportion of people. NICE data show that 34% of people using donepezil in the mild stages of Alzheimer's are responders (according to the 2001 NICE guidance definition of response), compared to 31% in the moderate stage.²⁷ However, NICE questions the cost-effectiveness of the acetylcholinesterase inhibitors in the mild stages of Alzheimer's. NICE also questions the clinical efficacy of Ebixa, which is particularly puzzling in that it contradicts the findings of the gold standard Cochrane review. Because NICE queried the clinical effectiveness of Ebixa, its cost-effectiveness analysis of the drug was not thorough.

2.3 The Society was involved as a consultee in the first appraisal of the acetylcholinesterase inhibitors in 2001 and has been extensively involved in the review of that guidance which was extended to include Ebixa. The current review began in 2004 and the Final Appraisal Determination was published in May 2006. Five appeals were lodged against this guidance, from patient groups, professional bodies and manufacturers. The key points of the Society's appeal were:

- NICE's failure to take important benefits of the drugs into account, particularly benefits to carers and reduced need for harmful neuroleptic drugs.
- Failures in the economic model, for example it does not measure quality of life of people with dementia properly.
- The decision is contrary to good practice in dementia care—treatment in the early stages is what people want.

2.4 These appeals were unsuccessful and permission has been given for a judicial review of the decision. The Alzheimer's Society has registered as an interested party in this judicial review. We have also acted as consultees in the development of the NICE/SCIE clinical guideline on dementia and Society representatives were members of the Guideline development group.

3. WHY NICE'S DECISIONS ARE INCREASINGLY BEING CHALLENGED

3.1 NICE is challenged because it is a very powerful body. Its decisions have an enormous impact on people's lives. However, it is important to note that NICE is not challenged because patient organisations simply dislike its decisions. Groups such as the Alzheimer's Society are challenging NICE because they believe the decision making process was flawed.

²⁴ Knapp, M and Prince, M, 2007, Dementia UK (A report to the Alzheimer's Society on the prevalence and economic cost of dementia in the UK produced by King's College London and London School of Economics). London.

²⁵ Birks J, 2007, cholinesterase inhibitors for Alzheimer's disease, *The Cochrane Database of Systematic Reviews*, Issue 1.

²⁶ McShane R, Areosa Sastre A, Minakaran N, 2007, Memantine for dementia, *The Cochrane Database of Systematic Reviews* 2007 Issue 1.

²⁷ National Institute for Health and Clinical Excellence, 2006, Donepezil, galantamine, rivastigmine (review) and memantine for treatment of Alzheimer's disease (final appraisal document). <http://www.nice.org.uk/page.aspx?o=322952>

NICE do not give sufficient weight to patient/professional evidence

3.2 NICE has difficult decisions to make and it has developed sophisticated but complex mechanisms to arrive at estimates of cost effectiveness. However, health economic analysis must be placed in the context of clinical practice and the lives of the people who are prescribed the drug treatments. NICE's final decision to allow access to Alzheimer's drugs only in moderate stages is completely out of step with what carers and people with dementia want and the recent direction of dementia policy—early diagnosis and treatment. The knowledge and experience of clinicians with expertise in the disease area has also been ignored, resulting in guidance that does not translate easily to clinical practice. It is therefore not surprising that there was such a huge outcry.

3.3 NICE was certainly made aware of the strength of feeling of patients, carers and clinicians during the Alzheimer's appraisal via its arrangements for consulting with stakeholders. However, it is questionable whether this has influenced appraisal committee deliberations.

3.4 In response to the comments from stakeholders NICE did look at different approaches to estimating costs effectiveness and a range of factors that should be included in the economic analysis. However, there is limited formal data around many of these issues and based on this NICE concluded there was no evidence that factoring in these considerations would make the drug treatments cost-effective. NICE failed to consider that the evidence from patients, carers and professional might be considered on its own merits rather than as pointers for the committee to consider further published research.

3.5 Patient groups put significant resource towards participating in NICE appraisals and the number of responses received from individuals show that the public is also keen to input. It is essential that NICE examines whether it is putting the information it gathers to effective use. We would welcome a debate around how NICE uses patient evidence, both when there is a lack of formal published data and when patient evidence contradicts the published evidence. Firstly, methods should be developed to incorporate the evidence into the economic analysis. Consensus methodology such as Delphi (a technique which aims to find a reliable consensus opinion from a group of experts) is a potential way of doing this. Secondly, when there is uncertainty around cost per QALY estimates, patient evidence must be given more weight. In our experience, the balance between the weight given to results of a much-criticised economic model and the evidence of people with dementia, carers and professionals has been wrong.

Issues with transparency of decision-making

3.6 Challenges are also likely where there is inadequate explanation as to how the appraisal committee arrived at a decision. During the appraisal of Alzheimer's drugs it has been impossible to understand how a number of decisions have been reached. Proper explanation must be provided so that consultees can either understand a decision, or challenge the basis of that decision. For example, the Alzheimer's Society was very concerned that withdrawing access to licensed Alzheimer's drug treatments would increase the prescription of dangerous neuroleptic treatments, which increase falls and stroke and can reduce quality of life through over-sedation. We argued strongly that the costs associated with increased prescription of these drugs should be factored into the economic analysis. NICE responded to this by saying: "it was not convinced that inclusion of an element of harm in the economic analysis from further prescribing of antipsychotics as a result of their recommendations was appropriate." (ACD2 and FAD para 4.3.10.4) No explanation was given as to why it was considered inappropriate, making it impossible for us to engage with NICE on this point. If a more constructive dialogue around points of disagreement could take place during the development of guidance it might be that appeals and challenges could be avoided.

3.7 The lack of depth of explanation in ACDs and FADs is a particular problem given that it is difficult to enter into a dialogue with NICE outside of the consultation process. If a consultee is not satisfied that an argument has been understood or properly considered, there is little opportunity to discuss this with NICE. When we have had specific questions we have been told to put those questions in our comments to the next consultation. While clearly NICE have to control dialogue with stakeholders in order to keep the appraisal process manageable, it would be helpful to have an opportunity to raise questions outside of the consultation process.

3.8 These problems can leave no option but to follow the appeal process. This is a hugely costly process for patient groups, which any organisation would want to avoid if possible. We believe more transparency in the decision making process could help reduce the number of appeals and we would recommend the following to enable this:

- Representatives of patient groups should be able to act as non-speaking observers at appraisal committee meetings at which a relevant technology is discussed.
- A full minute of the meeting should be available, with sufficient detail so that it is possible to understand how decisions were reached. We did request a record of the appraisal committee meeting through a freedom of information act request, but this was refused.
- Fuller explanations should be provided as to how a decision was reached in FADs and ACDs. "Considered not appropriate" is not good enough.

4. WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING AND IF SO WHY?

4.1 Frequent, high profile challenges to NICE will undermine the Institute's authority and reputation. Given the important role of NICE, we believe the Institute must respond to this by seriously addressing the criticisms raised by stakeholders.

4.2 We believe the failure of guidance to reflect the views of people with experience of treatments seriously damages public confidence in the Institute. Little weight has been given to the evidence of these individuals in the Alzheimer's drugs appraisal. This is extremely concerning given that NICE's decisions have such serious implications. The experience of people living with the condition should be the starting point of any technology appraisal.

4.3 If clinicians are to have full confidence in NICE, guidance needs to be both evidence based and workable in clinical practice. The guidance on Alzheimer's drugs fails in this respect and therefore it is not surprising that the Royal Colleges of Nursing and of Psychiatry and the British Geriatric Society appealed against the final decision. In addition, implementation of the NICE guidance on Alzheimer's drugs means that the UK is virtually the only country in Europe that does not allow access to the drug treatments in the mild stages of illness.

5. NICE'S EVALUATION PROCESS AND WHETHER ANY PARTICULAR GROUPS ARE DISADVANTAGED BY THE PROCESS

5.1 NICE have developed a complex evaluation process that is primarily based on generating a cost per quality adjusted life year (QALY). NICE use this generic measure to allow comparative judgements across diseases. We understand the need for NICE to be consistent, however there are specific methodological challenges in using QALYs in dementia, many of which are also found in other long-term conditions. Unless in these cases the wider benefits of the technology are given more weight and the QALY estimates less, we believe people with dementia and their carers will be strongly disadvantaged. There is precedent for this—in the 2001 appraisal of Alzheimer's drugs QALY estimates were considered unreliable by the appraisal committee and given little weight.

5.2 The problems of applying traditional health economics to dementia include:

Measuring quality of life in dementia

5.3 The calculation of cost per QALY relies on the measurement of health related quality of life (HRQL) in different disease states. Although key symptoms such as functional ability strongly correlate with quality of life and could be used as a proxy measure, there are currently no validated methods of measuring HRQL in Alzheimer's disease. NICE used an unvalidated method. This fundamental problem seriously compromises the robustness of NICE's model.

5.4 Furthermore, as the individual begins to lose capacity as dementia progresses, proxy judgements of the person's quality of life are used. This is far from ideal. There is no consensus on who is the best proxy—the literature suggests that professionals may be better proxies than carers on some subscales and family carers better on others.²⁸

Benefits to carers

5.5 Family carers are the mainstay of support for people with Alzheimer's disease. Although providing this support is something that most carers gladly do, it is extremely stressful, and takes a large toll on people's physical and mental health. If a drug means that the person they care for can, for example, be left alone in the house, regains a sense of humour, cooperates in tasks like bathing, the benefits to carers are immense.

5.6 While NICE's evaluation processes are focused on the individual receiving the intervention NICE do acknowledge that benefits to carers should be incorporated. However, in our experience, NICE have not adequately incorporated these benefits.

5.7 Despite the deluge of evidence from carers that effective drug treatment benefits carers as much as individuals with dementia, NICE chose to rely on the very limited and weak published evidence around carer quality of life at different stages of dementia. This suggested carers' quality of life does not vary significantly as a person's disease progresses. Based on this NICE chose to assign the very small utility gain of 0.01 to carers when calculating a cost per QALY. We believe NICE should not have accepted this finding unquestioningly, particularly given the strength of evidence from carers contradicting this. NICE must address how to properly incorporate benefits to carers if they are to produce equitable evaluations of interventions. Certainly, in the case of treatments for Alzheimer's disease NICE's evaluation methods have failed carers.

²⁸ Coucill W, Bryan S, Bentham P, Buckley A, Laight A, 2001, EQ-5D in patients with dementia: an investigation of inter-rater agreement. *Medical Care* 39:760-771.

Costs of dementia care

5.8 The exclusion of costs outside those borne by the NHS and social services is also likely to disadvantage groups where the individual and their family meet a considerable proportion of costs. Unlike other illnesses, people with dementia are disadvantaged by the current system of health care in the UK. The vast majority of formal care is provided by social services and is therefore means tested. In addition, the cost of informal care provided by family members and other unpaid carers makes up one third of the £17 billion that dementia costs each year.

5.9 NICE has not considered reduced benefit dependency and improved ability to work following effective drug treatment both for patients and their carers, despite this being a recommendation of the Health Select Committee 2002 inquiry. The Dementia UK report concluded that annually carers lose £690 million in income through having to give up employment or cut back their work hours. This lost employment means a loss of £123 million in taxes paid to the Exchequer.

5.10 NICE has a duty to include the costs and benefits that most fair-minded people would deem appropriate.²⁹ In cases such as dementia where such a significant proportion of costs are met by individuals and their families, there is a strong case for going beyond costs to NHS and personal social services.

Capturing benefits of the drug treatments

5.11 The survey carried out by the Society to inform our submission demonstrated that the benefits of the drug treatments extend well beyond outcomes commonly captured in clinical trials such as stabilisation of illness and improvements in function and cognition; and include other key benefits such as being more aware and more active, calmer, taking more interest in things, improved conversation, better quality of life and restored confidence.³⁰ However, it is difficult to incorporate these types of benefits reported by users and carers into the health economic analysis.

5.12 NICE's processes are heavily weighted to outcomes measured in clinical trials to the exclusion of other, harder to statistically measure, benefits. This approach will inevitably disadvantage groups where benefits of drug treatments are heterogeneous and hard to capture within a clinical trial. User-defined outcomes reveal what patients and carers think about an intervention in terms that are meaningful for their own lives. This kind of evidence is vital if NICE is to come to proper decisions on the basis of a fully rounded view of new health technologies.

Additional problems in using QALYs in dementia include:

5.13 The long-term nature of the condition. While people can live with dementia for up to 10 years most clinical trials last for only 6-12 months, meaning that the long-term effects of treatments have to be projected using modelling techniques. This increases the risk of introducing errors. Furthermore, oversimplified models should be avoided if the complexities of a disease and intervention experienced over a long period of time are to be captured. For the Alzheimer's appraisal, NICE developed a model with one cost-driver—moving into full time care. This model is particularly weak at assessing benefits to the subgroup of people with mild dementia because there will be such a time lapse before these individuals move into full time care.

5.14 Many people with dementia have concurrent health conditions, mainly because they tend to be older people. This can mean that even if dementia was not present the person is less likely to achieve a high QALY score. The impact of this on the economic analyses of treatments should be considered.

5.15 At the appeal hearing the appraisal committee chair argued that despite the problems in calculating a QALY in dementia 'there was no plan B'. This is an inadequate response. The health and wellbeing of many thousands of people with long-term conditions such as dementia are suffering because NICE's model does not work for their condition. NICE have a duty to respond to this by appraising its methods and accepting the challenge of developing a new approach that works for all. We would be happy to work with NICE on developing such an approach.

5.16 Until such an approach is developed, the Institute has a duty to consider what weight is given to QALY estimates when the robustness of the model is in doubt.

Appeal process

5.17 Although changes were made to the NICE appeal process following the Health Select Committee inquiry of 2002, the process is still not independent given that it is made up primarily of non-executive directors of NICE. The Alzheimer's Society firmly believes that the Institute must establish a properly independent appeals process if it is to maintain the confidence of the public.

5.18 In relation to the Alzheimer's appeal, we have concerns around the transparency of the appeal panel decisions. Little explanation was given as to how decisions were reached and why points raised by appellants were ignored.

²⁹ NICE, 2005, Guidance document for consultation, *Social Value Judgements*, www.nice.org.uk

³⁰ Alzheimer's Society, 2004, *Drugs for the treatment of Alzheimer's Disease*, Alzheimer's Society, London.

RECOMMENDATIONS

1. Methods should be developed to incorporate patient evidence into the economic analysis. Consensus methodology such as Delphi (a technique which aims to find a reliable consensus opinion from a group of experts) is one way of doing this.
2. When cost per QALY estimates are uncertain, patient evidence must be given more weight. In our experience, the balance between the weight given to results of a much-criticised economic model and the evidence of people with dementia, carers and professionals has been wrong.
3. Representatives of patient groups should be able to act as non-speaking observers at appraisal committee meetings at which a relevant technology is discussed.
4. A full minute of the meeting should be available, with sufficient detail so that it is possible to understand how decisions were reached. We did request a record of the appraisal committee meeting through a freedom of information act request, but this was refused.
5. Fuller explanations should be provided as to how a decision was reached in FADs and ACDs. "Considered not appropriate" is not good enough.
6. The health and wellbeing of many thousands of people with long-term conditions such as dementia are suffering because NICE's model does not work for their condition. NICE have a duty to respond to this by appraising its methods and accepting the challenge of developing a new approach that works for all. We would be happy to work with NICE on developing such an approach.
7. Until such an approach is developed, the Institute has a duty to consider what weight is given to QALY estimates when the robustness of the model is in doubt.
8. The Alzheimer's Society firmly believes that the Institute must establish a properly independent appeals process if it is to maintain the confidence of the public.

Alzheimer's Society

March 2007

Evidence submitted by the American Pharmaceutical Group (NICE 89)³¹

EXECUTIVE SUMMARY

1. The American Pharmaceutical Group has a number of concerns about the effectiveness of NICE, including NICE's evaluation process, the speed of publishing guidance, the appeal system, and implementation. In our submission we illustrate these concerns through case studies. These specific instances give cause for concern that NICE would be ill-equipped to manage an extended remit as suggested by both the recent Office of Fair Trading report into the workings of the PPRS and the Cooksey Report.

INTRODUCTION

2. The American Pharmaceutical Group (APG) represents the 10 leading research based US-owned pharmaceutical companies who invest in the UK. APG member companies currently supply over a third of all branded medicines to the NHS. We welcome this inquiry and believe it is a crucial time for the Committee to conduct a review of NICE to address whether the organisation is fit for purpose.

3. The APG supports the objectives of NICE and we value its independence and stakeholder engagement. However we have a number of concerns about how NICE works in practice. The recent Office of Fair Trading report into the pharmaceutical pricing regulation scheme (PPRS) recommends a wider role for NICE. However, the industry is not satisfied about NICE's ability to deliver increased access, accelerated uptake of new medicines, and proper assessment of value. The newer NICE Single Technology Appraisal (STA) process raises particular concerns over NICE's ability to conduct equitable appraisals close after the launch of medicines.

4. The APG works closely with the Association of British Pharmaceutical Industry (ABPI) and we endorse their submission to the Committee's inquiry. Rather than replicate the points of principle made in the ABPI's memorandum, we have used this submission to illustrate some of these points by way of case studies.

³¹ The APG consists of the following companies: Abbott, Amgen, Bristol-Myers Squibb, Janssen-Cilag Ltd, Lilly, Merck Sharp & Dohme, Pfizer, Procter & Gamble Pharmaceuticals, Schering Plough and Wyeth.

NICE EVALUATION PROCESS

5. A decision from NICE is becoming increasingly dependent on whether the technology in question demonstrates cost-effectiveness against an implicit cost per quality-adjusted life-year (QALY) threshold. This can be a useful pointer, but does not capture all dimensions of the value of a particular medicine or therapy, both to patients, carers and society at large. Although other measures of value can technically be included in HTA appraisals, almost all of the key decisions seem to be determined by the cost per QALY. The current implicit thresholds (£20,000–£30,000) are set by the HTA bodies themselves, are not subject to public scrutiny and do not appear to be linked to any kind of inflation adjustment over time. They have never been the subject of public debate or Parliamentary approval. This growing arbitrary dependence on a cost per QALY threshold approach appears to be a back-door means of NHS cost containment. While cost per QALY analysis has a part to play in HTA, the APG does not believe it should be pivotal to whether or not a product is recommended for use. The Cost per Life Year, for example, may be a more appropriate measure in certain circumstances. Affordability, innovation, burden on carers, value to society and contribution to economic productivity are all important factors that should be taken into account.

Case Study A: Cost effectiveness: the treatment of mesothelioma with alimta (pemetrexed)

6. Exposure to asbestos is the main cause of mesothelioma (a cancer of the lining of the lungs). Although relatively rare, the number of mesothelioma cases in the UK is steadily rising and is expected to peak between 2011 and 2015 and decline thereafter. Anticipated patient numbers will be between 1,950 and 2,450.

7. Alimta (pemetrexed), in combination with another drug called cisplatin, is the first and only treatment (chemotherapy) to be licensed in the UK for patients with mesothelioma. Some patients have been given the treatment since its launch in November 2004 but many other hospitals have been waiting for the final guidance from NICE before using it, resulting in widespread geographical inequalities in its availability.

8. Alimta (pemetrexed) entered the NICE process in August 2005. Released on the 26 June 2006 the first draft of the NICE guidance stated that the use of Alimta (pemetrexed) for the treatment of mesothelioma is not cost effective. The ruling was the subject of an appeal hearing in October 2006. The manufacturer, Lilly, and the Royal College of Nursing (RCN) were both appellants.

9. A number of Lilly's appeal points have now been upheld. The most significant was where Lilly successfully argued that the failure to consider the benefits of Alimta (pemetrexed) by reference to the Cost per Life Year Gained was discriminatory. The Appeal Panel upheld the appeal on this point and requested that the Appraisal Committee reconsider the use of life years gained.

10. Other appeal points upheld were:

- NICE failed to disclose a written perspective prepared by a clinical specialist who attended the meetings of the Appraisal Committee.
- The initial Appraisal Committee hearing on 7 March 2006 was inquorate. The Appraisal Committee should review all matters considered on 7 March.
- There was potential for misunderstanding the references to MSO1. The Appeal Panel requested that references to it be removed.

11. The Appraisal Committee met again to consider the issues upheld on appeal at a hearing on 8 March 2007. Having had four appeal points upheld against them, we question how the same committee can objectively reconsider the same issues again.

12. An Appraisal Committee Document is now available for comment by consultees. This document states that the preliminary view of the Appraisal Committee is not to recommend Alimta (pemetrexed) for use in the NHS. The appraisal committee will meet again on 8 May 2007 to consider the responses and issue the Final Appraisal Document. There is no further mechanism within the current NICE process to challenge these findings which will be presented to the NICE Board for ratification. The final Guidance is expected to be published in August or September 2007, fully two years after the start of the process. In the last year alone Lilly estimates that 300–350 patients who could potentially have benefited from treatment with Alimta have effectively been denied it.

13. If the current guidance is confirmed it will prevent patients receiving the medicine on the NHS. This would be the first time that NICE had denied patients access to the only licensed treatment for a condition on the NHS.

14. The Scottish Medical Consortium (SMC), the Cochrane Centre, the London Cancer New Drugs Group and the Drugs and Therapeutics Bulletin have all already positively appraised the use of Alimta (pemetrexed). However, the SMC's advice is usually superseded by final NICE Guidance, meaning that if the preliminary views of NICE are finalised, patients in Scotland could also be denied the only licensed treatment for mesothelioma from August–September 2007. Ironically, if NICE had appraised Alimta for mesothelioma as a Single Technology Appraisal this would not be the case.

15. The approach followed in considering Alimta (pemetrexed) is inconsistent with other similar appraisals. The draft guidance did not reflect the benefits of Alimta (pemetrexed) in a difficult to treat tumour in a small sub-set of the population for which no other therapy is licensed or, more importantly has

shown comparable effects in medical practice to those shown in phase III clinical trials. NICE's position is a clear disincentive to future innovative research, commercial or academic, in difficult to treat diseases. The overall budget impact submitted to NICE estimates at most £3.2 million in 2006–07, increasing to approximately £5.2 million in 2009–10. The current UK price of Alimta (pemetrexed) is also the lowest in Europe.

16. The Government and Parliament have voiced sympathy for people with mesothelioma—mostly victims of workplace exposure to asbestos—through the passage of the Compensation Act 2006. It would be disappointing if ultimately the only way to gain access to Alimta is to use compensation payments to fund private treatment.

Case study B: Verifying the research, data and models used in the NICE assessment: the treatment of Alzheimer's disease with anti-cholinesterase drugs

17. In March 2005 NICE issued initial guidance that three anti-cholinesterase drugs (Aricept, Exelon, Reminyl) should not be funded by the NHS for patients with Alzheimer's disease. In early 2006 NICE amended this decision so that the three drugs would only be funded for people in the moderate stages of Alzheimer's disease. NICE also recommended that Ebixa, the only treatment available for distressing behavioural symptoms in late dementia, should not be funded.

18. The initial decision and subsequent revision, limiting use to moderate patients, has repeatedly ignored the views of patient and professional groups about the value of these medicines in early disease. The most recent guidance (2006 FAD) requires patients to experience irreversible and debilitating decline in health status before treatment is initiated.

19. Residential care costs borne by patients and their families were excluded in the Alzheimer's appraisal, which has the effect of systematically under-estimating the value of Alzheimer's disease medicines to society.

20. The use of QALYs in healthcare decision making remains controversial. NICE rejected using the QALY approach in its original Alzheimer's disease assessment as it was not considered sufficiently reliable. NICE has used QALYs in subsequent appraisals despite there being no evidence since the original appraisal to demonstrate that this is a robust approach.

21. The Alzheimer's disease economic model used by NICE to assess the three drugs contains numerous assumptions and parameter estimates that do not reflect current practice, resource use and costs. The economic model can generate cost-effectiveness estimates above and below the notional £30,000 per QALY threshold used by NICE, depending on which parameter estimates are used.

22. Repeated refusal by NICE to provide a working version of the Alzheimer's economic model has prevented the manufacturers from properly appraising NICE analyses. Given concerns about methodology and assumptions, and errors in the Technical Assessment Report, the industry is not confident that this model does not also contain additional errors. Furthermore, the manufacturers were given just two days to review and comment on some of the later analyses, further hindering ability to engage properly in the appraisal.

Case Study C: Evidence used in the NICE evaluation process: NICE appraisal of erythropoietin (alpha and beta) and darbepoetin for the treatment of cancer-treatment induced anaemia

23. Erythropoietin (alpha and beta) and darbepoetin for the treatment of cancer-treatment induced anaemia was referred in the 9th wave, and commenced with the scoping in June 2004. The latest estimate for Guidance publication is November 2007.

24. The European Organisation for Research and Treatment of Cancer (EORTC), the American Society of Clinical Oncology (ASCO) and the US National Comprehensive Cancer Network (NCCN) all recommend Erythropoietin for cancer-treatment induced anaemia within the licensed indications for the products. NICE's preliminary decision was not to recommend the use of EPO for patients with anaemia induced by cancer treatment, although this is currently the basis for an appeal. Withdrawing the option of treatment with this medicine would be a major blow for people with cancer at a time when their health is already under serious test.

25. There are a number of concerns about NICE's evaluation process:

Government priorities on blood use

The UK has relatively low blood stocks and the cost of producing safe blood is increasing. Despite being a requirement for all NICE appraisals, NICE did not take into account the recommendations from other Government bodies on preserving blood supplies. This includes the 2002 Health Service Circular that instructed trusts to take action to avoid unnecessary use of donor blood and to consider effective alternatives.

Substantial errors in survival analysis undertaken by NICE

NICE was instructed to perform a meta-analysis of EPO trials consistent with the licensed indication to see if a survival advantage existed. NICE concluded none of the EPO trials was consistent with the current marketing authorisation and therefore rejected all EPO clinical trials. NICE failed to distinguish between *indications* for the use of EPOs and the *other information* included in the Summary of Product Characteristics (SmPC) which evolved post-marketing and after the trials programme was completed. This was inconsistent with the remit. The approach NICE used for this analysis was unscientific using a method we have never seen before. If you include all clinical trials with a population, dose and Hb level in line with the 2005 SmPC there is good evidence of a survival benefit.

Iron data

NICE did not consider the new data emerging that indicates a higher response rate when EPOs are administered with iron.

Patient preference

NICE did not properly consider patient preference and convenience. Evidence shows patients prefer EPO treatment due to improved convenience of home treatment and concerns over the increased risks associated with transfusion.

THE SPEED OF PUBLISHING GUIDANCE; THE APPEALS PROCESS

26. There are often delays in uptake of innovative medicines due to the time taken to publish guidance and the length of the NICE appraisal process.

Case Study D: Length of NICE process: the treatment of rheumatoid arthritis and of severe ankylosing spondylitis with adalimumab

27. Adalimumab was granted its European licence in September 2003 for the treatment of rheumatoid arthritis. Abbott submitted evidence on 8 June 2005 for the multiple technology appraisal of adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis but NICE has yet to publish its guidance—some way over the expected timeframe from submission of evidence to final guidance.

28. The use of adalimumab for the treatment of severe ankylosing spondylitis has followed a similar process. Abbott originally submitted evidence for this indication in January 2005 and the expected date for release of final guidance is currently unknown, as the third appraisal committee meeting requested additional analysis to be conducted to inform the cost-effectiveness estimates. The ongoing delays to NICE guidance for this indication are leading to increased variation in access to adalimumab in the UK, with the Scottish Medicines Consortium guidance recommending adalimumab for treatment of these patients on 10 November 2006.

29. One of the problems with the appraisal process as currently constructed is that any appeal lodged has a major impact on extending the delay until final guidance is released. There is currently a lengthy delay between submission of a notice of appeal and the date of an appeal hearing (four months in the case of adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis). This appears to be due to resource constraints in terms of the number of panels available to hear appeals—NICE's guide to the appeals process indicates it will endeavour to hear appeals within 10 weeks of the appeal being lodged. There is a further delay in the time taken from the appeal hearing to final guidance. For MTA appraisals where only sections of the Final Appraisal Recommendations are being appealed against, we feel it would make sense to release final guidance on those recommendations which are not being contested to reduce delays.

30. NICE's STA process is aimed at producing guidance around the time of marketing approval for the medicine. However, the availability of time slots on NICE's appraisal committee meetings appears to be delaying the scheduling of topics until well after launch. For example, adalimumab for the treatment of psoriasis is expected to receive its marketing authorisation in the 4th quarter of 2007. However, NICE provisionally indicated to Abbott that no appraisal committee time slots would be available to review this product until February 2008.

Case Study E: Length of NICE process and change of remit: the treatment of primary and secondary osteoporosis

Technology appraisals for the treatment of primary and secondary osteoporosis have been ongoing for five years and are still not completed.

32. NICE is currently consulting on Appraisal Consultation Documents (ACDs) for both primary and secondary osteoporosis. The original technology appraisal for the prevention and treatment of osteoporosis commenced in 2002 and was divided into two appraisals during its development; one for primary prevention and one for secondary prevention. The appraisal for secondary prevention was published in January 2005, whilst the appraisal for primary prevention is still in development.

33. NICE Guidance for the secondary prevention of osteoporosis included recommendations for the initiation of treatment and recommendations for those patients withdrawn from initial treatments. Two years later, following the inclusion of another agent and additional data analysis, the latest ACD for the update of this guidance provides recommendations only for the initiation of treatment. No guidance at all is offered for patients who are withdrawn from initial treatments (ie unable to tolerate or respond to alendronate). The ACD for primary prevention produced in parallel also contains guidance only for the initiation of treatment. There has been a clear change in the scope of the review without consultation.

34. NICE has spent five years developing this guidance already. The large number of drafts published for this ongoing appraisal has led to increased confusion as to best practice and unfortunately the current proposal does nothing to resolve this. This is unhelpful to healthcare professionals and patients and the current recommendations are likely to deny patients access to useful treatments.

THE IMPLEMENTATION OF NICE GUIDANCE

35. Different categories of NICE guidance carry different weight. *Technical Guidance* is covered by a mandate from the Secretary of State for Health in England. Typically the stated timeline for implementation is three months from publication in both England and Wales, 18 months in Northern Ireland, and at the discretion of Health Boards in Scotland. NHS bodies have a duty to make plans to implement *Guidance* issued by NICE and to fund the treatments involved. However, the additional tier of local bureaucracy whereby each local trust and board decides whether to place a nationally approved medicine onto a local formulary serves to exacerbate the “postcode lottery”. The process of potentially making three separate national HTA submissions and then providing additional data for local drug and therapeutic committees also places a significant burden on companies, which goes against the principles of the Hampton and Arculus reviews. Even when all these hurdles have been cleared, implementation of NICE guidance is extremely variable. To some extent the Healthcare Commission monitors NHS adherence to this through the Core Standards in its “Annual Health Check”, but the process is currently weak.

36. *Clinical Guidelines* on the other hand are even weaker, since they do not carry the same mandate. The Healthcare Commission does not measure implementation of *Clinical Guidelines per se*; instead they encourage trusts to consider implementation as a developmental standard—one which they should be aspiring to achieve in the future.

37. NICE has indicated that it intends to begin incorporating *Guidance* into *Clinical Guidelines* at the review which usually occurs three years after guidance is issued. Feedback from NHS organisations suggests that, while they would like to prioritise the implementation of *Clinical Guidelines*, they do not have the funding or resources required to do so. Consequently implementation is patchy and dependent on available funds.

Case Study F: Guidance versus guidelines: the use of atypical anti-psychotics in the treatment of schizophrenia

38. NICE issued guidance on the use of atypical anti-psychotics in the treatment of schizophrenia in May 2002. As is usual, this guidance was published with the intention that it would be reviewed and re-issued after three years (May 2005). Instead, in May 2005, NICE issued proposals to incorporate this *guidance* into the *Clinical Guidelines*.

39. Even with mandatory status, the implementation of *Guidance* issued by NICE varies. Regional variations in use of atypical anti-psychotics and even variations between local mental health trusts of up to 70% exist. A Healthcare Commission report in January 2007 found a quarter of mental health trusts have yet to get the funding from Primary Care Trusts to fully implement the 2002 *Guidance*—despite the direction to implement within three months.

40. By incorporating this *Guidance* into a *Clinical Guideline*, the NHS is no longer obliged to fund the use of atypical anti-psychotics. Some NHS representatives have indicated to us they will be re-directing funds currently allocated to atypicals towards other technologies which do have mandatory status. This is not a deliberate attempt to withhold treatment from those who need it, but the only way they can balance the books. However, in an area such as severe mental illness this approach could directly compromise patient care, and patient and public safety.

41. At present the *Guidance* on atypicals is the only technology appraisal that is being incorporated into a *Clinical Guideline* on review. NICE has indicated it intends to extend this method to other technology appraisals when they reach their review date. Potentially, many other therapy areas outside mental illness will find that funding for medication is no longer statutory. That cannot be the intention of NICE which was established to set clinical standards of excellence and achieve parity of access to quality treatment.

CONCLUSION

42. These specific instances give legitimate cause for concern that NICE would be ill-equipped to manage an expanded remit as suggested by the OFT report into the workings of the PPRS. The current NICE process seems unnecessarily adversarial. For example, the process would be improved if stakeholders could have on-going dialogue on technical questions with both the external review groups and the relevant NICE

appraisal committee. It would also be beneficial if issues of substance, as opposed to process, could be revisited on appeal. The appeal process itself raises the wider issue of whether NICE should sit as judge and jury in its own court—and then send any “successful” case back to the same jury.

43. Ultimately the interests of patients should be at the heart of the NICE process. We have documented evidence of how it is falling short in delivering its aims in terms of restricted access to proven medicines and accelerated uptake of new medicines.

44. Under the recommendations of the OFT for therapeutic reference pricing, HTA assessment of value would still be pivotal in determining whether patients would receive medicines. Given that the OFT proposes a new collaborative approach to HTA between NICE, the Scottish Medicines Consortium and the All-Wales Medicines Strategy Group, we urge the Committee to take evidence from all of these bodies. Given the magnitude of the issues at stake we also urge the Government to conduct a wide-ranging independent review of HTA processes. Before a meaningful discussion on the reform of the PPRS can take place, the APG wants to have full confidence in the metrics used to determine the value of a medicine within the total healthcare system. These should take into account innovation, affordability, benefit to patients, carers, society, the science base and UK plc.

The American Pharmaceutical Group

March 2007

Evidence submitted by Amgen (NICE 58)

OVERVIEW

The National Institute for Health and Clinical Excellence (NICE) was established to ensure “Faster Access to Modern Medicines”. Amgen supports this objective, and welcomes the contribution the organisation has made towards ensuring national guidance is published to deliver equitable access to medicines. Since its formation, the Government and NICE have maintained dialogue with all stakeholders and collaborated widely to ensure NICE has evolved into an internationally recognised centre of excellence for health technology appraisal. However, there are areas around the organisation’s procedures that need reviewing if NICE is to ensure patients benefit from innovative medicines, and that the UK continues to be home to innovative research for serious illnesses. This Inquiry is timely given proposals for a wider role for NICE as set out in the Cooksey Review of UK health research funding and Office of Fair Trading report into the Pharmaceutical Pricing Regulation Scheme. The Health Select Committee’s recommendations and Government response will act as a blueprint for future reforms of NICE, which must be in place before any wider role is considered.

EXECUTIVE SUMMARY

Britain’s entrepreneurial bioscience sector is a leader in Europe, and bioscience is set to continue transforming patient health through the development of new, improved and targeted therapies. To ensure patients have access to these scientific breakthroughs, and to ensure the UK continues to support innovation, and be home to a thriving pharmaceuticals and biomedicines sector, there needs to be changes to the regulations and environment which currently delay uptake of innovative medicines. With our experience of NICE, the Scottish Medicines Consortium (SMC) and All Wales Medicines Strategy Group (AWMSG), Amgen have been able to make an assessment of the issues and barriers around four key areas:

- Over-reliance on cost/QALY (Quality Adjusted Life Year) as an assessment of the cost-effectiveness of medicines compared to current standard practice, especially considering significant “real world” data often exists.
- Delays in the issuing of guidance, and continued lack of access to the medicine pending referral of a technology to NICE, or during the appraisal process.
- The independence of NICE’s Appeals Process
- Barrier to effective implementation of NICE Guidance

Our experience and perspectives on these shortcomings are detailed in our recommendations below.

1. About Amgen

Amgen is a biotechnology pioneer established in 1980. We discover, develop and deliver innovative human therapeutics which have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to

dramatically improve people's lives. In the UK we continue to be an entrepreneurial, science-driven enterprise dedicated to helping people fight serious illness and employ 500 people at our development centres in Cambridge and Uxbridge. In recent years, many of our medicines have undergone appraisal by NICE, hence we are qualified to comment on and make recommendations on NICE's process in respect of technology appraisals.

2. *NICE's evaluation process, and whether any particular groups are disadvantaged by the process*

2.1 NICE methodology relies heavily on cost/QALY (Quality Adjusted Life Year), an assessment of the cost-effectiveness of the new technology compared to current standard practice. This parameter is only one of several metrics that can be used to assess value but favours medicines that offer survival benefit rather than quality of life benefit. As a result, NICE has issued negative guidance on many medicines even though they offer substantial quality of life improvements, as opposed to mortality benefits. Furthermore, NICE appraisals do not give full consideration to wider healthcare and societal costs outside the narrow definition of immediate prescribing budgets, for instance reduction in overnight hospital stays, reduced staff time elsewhere in the patient journey, or residential care costs.

- Amgen believes a stakeholder group of Government, NICE, industry and patient groups should undertake a comprehensive review to propose more efficient methodologies for evaluating drugs that improve quality of life or more broadly those drugs for which the QALY is an inappropriate measure. We recommend the review should include an evaluation of best practices from other Health Technology Assessments (HTAs) around the world as well as comparative centres of excellence.

2.2 Amgen believe the industry can be disadvantaged because the Evidence Review Group (ERG) and NICE Appraisal Committee have excessively high expectations of the quality and quantity of clinical and health economic data available that can be generated by launch. Furthermore, when a medicine is launched into the NHS, considerable uncertainty exists regarding the cost-effectiveness of that medicine, and this data can only be gathered once the medicine is being routinely used in the NHS setting. QALY values can change over time, as more is learned about the optimum use of a medicine.

- Amgen believes the NICE Appraisal Committee needs to fairly assess what evidence they should expect in their deliberations and factor that appropriately into their decision making process.

2.3 With the increased research breakthroughs and targeted therapies, innovative biotechnology medicines will be increasingly focussed towards sub-sets of patients for whom no existing therapy exists. Given the small number of appropriate patients, many of these will have minimal budget impact if routinely prescribed in eligible patients. The NICE appraisal process requires considerable resources from manufacturers and consultees alike.

- NICE should only appraise medicines which have a significant cost burden to the NHS, and for which significant "real world" data exists. This will ensure that industry, academic institutions and the voluntary sector continue to undertake innovative research in difficult to treat diseases.

3. *The speed of publishing guidance*

3.1 There are two types of NICE "blight" operating in the NHS. The first is when NICE announce they will be reviewing a specific product. Countless examples exist of PCTs refusing to fund medicines until NICE produce guidance on the specific product. The second type of "blight" is for products not selected for appraisal. In these cases, there are many examples of PCTs refusing to fund treatments as they are not a priority compared to medicines that have been subject to NICE appraisal. The Department of Health recently re-issued Good Practice Guidance on Managing the Introduction of New Healthcare Interventions, and although this is welcome we believe there are still unacceptable barriers to prescribing and disadvantaged patients that require access to new medicines.

- Amgen believes a fundamental review is required to determine the extent of continued NICE blight, and that the Department of Health should develop policy mechanisms to ensure patients are not denied new medicines in the period NICE is evaluating a medicine or if NICE choose not to review a medicine.

3.2 With many NICE appraisals there can be protracted delays in the issuing of guidance. The duration of the NICE appraisal process has been improved by the introduction of the Single Technology Appraisal (STA) process; however the Multiple Technology Appraisal (MTA) remains lengthy and results in NICE blight. The MTA process is more suited to reviewing established technologies or topics for disinvestment.

- Amgen believes only the STA process should be used for new products being introduced into the NHS. The MTA process should be limited to reviewing products with significant "real-world" data.

4. *The appeal system*

4.1 The current appeal system means the Appeals Panel is comprised entirely of NICE personnel. It is vital that any appeals system is seen to be independent of NICE to ensure that the appeal process, is truly objective and distinct from the Institute.

- To increase the independence and credibility of the appeal process, Amgen recommends the appeal process should be separated from NICE and constituted entirely from non-NICE personnel.

5. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this).*

5.1 While there is a statutory instrument requiring the NHS to initiate funding the implementation of NICE guidance, in reality there is still extensive postcode prescribing in the NHS. It represents an inefficient use of NHS resources to have an appraisal system in place that is not fully implemented by PCTs and trusts.

- Amgen believes adherence to NICE guidance should be a fundamental part of broader NHS performance measures such as the GP contract QoF measures, and audit by the Healthcare Commission. Only by doing this can we ensure NICE guidance is fully adopted in the NHS.

SUMMARY OF RECOMMENDATIONS

Amgen believes a stakeholder group of Government, NICE, industry and patient groups should undertake a comprehensive review to propose more efficient methodologies for evaluating drugs that improve quality of life or more broadly those drugs for which the QALY is an inappropriate measure. We recommend the review should include an evaluation of best practices from other Health Technology Assessments (HTAs) around the world as well as comparative centres of excellence.

Amgen believes the NICE Appraisal Committee needs to fairly assess what evidence they should expect in their deliberations and factor that appropriately into their decision making process.

NICE should only appraise medicines which have a significant cost burden to the NHS, and for which significant “real world” data exists. This will ensure that industry, academic institutions and the voluntary sector continue to undertake innovative research in difficult to treat diseases.

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To increase the independence and credibility of the appeal process, Amgen recommends the appeal process should be separated from NICE and constituted entirely from non-NICE personnel.

Amgen believes adherence to NICE guidance should be a fundamental part of broader NHS performance measures such as the GP contract QoF measures, and audit by the Healthcare Commission. Only by doing this can we ensure NICE guidance is fully adopted in the NHS.

Amgen

March 2007

Evidence submitted by Archimedes (NICE 68)

EXECUTIVE SUMMARY

1. Although we agree in principle with the aims of NICE we have concerns with certain aspects of the existing evaluation process. Our major concerns include:

- (a) The one size fits all approach disadvantages innovative products indicated for diseases with small patient populations and where survival rates are low;
- (b) The lack of dialogue with NICE at an early stage of clinical development means that the data required to satisfy a NICE appraisal may not be available;
- (c) Expert opinion should be called upon when necessary to address technical issues which are not well understood by the appraisal committee;
- (d) The time to produce guidance should be reduced;
- (e) The criteria for evaluation of cost effectiveness have not changed.

All these points are explored further below.

ARCHIMEDES

2. Archimedes is a British pharmaceutical company, set up in 2004, to develop and bring to market new drugs for neglected conditions. The company has grown from its three founders to employ 100 people and specialises in treatments for patients with cancer and other rare diseases. To date it has invested almost £40 million through its R & D facility based in Nottingham.

3. We make reference in our submission to some of our experiences with a product from our portfolio, Gliadel, which is currently the subject of two separate NICE appraisal processes. Gliadel is one of only two treatments for patients with newly diagnosed high-grade glioma (brain tumours), a condition which affects around 2000 patients per year, and the current NICE position is that Gliadel will not be recommended for use in NHS patients with newly diagnosed high-grade glioma. This review process commenced in February 2005 and according to NICE is now set to end in Q1 2008 which has greatly restricted the use of Gliadel across the UK. We outline below our concerns on the way NICE operated to reach the decision to date and the wider ramifications for similar high cost treatments for neglected conditions.

COMMENTARY ON NICE'S EVALUATION PROCESS

One size fits all

4. NICE's technology appraisal process adopts a "one-size-fits-all" approach. While it is right that the procedure should be rigorous, and desirable that the number of alternative procedures is minimised, it is:

- (a) wasteful of resources to apply the same extensive and time-consuming process of appraisal to a drug that may cost the NHS a maximum of £1–2 million a year as is applied to a "blockbuster" treatment that might cost tens or even hundreds of millions of pounds;
- (b) counterintuitive to apply the same appraisal methodology to innovative products indicated for rare diseases with small patient numbers where clinical practicalities restrict the quantity and type of evaluable data;
- (c) unreasonable to expect that innovative medicines in small therapeutic areas should satisfy the same cost-effectiveness threshold as those indicated to treat much larger numbers of patients;
- (d) the current NICE processes make no allowance for the above factors. We suggest that below a certain threshold (perhaps 0.1% of the total budget—currently about £11 million), a quicker and more straightforward appraisal mechanism should be developed;
- (e) cost effective thresholds were set several years ago and have not been adjusted for inflation or innovation.

Lack of Dialogue

5. The current process allows no dialogue between NICE and the manufacturer. The products to be reviewed by NICE are often identified during development and a NICE review announced. If companies were able to meet with NICE at early stage in the clinical development process to define the scope of an appraisal they could ensure that the data which NICE needs is built into the on-going lengthy and expensive clinical studies. Equivalent organisations in other European healthcare systems do consult with manufacturers during their appraisal processes in order to facilitate the availability of data with which to support reimbursement. Additionally, there is currently no opportunity to discuss key issues that arise throughout the process and in particular as a result of appraisal committee meetings. The only way in which a consultee can respond through the existing process is via a written submission and without the benefit of a response other than through the appraisal documents.

Expert Advice

6. NICE does not always appear to ensure that it is availing itself of the appropriate expert advice. For example, at the meeting of the Appraisal Committee held on 22 November 2006 to consider NICE's preliminary view on Gliadel as one of two brain tumour therapies, no experts on brain tumours were invited to attend. This occurred despite clear indications from us and numerous clinical experts in our submissions prior to this that a major point in the appraisal of our product hinged upon a technical point requiring specialist knowledge.

Speed of Publishing Guidance

7. The length of time which NICE takes to appraise new treatments is a serious handicap for companies with high value innovative products. Often, such "biotech" products are in therapeutic areas which are not usually being researched by larger pharmaceutical companies and represent exciting new medicines. The assessment of Gliadel has now been running for over 2 years and is scheduled to run for at least another 12

months; a lack of a decision has prevented use of the product in a number of hospitals over this time period. Only 125 patients have been treated with Gliadel over two years in England and Wales, whereas for instance in France 4 times this number of patients have been treated over the same period.

CONCLUSIONS AND IMPLICATIONS

8. The UK biotech industry tends to focus on developing innovative products for conditions with high unmet medical need and where patient populations are comparatively small. Very often efforts are concentrated on one product which has been subject to many years of research and investment. NICE's current process increases the risk that such products will not be made available to NHS patients when they have already past all regulatory approval hurdles. This can also have a significant effect on the viability of UK biotech companies and the decision of whether to commercialise such products in the UK.

9. The NICE process could therefore be improved by:

- Adapting the criteria for affordability to reflect differences between diseases and options available for patients;
- Allowing the industry to discuss product technology appraisals with NICE at an earlier stage in order that the data required for the appraisal is generated as part of the clinical development programme;
- Discussing the technology appraisal at regular intervals to avoid misunderstandings and mistakes such as the use of experts;
- Updating the parameters used to assess cost effectiveness including financial thresholds.

Archimedes Pharma Ltd

March 2007

Evidence submitted by the Arthritis and Musculoskeletal Alliance (NICE 97)

INTRODUCTION

1. The Arthritis and Musculoskeletal Alliance (ARMA) is an umbrella body bringing together 33 national organisations working in the field of arthritis and other musculoskeletal conditions. This includes service user groups, professional associations and research bodies. It is a registered charity.

2. ARMA welcomes the opportunity to respond to the Health Select Committee's inquiry. Although drawing its membership from a number of fields, ARMA unites them around a common purpose of improving quality of life for people with arthritis and other musculoskeletal conditions.

3. In this submission ARMA will comment on the following questions:

- Why NICE's decisions are increasingly being challenged.
- NICE's evaluation process and whether any particular groups are disadvantaged by the process.
- The implementation of NICE guidance, both technology appraisals and clinical guidelines.

Why NICE's Decisions are Increasingly Being Challenged

4. ARMA does not wish to present a comprehensive list of reasons for NICE's decisions being challenged; however there is one particular area of concern for ARMA.

5. NICE health economics focus on the costs to the NHS without sufficient regard for the wider societal impact of recommendations for the use of certain treatments. Not having access to a particular drug might mean that someone is unable to work, but no consideration is given to the economic impact of their having to claim incapacity benefit and not contributing income tax.

6. Patient representative organisations come into contact on a daily basis with people who would describe their lives as being of poorer quality as a consequence of the scenario described above, hence more challenges and questions about the effectiveness of NICE. Whilst the NICE regime might not be able to share patient representatives' sense of frustration and injustice about the plight of such people, it should at the very least take into account the impact on the public purse of these circumstances.

NICE's Evaluation Process and Whether any Particular Groups are Disadvantaged by the Process

7. Organisations such as ARMA do not currently have sufficient resources to participate in the volume of appraisals relating to the group of conditions in which it is interested. ARMA has an annual income of approximately £140,000 and employs three staff. Much of its work on NICE appraisals is led by volunteers.

8. Small organisations like ARMA often have staff who are generalists across a range of work areas. Such organisations, especially smaller patient representative bodies, are therefore unlikely to have any staff that have sufficient depth of specialist knowledge of disciplines such as health economics to have the capacity to engage effectively in NICE evaluation processes.

The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines

9. ARMA has evidence from three studies conducted in 2003, 2005 and 2006 that demonstrate that there is significant non-implementation of NICE guidance.

10. In March 2002, NICE approved the use of TNF-a inhibitors for people with severe rheumatoid arthritis (RA) who had failed existing treatments.

11. Since then, three studies conducted by Arthritis and Musculoskeletal Alliance (ARMA) and the British Society for Rheumatology (BSR) have demonstrated that there are persistent problems in obtaining access to this treatment for a significant number of people who meet the strict eligibility criteria and would benefit from it.

12. This is despite the Department of Health issuing directions in December 2001 to place statutory obligations on the NHS to provide appropriate funding for recommended treatments within three months of NICE guidance being issued.

13. The third and most recent study was conducted in Spring 2006, which found that:

13.1 Four years on from NICE's original decision, people with rheumatoid arthritis were still being affected by post-code prescribing.

13.2 Twenty percent of the 81 rheumatology units who responded stated that they were unable to prescribe TNF-a inhibitors to every rheumatoid arthritis patient they identified as being eligible in accordance with NICE guidance. The larger surveys in 2003 and 2005 demonstrated that around one-third of consultants were unable to prescribe the treatment in both those years as well.

13.3 In those units that were unable to prescribe TNF-a inhibitors to every RA patient they identified as being eligible, waiting lists ranged from 10 to 126 patients.

13.4 Fifteen% of units stated that a cap had been imposed on the number of RA patients for whom they could prescribe TNF-a inhibitors. In some units funding was only available for 10 patients. In units where there was no cap; as many as 500 patients were being prescribed TNF-a inhibitors.

13.5 The top three barriers to prescribing TNF-a inhibitors were cited as:

- PCT has overspent and will not release funding—28%;
- PCT has not released funding yet—21%; and
- Trust has allocated funding for TNF-a inhibitors, but is lacking nursing support to deliver treatment—17%.

14. It was easy to generate these data and give voice to problems in non-implementation. What has been more difficult has been finding an effective authority that will do something about it. Ministerial interest came with the caveat that it was ultimately a local matter and it is beyond NICE's power to deal with non-implementation.

15. ARMA would welcome greater clarity and government interest in dealing with significant matters of non-implementation, not just for organisations, but for individual patients who may believe that they are being treated contrary to NICE guidance.

Bill Freeman

Director, The Arthritis and Musculoskeletal Alliance

March 2007

Evidence submitted by the Association of British Healthcare Industries (NICE 85)

The Association of British Healthcare Industries (ABHI) has always sought to be a supportive partner to NICE and these comments are intended to be constructive in the manner of open and transparent feedback, rather than negative criticism.

Why NICE's Decisions are Increasingly Being Challenged

The perceived increase in challenges to NICE decisions may have a direct correlation to the volume of guidance currently being produced by NICE. NICE has increased the volume of guidance published with the introduction of the STA process. There is now a reduction in the time taken to complete an appraisal and an increase in the quantity completed. One could argue that there is not sufficient time available during the STA process for an adequate consultation so some stakeholders may feel that their issues are not being addressed during the process and would therefore be minded to challenge the final decision.

Whether Public Confidence in the Institute is Waning, and if so Why

The ABHI is not able to confirm this one way or another but would speculate that the publicity surrounding each challenge may have a negative effect on the public perception of NICE as an organisation especially when there are headlines indicating a particular patient group is disadvantaged by the restriction of a technology.

NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process

As indicated above under the newly introduced STA process, the time constraint does not allow sufficient opportunity for stakeholders to adequately address issues that may develop during the process.

We feel that in general, manufacturers are at a disadvantage because of their absence at appraisal committee meetings. The inability of manufacturers to address issues that may have come up during review is a major flaw in the system.

Whilst it is recognised that NICE appraisal managers would not want to be constantly bombarded by parties with particular interests it would be beneficial to have an ongoing dialogue throughout an appraisal rather than just at the beginning of the process. Therefore the "consultee workshop" should incorporate the ongoing dialogue.

The Speed of Publishing Guidance

NICE has made many moves to reduce the timing for the development and publication of its guidances. However under the STA process, stakeholder involvement and consultation has been reduced which has the potential to lead to less robust decisions.

The Appeal System

Under the STA, the opportunity for stakeholders to comment on the academic group report has been removed. We would strongly suggest some form of interaction following this report will give stakeholders the confidence that they have some form of recourse.

Comparison with the Work of the Scottish Intercollegiate Guidelines Network (SIGN)

Our knowledge of the work undertaken by SIGN is limited. We do know that SIGN will look at a NICE appraisal to see how this might fit within the Scottish environment. This process is usually shorter than the NICE process.

The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines (Which Guidance is Acted on, Which is Not and the Reasons for This)

The value of the appraisal process would be enhanced if there were more robust methods for ensuring that guidelines were subsequently adhered to post-publication. We believe that specific recommendations and targets would help.

We would also like to make mention of the budget implications following a technology appraisal. Technologies are allocated mandatory funding. However when a technology appraisal is incorporated into a guideline this reference to mandatory funding is removed and we believe that there should be an ongoing obligation to monitor the funding of this technology especially in cases where there is a risk of the guideline not being implemented effectively.

John Wilkinson

Director General, Association of British Healthcare Industries

March 2007

Evidence submitted by the Association of the British Pharmaceutical Industry (NICE 72)

EXECUTIVE SUMMARY

- The ABPI supports the objectives set out for NICE at its inception. It has built up some core strengths over the years that we value and would not wish to lose: its focus on clinical excellence in public health priority areas; the breadth and coherence of its work programme; inclusion in its remit of support for diffusion of innovation; independence from pricing negotiations and decisions; its systematic engagement of stakeholders, including industry representation on many of its committees and regular dialogue with the ABPI; its respect for commercial-in-confidence information; and the ability to appeal its decisions.
- However, there are shortfalls in the way NICE operates that have compromised public confidence, and which need to be addressed. This need would become more acute were any expansion in its reach to be considered, eg as envisaged in the Cooksey Review and implementation of the OFT's recommendations. We believe these shortfalls are leading to a situation where patients in England and Wales may be permanently disadvantaged in their ability to benefit from major and incremental medical innovation, available in other countries, because the bar to positive recommendation is becoming unrealistically high or there is pressure to take decisions on the basis of very limited clinical effectiveness or cost-effectiveness data.
- This submission outlines these concerns in particular:
 - Over-reliance on cost/QALY, a mathematical prediction of potential future benefit, in making (rather than informing) decisions
 - Expectations of certainty in decision-making that cannot be achieved, particularly early in a product's lifecycle
 - Issues of quality and consistency in the work commissioned from Assessment Groups/Evidence Review Groups (AGs/ERGs), including transparency issues
 - An unnecessarily adversarial approach to industry within some AGs/ERGs, which can colour assessment and appraisal
- These issues result in an increasing trend to resort to an appeal process that is itself seriously flawed, and which has resulted in the past two years in no significant changes to NICE guidance.
- No doubt there are frustrations for all in the relationship between NICE, AGs/ERGs and industry. The ABPI wishes to constructively address these through engagement with NICE and the ERGs from the outset of appraisal.
- NICE has devoted significant resource to helping the NHS improve implementation of its guidance, which after eight years since NICE was created remains slow and patchy. Reasons for this include poor local financial planning, clinical resistance, and little in the way of sanctions if guidance is not implemented. The major levers in improving implementation are joined-up commissioning and financial incentives, removing prolonged and duplicative local evaluation processes, and more robust HCC assessment. The latter focuses on process rather than outcome, and implementation is not high in the HCC's priorities.

RECOMMENDATIONS

- More evenly-balanced NICE decision-making to recognise the imprecision in cost/QALY calculations and to encompass broader factors than cost/QALY. Final guidance to contain a clear explanation of how these factors were taken into account
- NICE to include broader parameters and costs when calculating value: eg societal benefits and costs, including carer and return-to-work factors; social security costs
- Industry to be invited to participate in Appraisal Committee meetings to answer questions and provide clarification on areas of uncertainty
- An independent review of the quality of Assessment/ERG Reports with recommendations including:
 - accountability for quality being brought under NICE;
 - production (for STAs) of a detailed methods manual setting out standards, expectations, and approaches;
 - introduction of more robust quality control systems
- A joint committee of industry, NICE and AGs/ERGs to contribute to the above review and to identify and address quality and process issues on an ongoing basis
- A more constructive, and less adversarial, approach to be taken to appraisal, including dialogue, from the outset of each appraisal, between manufacturers, NICE and AGs/ERGs on methods, data quality and sources used

- A root-and-branch review of the appeal process, which examines the grounds for appeal, its independence and its operation
- A review of NICE guidance implementation with recommendations that result in tangible action, eg greater HCC attention; “joined-up” commissioning and financial incentives; NICE-approved medicines automatically included in local formularies; mandatory funding for medicines, where reviews of technology appraisals have been moved into clinical guidelines and where positive recommendation remains

INTRODUCTION

1. The ABPI welcomes this Inquiry into NICE. Whilst we support the objectives set for NICE when it was created and recognise much good practice, we share with other stakeholders concerns about aspects of its methods and decision-making—recently made even more acute by recommendations in the reports by the OFT on the PPRS and by Sir David Cooksey on research funding. Both envisage broader roles for NICE that could have a major impact on the future health of the nation and the UK pharmaceutical industry.

NICE DECISION MAKING

Use of Cost/QALY

2. NICE decisions have become overly reliant on one parameter: the cost/QALY, an assessment of the incremental cost-effectiveness of a new technology compared to that of standard practice. Although the ABPI recognises the usefulness of this approach as a means of comparing the cost-effectiveness of a broad range of technologies, it is generally derived from a complex mathematical prediction of potential future benefits and costs, and therefore should be used as one important factor to inform decisions rather than make them, in line with Principle 4 of NICE’s social value judgements.³² More balance should be struck between cost/QALY and other important factors (listed in Appendix 1),³³ such as clinical need.

3. There are a number of issues in the application of QALYs:

- Cost-effectiveness assessment is an imprecise and emerging science and is usually reliant on complex economic modelling, incorporating data and assumptions from a wide range of sources. Modelling results in wide-ranging estimates of cost-effectiveness depending on the methodology and assumptions used. For example in the appraisal of Exubera@, cost/QALY estimates presented to the committee ranged from £24,184 to £1,260,325 and for Alimta@ in Lung Cancer from £9,010—£1.8 million.
- The QALY is based on the measurement of two key elements of benefit: quantity and quality of life. Although not without challenges, given time, quantity-of-life estimates are relatively straightforward; but measurement of quality of life is much more difficult, subjective and approximate. The wide range of methodological approaches and definitions results in significant uncertainty in the accuracy of absolute values or reproducibility between different appraisals. Also, the generic (rather than disease-specific) approach required by NICE (as illustrated by its preferred questionnaire, EQ5D (Appendix 2))³⁴ is relatively insensitive to incremental changes in quality of life and does not fully reflect the range of benefits that are important to patients.
- Other aspects of value may not be fully reflected in the QALY estimate, eg the impact of an improved safety profile, the benefits of an oral product that may reduce pressure on hard-pressed hospital services, or the advantages of improvements that enhance compliance.

4. In practice, these limitations mean that it is generally more difficult for medicines which deliver quality rather than quantity of life to demonstrate a large enough incremental benefit to be deemed cost-effective, eg in treatments at the end of life, for the elderly, and for long-term conditions, where apparently small quality-of-life benefits can make a significant difference to patients.

5. In some cases, it may never be possible to demonstrate cost-effectiveness at a price that secures a return on investment, particularly in areas that have suffered from historically low levels of innovation and where comparators used are old, generic, and very inexpensive. In the recent Velcade@ appraisal, the main comparator cost £74/patient/year. In osteoporosis, new provisional guidance compares innovative treatments with generics. This approach means that innovative treatments, available in other European countries, may never be available to patients in England and Wales. Comparing medicines with novel mechanisms and/or better side-effect profiles to the cheapest available therapy in a disease area would effectively halt further innovation. Were such an approach to have been followed historically, few of today’s “best-in-class” medicines would be available.

³² Principle 4: In the economic evaluation of particular interventions, cost-utility analysis is necessary but should not be the sole basis for decisions on cost-effectiveness. NICE states its position “that while it endorses the use of cost-utility analysis in the economic evaluation of particular interventions, such information is a necessary, but not sufficient, basis for decision-making”. Social Value Judgements, Principles for the Development of NICE Guidance, December 2005.

³³ Not Printed Here

³⁴ Not Printed Here

6. The perspective of cost-effectiveness taken by NICE is limited to the NHS and Personal Social Services; this excludes important benefits such as the impact on carers or enabling people to return to work and contribute to society. In Sweden, for example, LIF economic evaluation guidelines state “... *all relevant costs and revenues for treatment and ill health, irrespective of the payee (county council, local authority, state, patient, relation) should be considered.*” The current approach is inappropriate in diseases such as Ankylosing Spondylitis, which can strike patients in their 30s, lead to progressive disability, and have major effects on people’s ability to work, resulting in incapacity benefit, sick leave and loss of employment.

7. Patients with rare diseases treated with orphan medicines³⁵ are disadvantaged by the NICE process. Orphan medicines appear expensive on a “per-treated-patient” basis because development costs are relatively high and an adequate return is necessary to sustain research.

8. As of January 2006, NICE had appraised 16 EMEA-designated orphan medicines, of which four (25%) were rejected, nine (56%) recommended for restricted use, and three (19%) recommended for general use. This compares to 6% rejected, 48% restricted-use, and 46% recommended-for-general-use rates in the 116 non-orphan medicines appraised over the period, a statistically significant difference.³⁶

9. The combination of limited data at launch and relatively high per-patient prices means it is challenging for orphan medicines to meet NICE cost/QALY criteria. The current methodology requires re-evaluation, with distinct decision rules focusing more on unmet need, innovation, clinical effectiveness and budget impact, and less on cost/QALY.

CONSISTENCY AND QUALITY OF ASSESSMENT

10. In order to produce credible and defensible guidance NICE requires top-quality analysis of the evidence submitted to it. This is synthesised in the assessment report, for MTAs a review of clinical and cost effectiveness based upon a systematic review of the literature, a review of the manufacturer/sponsor submissions, and frequently a de-novo assessment of cost-effectiveness, involving the generation of an economic model; and for STAs in the ERG Report, which is a critique of the manufacturer’s submission. NICE obtains these reports from a number of AGs/ERGs, commissioned via the NHS R&D HTA Programme. The assessment reports are the property of the AGs/ERGs, and their quality is the responsibility of the authors.

11. The approaches taken, particularly by ERGs, are inconsistent—most likely because there is no comprehensive STA “methods manual” to ensure consistency of standards and methods, and ERGs wish to exercise academic freedom. Concerns include the adequacy with which assessment reports address the scope of appraisals; the appropriateness of the structure and inputs to economic models; and the extent to which comments from stakeholders are addressed.

12. A key issue is how the Groups handle uncertainty, which is greatest early in a product’s lifecycle. Given that effectiveness and cost-effectiveness data are derived from highly structured clinical trials and economic models based on a wide range of assumptions and inputs, it is inevitable that different conclusions will be reached by different assessors. It is how these uncertainties are managed and the transparency with which they are addressed that are important. Rather than seeking to constructively outline and address them, some centres present them as fatal flaws in the manufacturer’s case.

13. Quality control is another important issue. Addenda correcting errors in original assessment reports have been required for six (30%) of the 20 MTAs published since the beginning of 2006. These addenda have corrected errors in the modelling of costs and utilities; amended (increased) the value placed on clinical effectiveness, and included additional benefits not originally modelled. NICE or its Decision Support Unit were required to undertake further analysis and/or address deficiencies in the assessment report in half of these cases.

14. One simple, but essential, quality control step is missing in the STA process. The ERGs prepare a report which is considered by the Appraisal Committee to formulate draft guidance. No opportunity is provided to stakeholders to comment on its technical accuracy before the Appraisal Committee uses it to make recommendations. Apart from being inconsistent with the MTA process, the opportunity for manufacturers to correct inaccuracies in an STA is particularly important, as the ERG report is based solely on the company’s submission. Factual errors are translated into draft and final guidance leaving appeal as the only route to make corrections. NICE has resisted this step on the grounds that it leads to unequal treatment of stakeholders.

15. The consequence of poor quality assessment reports is a delay in issuing appropriate guidance at best and the production of non-transparent and possibly incorrect guidance at worst. Without doubt, more appeals result.

³⁵ The EMEA defines orphan medicines as those to treat rare diseases which are serious, life-threatening or chronically debilitating, with prevalence < 5 per 10,000 population. NICE defines “ultra-orphan” diseases as those affecting up to 1000 people in the UK.

³⁶ Working paper by the Office of Health Economics: “HTA for orphan drugs: A review of the Issues and of NICE and SMC Decisions (to be made available in April 2007)

16. The situation is exacerbated by the inability to challenge the methods and models developed by the AGs/ERGs. Whilst the AGs/ERGs have access to the full working models produced by manufacturers, manufacturers sometimes do not have access to the models created by the AGs/ERGs, the results from which form the primary evidence upon which the Appraisal Committee decides on cost-effectiveness and patient access. If the model is made available, it may be “locked”, which significantly hinders the ability to understand the basic assumptions upon which the cost-effectiveness calculation is made.

17. The ABPI believes that, underlying these issues, there is an adversarial approach to industry in appraisal, which is not helpful. The ABPI would prefer a more collaborative approach, with a constructive dialogue between the AG/ERG, NICE and the company from the outset of appraisal, allowing discussion and debate on methods, data quality and sources used. This would reduce inaccuracies, address unnecessary misunderstandings, speed up the process, and reduce the number of appeals.

WORKINGS OF THE APPRAISAL COMMITTEE

18. Currently clinicians and representatives of patient organisations are invited to attend Appraisal Committee meetings to give their views and respond to questions. This invitation is not extended to manufacturers, who have spent years amassing the evidence upon which NICE guidance is based. This is inherently inequitable, can lead to misunderstandings and, in some cases, unnecessary re-work and appeals. In STAs, where appraisal is based on the manufacturer’s submission, a level playing field should be adopted so manufacturers can help clarify areas of uncertainty and answer questions.

19. NICE has consistently rejected the industry view (particularly for STAs) that the Appraisal Committee should give proper consideration to the lack of maturity of the evidence for products early in their lifecycle. Unreasonable expectations of clinical and economic certainty lead to “all-or-nothing”, “yes-no” decisions. This is dangerous for two reasons: 1) patients are being denied access to important treatment advances; and 2) denying access so early in the life of the product means that learning and incremental innovation through normal clinical experience will not happen.

20. In the case of MTAs, the assumption in “class” appraisals is that all products are essentially similar. This is done to enable cost comparison, but fails to take into account that some products may have more robust evidence than others. This opposes NICE’s principle of evidence-based assessment and can lead to patients being denied access to a technology which has the best evidence, merely because it is more expensive. The approach is anti-innovative because the innovator entrant demonstrates clinical and cost-effectiveness only to have their evidence translated across the class, negating their advantage on price alone.

APPEAL PROCESS

21. The deficiencies described above are leading to an increasing number of costly and time-consuming appeals, which further delay patients’ access to medicines.

22. Of the 279 appeal points heard since NICE appeal hearings became public, not one has resulted in any significant change to guidance.³⁷ One reason for this is that the grounds for appeal are based on procedure rather than a difference of scientific opinion. Ground 2 (perversity) allows an appeal where the conclusion in the FAD is so unarguably wrong as to be “perverse”, which is a very high hurdle. NICE procedures explain that it is theoretically possible for two Appraisal Committees to reach different conclusions based on the same facts, without either being perverse. There is no scope, therefore, to challenge where a conclusion appears to be incorrect, but is not frankly perverse.

23. The process is not independent, with NICE deciding which grounds for appeal can be heard, constituting the Appeal Panel (which includes at least two NICE directors including the chair), and administering the process. NICE is therefore sitting as judge and jury over its own guidance. Appendix 3 sets out these concerns and others relating to how appeals are conducted. A root-and-branch review of the process is required.

IMPLEMENTATION OF NICE GUIDANCE

24. NHS implementation of NICE guidance remains slow and patchy, in spite of considerable efforts by the NICE Implementation Team to improving it, and the inclusion of implementation in NHS core and developmental standards, against which local NHS organisations are assessed by the HCC. A number of factors contribute to this, the most important being poor NHS financial management, clinical resistance, and lack of sanctions against poor implementation.

25. Two studies commissioned by NICE looked at financial planning,³⁸ and found inappropriate use of allocated funding, lack of horizon scanning for future NICE guidance, and poor planning. Organisations perceived that NICE guidance was unaffordable, but where robust implementation systems were in place funding was found not to be the biggest barrier.

³⁷ ABPI can supply a detailed analysis of appeal decisions from the period October 2004—November 2006 (since hearings were held in public) on request.

³⁸ Audit Commission, 2005, *Managing the financial implications of NICE guidance*; Howard S and Harrison L, 2005, *NICE Guidance Implementation Tracking, Data Sources, Methodology & Results*.

26. In contrast to implementation of technology appraisals, there is very little understanding of how clinical guidelines are implemented. Research is needed.

27. Implementation of guidance is not an HCC priority in its Annual Health Check. Assessment takes the form of ensuring that processes are in place rather than measuring tangible evidence of implementation.

28. There is little point in investing in NICE, and the resources required to meet its requirements, if its guidance is not implemented. The major levers to improve implementation are more rigorous HCC measurement and inspection systems that provide a clear picture of both the quality and extent of implementation, and “joined-up” commissioning and financial incentives, eg inclusion of an implementation component in the QOF, automatic inclusion of NICE approved medicines on local formularies.

REVIEWS OF TECHNOLOGY APPRAISALS (TAs)

29. TAs are accompanied by mandatory funding within three months of guidance being published. There is no such mandatory funding for Clinical Guidelines. There has been a recent trend for reviews of TAs to be carried out “within the context of a clinical guideline”, with express information from NICE that mandatory funding will be removed, even if the guideline continues to recommend use. An example of this policy is given in Appendix 5.³⁹

30. The reason given by NICE is that the average length of time for a TA to be reviewed (about three years) should be sufficient for the NHS to embed it into clinical practice. However, as we discuss above, implementation is patchy and slow, and three years are simply not sufficient for use of a (new) intervention to have become routine. We call for continued mandatory funding for a medicine whose use remains recommended when reviewed as part of a guideline.

David Fisher

ABPI

March 2007

APPENDIX 3

DEFICIENCIES IN THE CURRENT APPEAL PROCEDURE

BEFORE THE APPEAL HEARING

Lack of Transparency

A recurrent difficulty in relation to NICE appraisals is the lack of proper reasoning to explain the conclusions reached in the FAD. It is therefore difficult for consultees to assess the content of the FAD and whether the conclusions reached may be characterised as perverse. The result of this is that:

- (a) where consultees seek to argue a point as lack of transparency, NICE will frequently rule that, by seeking to engage with the issue, consultees have demonstrated an understanding of the matters raised and the question should therefore be considered under perversity (even though insufficient reasoning is provided to enable a consultee fully to understand the basis for the Appraisal Committee’s conclusion and therefore to prepare a perversity argument);
- (b) where an argument is presented under perversity, a further explanation is then provided by the Appraisal Committee verbally at the Appeal Hearing, often in a way that cannot be anticipated, therefore prejudicing the ability of the Appellant to respond.

The Initial Scrutiny of Appeals

The initial scrutiny of appeals by the Chairman of the Appeals Committee is intended to confirm that an appeal (a) falls under one or more of the permitted grounds; and (b) whether sufficient detail is provided to demonstrate an arguable case. In practice, however, the initial scrutiny often appears to go beyond the requirement that an arguable case be demonstrated and to constitute an assessment of the merits of the appeal.

This is particularly the case in relation to points argued as a lack of transparency and brought under Ground 1, where the Chairman of the Appeal Committee will frequently form a view of the adequacy of the reasoning provided in the FAD and conclude that the point should be brought under Ground 2. In our view, the adequacy of the reasoning provided in the FAD should not be determined at the admissibility stage.

³⁹ Not Printed Here

The rulings made at the initial scrutiny stage with respect to admissibility are not always consistent, suggesting that greater guidance needs to be provided by the Institute in relation to the admissibility of appeals.

The Involvement of the Chairman of the Appeal Committee

The Chairman of the Appeal Committee undertakes the initial scrutiny of appeals, to assess admissibility. As indicated above, this appears to involve a preliminary assessment of the substantive merits of the appeal and further correspondence about whether or not the Appellant's points are admissible. In these circumstances, we believe it is unfair for the Chairman of the Appeal Panel to participate in the appeal hearing as a member of the Panel.

THE APPEAL HEARING

Constitution of the Appeal Panel

Concern has been expressed regarding the constitution of Appeal Panels and, in particular, the fact that two or three members of the five person Appeal Panel (including the Chairman of the Panel) will be members of NICE's own Board. (It should be noted that the 2004 procedures introduced a change in this respect. The previous procedures, issued in 2001, provided that three members of the five person Panel would, in all cases, be members of NICE's Board. The 2004 procedures however raise the possibility that one of those three persons may instead be an NHS representative.)

In spite of the fact that the majority of appeal points relate to interpretation of cost-effectiveness evidence, there is no Health Economist on the Panel, suggesting a deficiency in expertise in addressing the complex points raised.

Lack of any Substantive Review of the Recommendations

NICE appeal procedures do not allow for any review of the scientific merits of its recommendations. While appeals are permitted under the three identified grounds these do not include a challenge based simply on a difference of scientific opinion.

Ground 2 (Perversity) allows an appeal to be brought where a conclusion expressed in the FAD is so unarguably wrong as to be perverse, but this is a very high hurdle. NICE procedures explain that the Appeal Panel will not substitute its own view for that of the Appraisal Committee and that it is theoretically possible for two Appraisal Committees to reach different conclusions based on the same facts, without either being perverse.

The effect of this limitation is that there is no possibility within NICE procedures for any challenge to be brought where a conclusion appears to be incorrect, but is not frankly perverse. This unsatisfactory situation is exacerbated in the following circumstances:

- (a) In some cases, guidance is changed between the ACD and FAD and, in those circumstances, there may be no possibility to submit a challenge to the substantive scientific conclusions that are expressed for the first time in the FAD;
- (b) The position described in (a) above is particularly acute in circumstances where new evidence is obtained by the Appraisal Committee and disclosed to consultees for the first time within the FAD (eg as occurred in the appraisals of Alzheimer's Disease Treatments and Erythropoietins for the Treatment of Cancer Treatment Induced Anaemia). In these circumstances, a consultee has no opportunity to challenge the new evidence or, in view of the fact that new evidence may not be introduced at the appeal stage, to introduce its own new material to counter it;
- (c) The fact that a challenge to the substantive conclusions expressed in the FAD is not possible at appeal is particularly unfair to manufacturers who, in contrast to other consultees, have had no opportunity to attend earlier meetings with the Appraisal Committee to ensure that their case is fairly and accurately represented;
- (d) The absence of any review of the substantive conclusions expressed in the FAD is not corrected by the fact that Judicial Review is available, because the Courts will also not review the substantive merits of the Institute's decision, but only the procedure by which it was reached.

Some of these concerns might be ameliorated if the appraisal process was more transparent and if manufacturers were permitted a greater opportunity to participate in the appraisal by attending Appraisal Committee meetings. In addition, the practice of disclosing new evidence together with the FAD should be discontinued and there should be a requirement that in all cases where there is significant change following consultation on an ACD, a second ACD should be issued for consideration rather than a FAD.

Approach to Issues of Transparency

In many cases, where an Appellant raises a point of appeal based on lack of transparency, the Appeal Panel will then give the Appraisal Committee an opportunity to explain its reasoning. The reasons provided by the Appraisal Committee at the hearing are often wholly new and have not been addressed at any previous part of the appraisal. When these reasons are provided for the first time at the appeal hearing, the Appeal Panel may accept them as providing justification for the conclusions reached, without apparently considering that the mere fact that further explanation was necessary supports an Appellant's appeal that the FAD, as drafted, lacked transparency. It is self-evident that the Appellant is unable to give a fully considered response to reasoning provided for the first time by the Appraisal Committee at an appeal hearing.

Way in which the Appeal Hearing is Conducted

The way in which appeal hearings are conducted is variable. While Appellants are permitted 10 minutes at the commencement of the hearing in which to make a short oral presentation, whether or not Appellants are then permitted to introduce each point of appeal varies. Appellants should be permitted to introduce each point of appeal, especially where the scientific arguments may be complex; without such an explanation the questioning from the Appeal Panel may not address the point raised by the Appellant.

In addition, it is a standard approach at appeal hearings that, where more than one Appellant is present, each Appellant may respond to the questioning, only when its particular point of appeal is under consideration. In circumstances where several Appellants may raise similar points of appeal, this may mean that an Appellant is prevented from engaging with issues relevant to its own appeal. The issue is highlighted by the circumstances of the Alzheimer's Disease Treatments Appeal where issues relevant to the clinical trial data of one manufacturer were raised by one of the professional groups. In that case, the manufacturer concerned was prevented from responding or commenting on their own clinical trial data because the Appeal Panel was not, at that time, considering their appeal.

Similarly, in some cases, particularly where there have been several Appellants present at an appeal hearing, the Panel has not given adequate time for all the issues to be adequately explored. There is no reason why an appeal hearing should be rushed and the Institute should be required to set aside adequate time so that each appeal point may be properly considered.

Overall, we believe that NICE should adopt a more flexible approach towards the hearing of appeals, with a willingness to hear submissions from other Appellants in response to points of appeal, in the format that is used for the Hearing and in the time permitted for considering the issues raised.

AFTER THE APPEAL HEARING

The fact that, following an Appeal, the same Appraisal Committee is asked to Review the Appraisal

Following a successful appeal, an appraisal will be returned to the Appraisal Committee for further consideration. However, the Appraisal Committee asked to perform this task is the same as the one that previously produced the unfavourable FAD, raising the possibility of lack of impartiality.

Timing between communication of Appeal Decision and publication of Guidance

Irrespective of whether an Appeal is successful or unsuccessful, the decision is provided to Appellants only two days prior to publication. This allows little opportunity for preparation of communication materials by companies. Furthermore, if an appeal is unsuccessful, the Appeal Decision will be published together with Guidance to the NHS and the two day period allows little opportunity for consideration of any legal challenge, including injunctive proceedings, prior to publication. We believe the two day period could be increased without detriment to the Institute.

The Guidance itself is not issued to consultees prior to publication

Following an appeal hearing, minor changes to the FAD may be effected by the Guidance Executive, without the appraisal returning to the Appraisal Committee, as a result of the decision of the Appeal Panel or on the Guidance Executive's own initiative. However, irrespective of such changes, the Guidance itself is not provided to consultees prior to publication. This means that changes to the FAD, made by the Guidance Executive, will be published with no advance notice to companies and no opportunity for challenge—even if they may not reflect the decision of the Appeal Panel or be otherwise controversial.

We believe there is no reason why a copy of the Guidance should not be issued to consultees together with the Appeal Panel decision for consideration in advance of publication.

The role of the Guidance Executive is poorly defined

NICE procedures merely state that the Guidance Executive will review Guidance before it is issued. There is no indication as to precisely the measures that the Guidance Executive may properly take and NICE's website includes no procedures for this body. We believe that NICE should be required to specify in more detail the purpose of the Guidance Executive review and the modifications that may be authorised by this body.

Evidence submitted by AstraZeneca (NICE 33)

SUMMARY OF KEY POINTS AND RECOMMENDATIONS

- AstraZeneca supports the objectives of NICE. There are core aspects of NICE that are fundamental to its working which should not be lost. For example, the commitment to raising standards of healthcare; the focus on areas of government health priority; the engagement with stakeholders; the overall transparency of process; the respect for commercial-in-confidence information, and; the ability to appeal decisions.
- However, we believe there are areas for improvement in the way that NICE operates. These areas have undermined private and public confidence in NICE and must be addressed before any expansion in the role and remit of NICE (such as that proposed by Cooksey/recent OFT report) is to be countenanced.
- This submission highlights the following shortcomings:
 - Over-reliance on cost per QALY as the tool for *making* rather than *informing* decisions.
 - Expectations of certainty in decision-making that cannot be achieved, particularly early in a product's lifecycle.
 - Quality and consistency in the work commissioned from Evidence Review Groups (ERGs), including important transparency issues.
- These shortcomings underlie an increasing trend for companies to resort to an appeal process that is itself seriously flawed, and which has resulted in the past two years in no significant changes to any NICE guidance.
- We believe these shortcomings are leading to a situation where English and Welsh patients may be permanently disadvantaged in their ability to benefit from absolute and incremental medical innovation, available as standard care in other countries, because the bar to positive recommendation is becoming unrealistically high.
- NICE has recently started helping the NHS to implement its guidance. Many reports have indicated that implementation remains inconsistent and patchy within the NHS even after these focussed attempts. Reasons for inconsistent implementation include poor local financial planning, clinical resistance and ineffective sanctions.

WHY NICE'S DECISIONS ARE INCREASINGLY BEING CHALLENGED

NICE Decision-Making—Cost per QALY

2. AstraZeneca adds its support to the ABPI view that over-reliance on the cost per QALY within decision-making within NICE is detrimental to the quality of NICE decision-making overall. Whilst the use of cost per QALY cost-effectiveness arguments are key to informing decisions regarding a technology, they are not the only component of a product's value. For example the following items comprise a (non-exhaustive) list of other considerations that can inform on the value of a product:

- Is the condition severe or life-threatening.
- Are there any other direct treatment alternatives.
- Does the medicine confer benefits/savings beyond those impacting health and social services, eg social security, carer benefits, ability to return to work.
- Factors that are identified by patients/carers to be of most value.
- Is the patient of an age where benefits may be wider than that conferred to the individual concerned.
- Does the medicine reverse rather than stabilise the condition.
- Timescale within which the benefits are anticipated.
- Overall budget impact (or lack thereof).
- Issues of health "equalisation" and equity.

We believe that these “other considerations” are overshadowed in the NICE decision-making process by the single “cost per QALY” value.

3. There are a number of limitations to the application of the QALY which have been fully addressed in the ABPI submission. However, it is useful to highlight the following points:

- Cost-effectiveness is a fairly new area of science which provides a single point estimate together with a range of values based on “likely assumptions”. Modelling results in wide-ranging estimates of cost-effectiveness depending on the methodology and assumptions used. As such, quite often the most important question is not, “What is the cost per QALY?” but more, “How certain are we that that cost per QALY value provided is true?” With the complex nature of modelling this subtlety can be lost in interpretation in favour of a single point estimate.
- The measurement of the quality of life component of the “QALY” is subject to a high degree of subjectivity and with a range of differing methodological approaches, the values garnered are often wide-ranging and hence contain a great deal of uncertainty. Additionally the generic approach to the measurement of quality of life, as required by NICE in the EQ-5D instrument, is relatively insensitive to incremental changes in quality of life and does not fully reflect the range of benefits that are important to patients.

4. In practice, these limitations mean that it is generally more difficult for medicines which deliver *quality* rather than *quantity* of life to demonstrate a large enough incremental benefit to be deemed cost-effective, eg in treatments at the end of life, for the elderly, and for long-term conditions, where apparently small quality-of-life benefits can make a significant difference to patients.

5. The perspective of cost-effectiveness taken by NICE is limited to that of the NHS and Personal Social Services; this excludes important benefits such as the impact on carers or enabling people to return to work and contribute to society.

6. Patients with rare diseases treated with orphan medicines⁴⁰ are disadvantaged by the NICE process. Orphan medicines are apparently expensive because development costs are relatively high on a “per-treated-patient” basis and an adequate return is necessary to sustain research. The combination of limited data at launch and relatively high per-patient prices means it is challenging for orphan medicines to meet NICE cost/QALY criteria. The current methodology requires re-evaluation, with distinct decision rules focusing more on unmet need, innovation, clinical effectiveness and budget impact, and less on cost/QALY, to ensure that the NHS principle of equal access based on clinical need is maintained for patients with rare diseases.

Consistency and Quality of Assessment

7. In line with the ABPI submission, AstraZeneca has concerns with the apparent consistency in approach and quality of the assessments carried out by the independent evidence review groups (ERGs).

8. A key issue is how the ERGs handle uncertainty, which is greatest early in a product’s lifecycle. Given that effectiveness and cost-effectiveness data are derived from highly structured clinical trials and economic models based on a wide range of assumptions and inputs, it is inevitable that different conclusions will be reached by different assessors. It is how these uncertainties are managed and the transparency with which they are addressed that are important. Rather than seeking to constructively outline and address them, some ERGs present them as fatal flaws in the manufacturer’s case.

9. Within the STA (Single Technology Appraisal) process there is an obvious omission in quality assurance which places it at odds with the MTA (Multiple Technology Appraisal) process. Within the STA process, no opportunity is afforded to stakeholders to comment on the technical accuracy of the report before the Appraisal Committee uses it to make recommendations. This technical accuracy aspect is particularly important in an STA as the ERG report is based solely on the company’s submission. Factual errors that are not rectified are translated into draft and final guidance leaving appeal as the only route to make corrections.

10. The situation is exacerbated by the inability to challenge the methods and models developed by the ERGs. Whilst the ERGs have access to the full working models produced by manufacturers, manufacturers frequently do not have access to the models created by the ERGs, the results from which form the primary evidence upon which the Appraisal Committee bases its decisions. If the model is made available, it is “locked”, which significantly hinders the ability of manufacturers to understand how it works and ultimately to challenge the working of the ERGs.

11. AstraZeneca support the ABPI’s wish for a more collaborative approach with the ERGs, based on constructive dialogue between the ERG, the NICE Executive and the company from the outset of the appraisal, allowing discussion and debate on methods, data quality and sources used. This would reduce inaccuracies, address unnecessary misunderstandings, speed up the process and reduce the number of appeals.

⁴⁰ The EMEA defines orphan medicines as those to treat rare diseases which are serious, life-threatening or chronically debilitating, with prevalence < 5 per 10,000 population. NICE defines “ultra-orphan” diseases as those affecting up to 1,000 people in the UK.

Workings of the Appraisal Committee

12. It is not clear how relevant clinical expertise, particularly from those who have hands-on experience of managing patients with the condition, is used in Appraisal Committee decision-making.

13. The discussion in the Appraisal Committee is almost solely focused on the economic case, presented by an economist, with the over-riding consideration being the cost/QALY. As stated previously, we believe there should be much greater balance between this and other considerations in the discussion and subsequent decision-making.

14. NICE has consistently rejected the industry view (particularly for STAs) that the Appraisal Committee should give proper consideration to the lack of maturity of the evidence for products early in their lifecycle. Unreasonable expectations of clinical and economic certainty for these products then result. This is dangerous for two reasons: (1) patients are being denied access to important treatment advances; and (2) denying access so early in the life of the product means that learning and incremental innovation through normal clinical experience will not happen.

15. For example, anastrozole is an anti-oestrogen used to prevent breast cancer recurrence. It was first launched in 1995 and subsequently use has evolved through 2nd line for advanced breast cancer (ABC), 1st line ABC, tamoxifen-intolerant patients with early breast cancer (EBC) (2002), to 1st line EBC (2005). The clinical benefits are different in each of these settings, and therefore cost-effectiveness will vary correspondingly.

16. The landmark ATAC study published in 2005 showed that after five years' treatment, anastrozole increased DFS (disease free survival) compared with tamoxifen, in women with EBC. DFS is used to model longer-term benefits (overall survival, life years gained and QALYs). This study of over 9,000 women commenced recruitment in 1996 and it will be several years before we are likely to see a statistically significant difference in survival (it took seven years to show a survival advantage of tamoxifen over placebo).

17. These challenges will be common to any cancer treatment where the prognosis is good, and survival rates high. The two most common cancers (breast in women, prostate in men) fall into this category.

Therefore:

- Estimating value (cost per QALY) at launch from surrogate markers will always be subject to a high level of uncertainty.
- Outcomes data cannot be generated until many years after launch.
- The value of drugs like anastrozole is likely to evolve with the patient population treated.
- A strict adherence to purely cost per QALY messages at launch may discourage the NHS from ever investing in products for chronic conditions. This will place UK patients at a disadvantage compared with their counterparts in other countries.

18. If an appraisal of anastrozole had been undertaken at launch, it is unlikely that it would have been found to be cost-effective due to the high level of uncertainty inherent in the data available at launch. A decision into its continued use on the NHS at this time could have led to access to a valuable product being blocked for UK patients whilst its usage became standard of care in other countries.

19. In the case of MTAs, the assumption in "class" appraisals is that all products are essentially similar. This is done to enable cost comparison, but fails to take into account that some products may have more robust evidence than others. This opposes NICE's fundamental principle of evidence-based assessment and can lead to patients being denied access to a technology which has the best evidence, merely because it is more expensive. This approach is anti-innovative because the innovator entrant demonstrates clinical and cost-effectiveness only to have their evidence translated across the class, negating their advantage on pricing alone. Longer term, this is likely to dis-incentivise UK investment in research into new treatments.

APPEAL PROCESS

20. AstraZeneca supports the ABPI's view on the current Appeals process with NICE. The main concerns include lack of independence, inconsistency of approach at appeal hearings, absence of health economic expertise on the Appeal Panel, and stakeholders' ability to understand and challenge new evidence disclosed for the first time in the FAD. We believe the more pragmatic system adopted by the SMC and AWMSG (which allows for appeals on "scientific grounds" as opposed to the more legalistic criteria employed by NICE) should be utilised for NICE.

IMPLEMENTATION OF NICE GUIDANCE

21. NHS implementation of NICE guidance remains slow and patchy, in spite of considerable efforts by the NICE Implementation Team for the past four years to improving it, and the inclusion of implementation in NHS core and developmental standards, against which local NHS organisations are assessed by the HCC. A number of factors contribute to this, the most important being poor NHS financial management, clinical resistance, and lack of sanctions against poor implementation.

22. Implementation of NICE guidance is not a HealthCare Commission priority in its Annual Health Check. Assessment takes the form of ensuring that processes are in place rather than measuring tangible evidence of implementation. Indeed implementation of NICE Clinical Guidelines remains merely a best practice standard to aspire to rather than a requirement for the NHS. AstraZeneca believes that implementation of guidance should involve rigorous HCC measurement and inspection together with joined-up financial incentives/penalties for lack of implementation. A system for improving this implementation could involve inclusion of an implementation component in the QOF or automatic inclusion of NICE approved medicines on local formularies. (We are aware of the potential difficulties for PCT funding flows that may be attached to this latter recommendation. We recommend further advanced planning for PCTs, with NICE providing suitable warning to the NHS regarding ongoing appraisals for the year and hence potential budget implications.)

REVIEWS OF TECHNOLOGY APPRAISALS (TAs)

23. TAs are accompanied by mandatory funding within three months of guidance being published. There is no such mandatory funding for Clinical Guidelines. There has been a recent trend for reviews of TAs to be carried out “within the context of a clinical guideline”, with express information from NICE that mandatory funding will be removed, even if the guideline continues to recommend use.

24. The reason given by NICE is that the average length of time for a TA to be reviewed (about three years) should provide sufficient time for the NHS to embed its use into clinical practice. However, as we discuss above, implementation is patchy and slow, and three years is simply not sufficient for use of a (new) intervention to have become routine. An example of this situation is the atypical antipsychotics for schizophrenia. A clinical guideline is currently underway which will update the existing appraisal which recommended use of these products within schizophrenia. AstraZeneca is aware that use of atypicals is not standard across the country. Removal of the mandatory aspect of the current TA will lead to fewer patients gaining access to these important drugs, even if the guideline subsequently recommends their use. This appears incongruous for the area of mental health which has been highlighted by the government as a priority area for England and Wales.

25. AstraZeneca supports the ABPI call for continued mandatory funding for a technology whose use remains recommended when reviewed within the context of a clinical guideline.

RECOMMENDATIONS FROM ASTRAZENECA UK LTD

- Recognition that economic modelling (cost per QALY) should comprise one element of decision-making rather than the single over-riding factor.
- NICE decision-making should include broader elements of “value”—for example those of most relevance to patients plus societal benefits.
- NICE to become directly accountable for the quality and consistency of the assessment/ERG reports.
- Mandatory funding for medicines, previously positively assessed within HTA but where reviews of technology appraisals have been achieved within the context of a clinical guideline, to become applicable where positive recommendation remains within the clinical guideline.
- Dialogue, from the outset of an appraisal, between manufacturers, NICE and ERGs on methods, data quality and sources used.
- A far-reaching review of the appeal process, with appeals allowed on the basis of scientific interpretation.
- A review of NICE guidance implementation with recommendations that result in tangible action, eg greater HCC attention; “joined-up” financial incentives; NICE approved medicines automatically included in local formularies.

AstraZeneca

March 2007

Evidence submitted by beat (NICE 06)

1. As the Eating Disorders Association, our name until February 2007, beat staff, volunteers and members were involved in the development of clinical guidelines for eating disorders published in January 2004. Chief Executive Susan Ringwood was a member of the Guideline Development Group and is currently a lay member of the NICE Topic Consideration Panel for Mental Health. These comments refer only to our organisation’s experience of NICE in relation to eating disorders.

2. The guidance development process was lengthy, but also very thorough. The outcome was a set of comprehensive recommendations which we were very willing to endorse and help promote.

3. Thoughtful consideration was given to representing the experience of treatment and care. Patients' views as well as those of care givers were sought and included in the final guidance documents. Members and stakeholders who had been sceptical about the guideline development process and even doubtful about the genuineness of the invitation to submit views were ultimately impressed by the outcome. Several individuals took the time to contact us and say that their opinions had changed and become more favourable towards NICE as a result.

4. We find that having guidelines to refer to is helpful in both raising awareness and in assisting families and individuals seeking appropriate treatment. Unfortunately, however, too many families still report having to make an individual case for treatment, especially where there is no locally available specialist resource.

5. We have families reporting conversations with their GPs that include statements such as "but of course, these are only guidelines, not requirements". Others have been told "the evidence in the guidelines is only expert opinion, and my clinical judgement is just as valid".

6. We recognise that we are more likely to hear from people whose experience of care has been less than ideal, but this still happens far too often. This could be one factor that leads to a loss of confidence in NICE by families—the failure to fulfil the promise raised by the guidelines' publication and the notion that guidance is not a requirement.

7. One area where we are particularly disappointed and have been critical of NICE is in the implementation of guidance. Not only in relation to the points made in paras 5 and 6 above, but that the need for a focus on implementation came rather late onto NICE's agenda. We have contributed to the implementation by publishing information for patients and carers. Together with the Collaborating Centre for Mental Health, we were awarded a BMA Patient Information Award for our NICE guidance information literature.

8. The full implications of implementation have also provided problematic to scope—particularly when training or professional development of staff is a necessary feature. An example from the eating disorder guidance is of Cognitive Behavioural Therapy. CBT is strongly recommended as the evidence based treatment of choice for people with bulimia nervosa, yet there are far too few qualified CBT therapists to provide this intervention. The Government's recent—welcome—commitment to increase the training in CBT lagged far behind the guidelines' publication.

9. An audit of clinical pathways and entry into specialist services for eating disorders published in February 2006 by the NHS Audit, Information and Analysis Unit revealed some very stark data. The researchers found that none of the 1,275 GPs surveyed were using NICE guidance of protocols of treatments. In depth interviews with primary care physicians revealed a number of themes:

- (i) ambivalence towards the use of guidelines in primary care—a feeling that protocols did not fit with the ethos of general practice by placing restrictions on clinical judgements and skills;
- (ii) the multiple and sometimes conflicting clinical and service priorities faced by general practitioners. GPs feeling overwhelmed, without enough time to review the number of guidelines; and
- (iii) for eating disorders specifically, the relative rarity of presentation in primary care was felt to be a significant issue in that the guidelines are more likely to be overlooked if not consulted frequently.

10. Given the vital role of GPs in diagnosing and providing access to secondary and specialist care—this ambivalence and sense of burden that NICE guidance places does need to be addressed with some priority. A suggestion is that summaries of primary care specific guidance be drawn together.

Susan Ringwood

Chief Executive Officer, beat

March 2007

Evidence submitted by the Bioindustry Association (BIA) (NICE 93)

EXECUTIVE SUMMARY

1. The BIA supports the work of the NICE and its objective of allowing "Faster Access to Modern Medicines",⁴¹ and welcomes this opportunity to make constructive comments to build on NICE's strengths.

2. Feedback from BIA members indicates that NICE's decision-making process is not fully transparent; this in itself is a highly likely reason why NICE decisions are being increasingly challenged. A system comparable to the US FDA with open and public advisory committee outcomes would be highly preferable.

3. NICE currently relies heavily on a methodology that is based on a one-size-fits-all measure of cost effectiveness.

⁴¹ Health Service Circular HSC 1999/176.

4. NICE's approach to cost-effectiveness analysis is often based on limited data generated at too early a stage in a product's growth. This can lead to higher levels of uncertainty, especially in highly innovative products. There needs to be agreement on the criteria against which therapeutic progress (or value) can be identified throughout a product's lifecycle.

5. Provision for early dialogue between companies and NICE would ensure a more efficient process. It would ultimately speed up the appraisal process, reduce inaccuracies and, consequently, reduce the number of appeals.

6. Once NICE guidance is issued, prescriber uptake implementation is poor and patchy.

7. Investing in NICE, and ensuring it has the resources it needs to do its job properly, is pointless if its guidance is not implemented.

INTRODUCTION

8. The BIA is the trade association for innovative enterprises in the UK's bioscience sector. We represent over 300 members, the majority of which are involved in realising the human health benefits that bioscience promises.

9. The UK is a world leader in biomedical research, second only to the United States. More than 250 million patients worldwide have already benefited from approved biotech medicines and therapies to treat or prevent conditions including heart attacks, multiple sclerosis, breast cancer, cystic fibrosis and leukaemia.

10. The BIA recognises the focus of this Inquiry but wanted to take this opportunity to highlight the fact that aspects of NICE's work impact on the bioscience sector and result in lower levels of uptake of innovative medicines.

11. The Ministerial Industry Strategy Group "Long Term Leadership Strategy Report", published in February 2007, reported NICE as having the most influence (in secondary care) in driving different uptake patterns. "The work of NICE can be one of the single biggest factors influencing uptake of new technologies in the NHS, and warrants a specific focus in the context of work to improve uptake."

12. The BIA hopes that the outcome of this Inquiry, and the Government response, will contribute to increasing the uptake of new medicines for improved patient health.

Why Are NICE'S Decisions Increasingly Being Challenged?

13. There is evidence that NICE is turning down an increasing number drugs, so it is perhaps unsurprising that the rate of challenges is also increasing.

14. Out of 15 recent decisions classified as appraisals under development, eight drugs were not recommended in all indications because they were not considered cost effective (most Incremental Cost Effectiveness Ratio (ICER) values were higher than £40,000)⁴². A central question here is the threshold for ICER values. The range is given between £20,000 and £30,000; this needs to be debated moving forward.

15. In addition, there are concerns over NICE's decision process. Feedback from BIA members is that the process is not fully transparent; this in itself is a likely reason why NICE decisions are being increasingly challenged.

Is Public Confidence in the Institute Waning, and If So, Why?

16. It would be uncommon for the public to fully understand NICE's activity beyond what is reported in the media. At a recent NICE Roundtable discussion in Birmingham it was suggested that an "FDA-like" open and public evaluation before an advisory committee could help increase the transparency of reviews by allowing all stakeholders to "have their say", which could improve transparency and trust in the NICE process and decisions.

Nice's Evaluation Process, and Whether Any Particular Groups are Disadvantaged by the Process

17. In this section the BIA has chosen to examine four different patient groups by way of examples. The BIA's comments on improvement the NICE evaluation process are covered in the section below on "Improving the Health Technology Assessment Process".

⁴² Office of Fair Trading. Annex B, Review of NICE, SMC and AWMSG. February 2007. OFT885bb

EPO

18. Quality Adjusted Life Years (QALY) values can change over time, as more is learned about the optimum use of a medicine. A good example of this is erythropoietin (EPO), a treatment for patients with kidney failure, which improves red blood cell count, reduces the need for blood transfusions and improves patients' quality of life. At the time of EPO's launch in 1990, the estimated cost per QALY was £103,000, a value which does not represent cost effectiveness under NICE's methodology. Over time, management of kidney failure using EPO has changed, as more has been learned about the drug and benefits, including improved quality of life for patients, have been found. Current estimates of cost per QALY for EPO show a dramatic reduction from the initial value.

19. On a related note, erythropoietin (alpha and beta) and darbepoetin for the treatment of cancer-treatment induced anaemia have been undergoing NICE appraisal, and is scheduled to be considered by the NICE appraisal committee for the fourth time in June 2007, with Guidance expected in November 2007. Preliminary Guidance from NICE does not recommend the use of EPO for patients with cancer-treatment induced anaemia. In the appraisal, NICE did not properly consider quality of life as they only used Quality of Life (QoL) estimates derived from clinical trials. RCT data is difficult to generalise to real life clinical practice and this may lead to an underestimate of the QoL benefits associated with EPO in the real treatment setting.

20. In the NICE health economic estimate of EPO, it was assumed blood transfusion would only be considered in patients whose Hb level fell below 10g/dl. The National Blood Service (NBS) have confirmed that transfusion is actually considered when the Hb level is approximately 8–9g/dl. Using the NBS estimates reduces the cost-effectiveness ratio by about one third. NICE did not consider the impact on cost-effectiveness that some patients with lower Hb levels would require more blood transfusions. Including published estimates of the amount of blood that would be used in a real life situation, halves the cost-effectiveness ratio.

21. NICE's decision ignores internationally recognised evidence based guidelines which are supported by a wealth of research. The European Organisation for Research and Treatment of Cancer (EORTC), the American Society of Clinical Oncology (ASCO) and the US National Comprehensive Cancer Network (NCCN) all recommend EPO for patients with chemotherapy-induced anaemia within the licensed indications for the products. As it currently stands, NICE's interim decision is also at direct odds with the Government's core objective of improving a patient's quality of life and a variety of further objectives laid out in the National Cancer Plan.

Gliomas

22. Every year, nearly 2,000 people in England and Wales are diagnosed with high grade glioma, a life-threatening form of malignant brain tumour which accounts for 2% of all cancers in the UK. This highly aggressive brain cancer has a devastating effect on patients (many of whom are very young) with at least half dying within 12 months.

23. Gliadel implants, produced by BIA member Archimedes Pharma, are used at the time of surgery. Clinical data show these implants can prolong meaningful quality of life and significantly increase survival rates. The use of Gliadel can increase the numbers of high grade glioma patients surviving three years from surgery by four- to five-fold.

24. Gliadel is the only treatment which allows patients to start chemotherapy immediately following surgery and prior to radiotherapy. This is particularly important as patients frequently face a five to six week delay for radiotherapy rather than the recommended two weeks post-surgery. Gliadel is also the only treatment that can be used in patients with grade 3 or grade 4 glioma; other treatments are indicated only for patients with grade 4 glioma.

25. The cost of Gliadel is just over £5,000 per patient. If all patients suitable for Gliadel received treatment the cost to the NHS would be around £2 million per annum. All the leading European countries and the US have approved and reimbursed Gliadel and Scotland has also approved Gliadel for reimbursement.

26. In January 2007, NICE issued a negative appraisal on Gliadel. If this negative appraisal is implemented, then around 25% of patients with high grade glioma will have no access to drug therapy.

27. It is of concern that the process of assessing Gliadel appears to have been significantly flawed—NICE have twice used the wrong data, producing inaccurate cost effectiveness ratios and have used incorrect assumptions about the neurosurgery involved. There also appears to have been limited discussion with experts on high grade glioma, particularly around the treatment of those specific groups of patients who have most to gain from Gliadel.

Orphan diseases

28. The EMEA's definition of orphan disease is a serious, life-threatening or chronically debilitating disease affecting fewer than five in 10,000 people in the EU.

29. Patients with rare diseases who could be treated effectively with orphan medicines are disadvantaged by the NICE process. Orphan medicines appear expensive because the cost of developing them is relatively high on a "per-treated patient" basis. There is also only limited data available on such medicines at launch. These factors combine to make it particularly difficult for orphan medicines to meet the ICER threshold. As a result they appear to be expensive but an adequate return is necessary to sustain research and medical progress in areas of high unmet patient need.

30. Simply because these patients are suffering from rare diseases, they are being denied an effective treatment for severe, often life-threatening conditions, which is at odds with the fundamental NHS principle of equity of access to treatments for all patients based on clinical need. Indeed, the slow uptake of orphan medicines in the UK is of concern to the EMEA.⁴³

31. As of January 2007, NICE had appraised 16 EMEA/FDA designated orphan Medicines, of which it rejected four (25%), recommended nine (56%) for restricted use and recommended three (19%) for general use. In comparison, of the 116 non-orphan drugs appraised by NICE, seven (6%) were rejected, 56 (48%) recommended for restricted use, and 53 (46%) recommended for general use.⁴⁴

32. The current methodology therefore needs to be re-assessed, with more emphasis attached to unmet need, innovation, clinical effectiveness and budget impact, and less on cost/QALY.

Ultra-orphan diseases

33. Ultra-orphan medicines are described by NICE as medicines for the treatment or prevention of a disease affecting fewer than 1,000 people in the UK.

34. The conventional NICE evaluation process disadvantages individuals with ultra-orphan diseases, for which products that are available for treatment are characterised by:

- high acquisition costs;
- high ICER;
- use is limited to an ultra-orphan disease that are chronic, severely disabling and/or life-threatening; and
- potential for life-long use.

35. Currently there is no process outside the conventional evaluation for this class of products. It has been suggested that NICE establish an Ultra-Orphan Drugs Evaluation Process and Committee. The process would be modeled on the existing conventional process but be tailored for ultra-orphan drugs. The reference ICER would be developed from currently marketed ultra-orphan drugs that are in the range of £200–£300K per QALY. The BIA would support such a development, and would also support a similar development for orphan drugs.

*Improving the Health Technology Assessment Process**Definition of value*

36. A broader definition of value is needed in the NICE evaluation process. NICE currently relies heavily on a methodology that is based on a one-size-fits-all measure of cost-effectiveness, an ICER based upon a cost per QALY. This attempts to apply the same parameters to a wide range of health interventions and subjective outcomes such as quality of life.

37. While such a measure has a role, it is but one of a number of parameters. Over-reliance on this single measure can have a profound impact on patients, who can be denied treatment on the basis of theoretical assumptions.

38. Not only are QALYs not always objective, they can also change over time and, importantly, they do not take into account the indirect benefits of a new therapy, such as productivity gains, reduction in caregiver and personal time costs, shorter hospital stays, enabling people to return to work and contribute to the economy. The priorities of the patient population, the nature of the therapeutic market and availability of alternative treatments, the perspective of medical specialists, affordability concerns and effects on macro-economic growth should all be recognised in decisions about price and reimbursement.

⁴³ http://ec.europa.eu/health/ph_threats/non_com/docs/EMEA_chart_en.pdf

⁴⁴ "Working paper by the OHE: 'HTA for orphan drugs: A review of the Issues and of NICE and SMC Decisions'".

39. A particular concern for innovative companies is that NICE's approach to cost-effectiveness analysis is often based on limited data generated at too early a stage in a product's growth. This can lead to higher levels of uncertainty, especially in highly innovative products. There is a real risk that smaller companies will either be penalised for failing to generate insufficient health economic data, or forced to use limited data from RCTs that will give uncertain outcomes.

40. There needs to be agreement on the criteria against which therapeutic progress (or value) can be identified throughout a product's lifecycle—this can include mortality and morbidity data, side-effects, tolerability, predictive surrogate parameters, pharmaceutical form, route of administration, compliance, ease of use, impact on the healthcare service, disease severity, medical need, quality of life and patient preferences. Improvements under any of these headings may constitute innovation that is of value to sub-groups of patients.

Early interaction

41. The BIA welcomes the recommendation in the recent Cooksey review of UK health research funding to involve NICE earlier in the process of development to accelerate assessment of clinical and cost-effectiveness.

42. Provision for early dialogue between companies and NICE would ensure a more efficient process. It is likely that the burden of more reviews will mean that more companies will be impacted by the NICE process, and it is important that companies gain an early understanding of what is expected of them.

43. Engaging with companies from the start of the appraisal would allow discussion on methods and data. This would ultimately speed up the appraisal process, reduce inaccuracies and, consequently, reduce the number of appeals.

Speed of publishing guidance

44. There are significant concerns over the speed of publishing decisions. For example, one BIA member company has been waiting NICE's guidance on Osteoporosis Primary Prevention which has been in progress since March 2002.

45. Certainty, to which positive NICE guidance contributes, is important for innovative companies to grow. A long wait for NICE guidance will not create an overall innovation-friendly environment. Many emerging biotechnology companies are working largely on single product development, so delay, not to mention negative appraisals, can be catastrophic for such companies.

46. The BIA welcomed the announcement in November 2005 of a new NICE Single Technology Appraisal, which will be used initially to produce faster guidance on certain life-saving drugs which have already been licensed and on new medicines referred to NICE.

47. Two of the first five medicines to go through the new process are biotech medicines—Herceptin, for breast cancer, and MabThera, for non-Hodgkin's lymphoma. This is a positive step towards ensuring that patients have the best possible access to innovative medicines. It is important that the new procedure is extended to other medicines for debilitating and life-threatening diseases.

48. The take-up of innovative drugs would be improved by the further improvements to the fast-track system of NICE appraisals for innovative medicines. For example, the STA submission word limit makes it difficult to ensure the submission is sufficiently comprehensive, and creates a risk that the appraisal committee cannot adequately understand and correctly analyse the data.

The Implementation of Nice Guidance, Both Technology Appraisals and Clinical Guidance (Which Guidance Is Acted On, Which Is Not and the Reasons For This)

49. Negative appraisals almost certainly result in non-implementation, however, positive appraisals do not mean universal implementation within NICE timelines.

50. There are two kinds of "NICE blight" that are leading to reduced access to modern effective treatments:

- (a) where PCTs hold back decisions on funding of a product on the NICE work programme pending a decision by NICE, which is often issued months or even years after grant of a licence; and
- (b) when PCTs hold back funding for new treatments that are not short-listed for consideration by NICE on the assumption that they will at some stage be the subject of an appraisal.

51. Government policy is that patients should not automatically be denied funding for medicines that are awaiting NICE guidance. NHS organisations are supposed to use local arrangements for the managed introduction of new technologies where NICE guidance is not yet available. However, funding decisions are routinely delayed until guidance is available, meaning that patients are often denied access to medicines for months or years.

52. A good example is the use of bortezomib for multiple myeloma, which was licensed in April 2004 and received CHMP positive opinion for the expanded indication in March 2005, although final NICE guidance on the expanded authorisation has still not been issued. In the meantime, patients are dependent on decisions made by local PCTs which leads to inequality of access across the UK.

53. In this, as in other instances, even once NICE guidance is issued, prescriber uptake implementation is patchy. The reasons for this are varied, but do not simply relate to the cost of implementing NICE guidance—factors such as poor NHS financial management and clinical resistance are key.

54. Investing in NICE, and ensuring it has the resources it needs to do its job properly, is pointless if its guidance is not implemented. The BIA would support more joined-up financial incentives and measures to measure tangibly the extent and quality of guidance implementation, eg by including this in the Healthcare Commission's Annual Health Check, which is not currently the case.

The Appeal System

55. The BIA would like to bring to the Committee's attention an issue with the appeal process insofar as companies have to deal with the same people that actually made the decision in the first place, so it is questionable whether it is an objective process.

Laura Gilbert

Public Affairs Director, Bioindustry Association

March 2007

Evidence submitted by Bowel Cancer UK (NICE 38)

BOWEL CANCER UK

Bowel Cancer UK is a leading charity dedicated to raising awareness of bowel cancer, improving the quality of life of those affected by the disease and, ultimately, reducing deaths from the second most common cause of cancer death in the UK, affecting men and women equally.

Bowel Cancer UK commemorates its 20th anniversary this year: 20 years in which we have sought to represent and help those affected by bowel cancer—patients and those who care for them—including in helping them to gain access to the treatments, care and services that are right for them.

EXECUTIVE SUMMARY

As you will see, we have responded to each of the areas of particular interest that the Committee has drawn attention to, as set out in your press notice number 11. We have also added points that we believe will be of use to the Select Committee in its Inquiry. All our responses are based upon our considerable experience of working with NICE and taking part in their appraisals of bowel cancer treatments over the last seven years.

1. Why NICE's decisions are increasingly being challenged

NICE's decisions are increasingly being challenged—including, where appropriate, by ourselves—because their guidance is often negative and flies in the face of the medical evidence supporting the efficacy of the treatments they are appraising. NICE is also being challenged more because their decisions seem to be based solely on grounds of cost not efficacy. This is not only wrong; it also goes against why they were set up in the first place, in their own words: "*NICE is an independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health.*"

2. Whether public confidence in the Institute is waning and if so why

Public confidence in NICE is waning for the above reasons and because NICE is increasingly seen as not being "*an independent organisation*" but an agent of government, whose sole purpose is to restrict NHS spending on treatments, rather than, as should be the case, make these treatments available to the patients who need them and could benefit from them.

3. *NICE's evaluation process, and whether any particular groups are disadvantaged by the process*

Speaking from the perspective of bowel cancer patients and carers, I can definitely say that they have been disadvantaged by the NICE process. The recent revolution in new treatments for the disease—after 50 years of only one treatment being available—has not benefited patients on the NHS. Bowel cancer treatments that are routinely made available to patients in Europe, the United States and in the private setting are being denied to patients in the UK as a result of negative NICE guidance. It is no surprise, therefore, that we lag far behind other countries in terms of how long our patients survive with the disease.

As we've said previously, in response to a specific negative NICE verdict, it is ironic that the UK is at the forefront in developing these treatments and yet at the very back of the queue when it comes to patients gaining access to them. It is also worth noting that even though NICE guidance is just that—"guidance" and not law—PCTs treat it as law and usually refuse to go against it.

4. *The speed of publishing guidance*

While NICE guidance has speeded up in recent years, following pressure from voluntary groups and others, this is, in effect, academic when, as in the case of bowel cancer, their guidance is often negative.

5. *The appeal system*

I will refer to a summary of the comments of lawyer Peter Telford on this point, who has been working pro-bono with Bowel Cancer UK on patients' behalf in seeking to help them gain access to treatments. Peter says the following:

NICE's current system of decision making and review offers no opportunity for relevant and current material and facts to be considered in any appeal.

The NICE appeal system is, in fact, not an appeal system at all. It is a review of the material that was available to NICE at the date of the original decision only. A proper appeal would involve a reconsideration of the facts on the basis of the best available evidence at that time.

The present NICE appeal system is based on the model of a judicial review and the only legal avenue of appeal from the final decision of the appeal panel is itself by way of judicial review. Judicial review, by its very nature, prevents new evidence being submitted. The evidence is limited to that which was before the original body.

Even if one were to successfully argue before a judicial review that the evidence before the appeal panel should have been taken into account, it would still not enable the judicial review body to come to its own conclusions on those facts. It could only refer the matter back for a fresh decision.

The danger of a "never ending" system of decision making is met by the wording of the rule that would apply when an appeal body reconsidering the matter looks at what evidence to take into account. This wording would be similar to that used in appeals in other legal fields, such as immigration (not asylum) or housing, where "the appeal body may take into account evidence of material facts which appertained as at the date of decision". These bodies continue to function and do not suffer from a "never ending" process due to admitting evidence.

While the rule of admissibility is a discretionary one and not an absolute right to new evidence, the person seeking to place it before the appeal body has the onus of establishing it as relevant and material. As is the present position, the appeal body would take legal advice on whether it should be admitted.

The appeal process is limited to an essentially "due process" review, which means that the merits of the decision are not reviewed. This artificial limit is not necessary. It also means that when coupled to excessive delay in the process, the decision can become out of step with the reality of rapid technological advances.

The fact that the appeal panel members are experts is somewhat wasted when they are forced to do little more than observe that the original panel went through the right process and—having made proper assumptions on the then available evidence—came to a decision by a logical and reasonable process.

In some areas, such as housing where there are alternatives to public housing, such a process may not lead to ultimate unfairness and injustice. In cancer care and oncology, where changes and improvements to drugs, technology and methodology are ever present, such a process can lead to nonsensical conclusions that are out of step with the, by then, available facts.

6. *An example of how the NICE Appeal system fails bowel cancer patients (also provided by Peter Telford, who was Counsel pro bono for Bowel Cancer UK and Cancer Backup at the hearing of the below appeal in November 2006)*

- Treatments: Bevacizumab (Avastin) and Cetuximab (Erbix), both biological agents for the treatment of advanced colorectal cancer.

- NICE announces intention to review guidance in April 2005.
- Evidence closed by August 2005.
- Internal (Sheffield based) panel organises evidence and reports to NICE by February 2006.
- Submissions end April 2006 (including comprehensive submission by Bowel Cancer UK).
- Draft guidance issued August 2006 (negative on both). Non reviewable before May 2009.
- Appeal heard for Cetuximab only November 2006 (no new evidence allowed).
- NICE appeal committee reject appeal (end January 2007).
- NICE appeal committee observes that they were unable to take account of new material evidence and would like NICE (not themselves but the original committee) to reconsider earlier than May 2009. However, no power in the appeal committee to order NICE (original) to review earlier as they were not informed of the merits of the decision.
- Final guidance issued end January 2007 (negative on both).
- Therefore a total of 21 months elapsed with no possibility of any new evidence for nearly 18 months.
- Of course, the decision depended in part on clinical trials which were not fully complete. During those 18 months some of those trials and new trials were completed.
- New evidence could mean that drugs originally advised negatively might be advised positively or at least neutrally.

7. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN) (and the SMC)*

While in the past SIGN—and the Scottish Medicines Consortium (SMC), which are between them the Scottish equivalent of NICE—have shown some independence from NICE, in recent times they appear to increasingly follow NICE's example, which, as most NICE bowel cancer related decisions are negative, again has a detrimental effect on bowel cancer patients.

8. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)*

Even when NICE approves treatments—such as oral chemotherapy and combination chemotherapy—implementation of their guidance is often patchy. There appears to be no incentive for PCTs to implement NICE guidance or monitor how guidance is implemented, beyond seeking to avoid the negative publicity that ourselves and other organisations might generate in the media and elsewhere.

9. *The “lowest common denominator” effect*

One of the saddest, and frankly shabbiest, aspects of NICE decisions is the way they appear to presume that if they approve a drug for use, clinicians are going to dish it out to their patients like sweets from a candy store. NICE seem to ignore the fact that clinicians have the best interests of their patients at heart, which means that if a treatment isn't working, they will stop giving it to them.

10. *NICE—Creating a two tier system*

As you'd expect, when bowel cancer patients—and those who care for them—are told they could benefit from a treatment but can't get it on the NHS, often because of negative NICE guidance, they will move heaven and earth to pay for it privately, making financial and other sacrifices to do so if they are able to. This creates a two tier system that totally goes against what the NHS stands for and what NICE was created for. Consequently, the system and NICE's role within it needs to change.

Bowel Cancer UK warmly welcomes this Review and is grateful for the opportunity to contribute to it.

Ian Beaumont
Bowel Cancer UK

21 March 2007

Evidence submitted by Breakthrough Breast Cancer (NICE 60)

1. INTRODUCTION

1.1 Breakthrough Breast Cancer is the UK's leading breast cancer charity and is committed to fighting breast cancer through research, campaigning and education. Breakthrough has established the UK's first dedicated breast cancer research centre, in order to realise our vision: *a future free from the fear of breast cancer*. Breakthrough campaigns for policies that support breast cancer research and improved services, as well as promoting breast cancer education and awareness amongst the general public, policy makers, health professionals and the media.

1.2 Breakthrough works closely with healthcare professionals, patient advocates, and researchers. Our memorandum incorporates the views of Breakthrough and members of its Campaigns & Advocacy Network (Breakthrough CAN)—which is made up of over 800 individuals and organisations. Many members of Breakthrough CAN have personal experience of breast cancer as well as being involved in and working alongside their local NHS to try to deliver better treatments and services for people affected by breast cancer and their families. Breakthrough CAN members are also involved in the work of the National Institute for Health and Clinical Excellence (NICE), for example by providing their views on NICE consultations, new technologies and clinical guidelines. Comments from Breakthrough CAN members are included throughout this submission.

1.3 Breakthrough welcomes this inquiry into NICE. Our memorandum focuses on the work of NICE, areas where NICE has developed and the challenges it currently faces. Breakthrough staff and CAN members would be willing to provide oral evidence to this inquiry, if the committee would find this useful.

2. THE ROLE OF NICE

2.1 NICE plays a vital role in reducing inequalities in access to quality care and treatment by establishing best practice guidance to be followed across the NHS in England and Wales. Breakthrough Breast Cancer believes it is very important that all patients receive the same standard of care no matter where they live.

2.2 By providing guidance that is based on both clinical and cost effectiveness, NICE also plays an important role in ensuring that patients receive effective treatments and care that also provide value for money.

2.3 It is important that all guidance produced by NICE continues to carry weight in order to reduce the post code lottery in accessing services, standards of care and treatments. Many Primary Care Trusts (PCTs) will wait until NICE has published guidance on new treatments before it prescribes to patients. It is only then that they have a statutory duty to do so. However, as clinical guidelines produced by NICE are not mandatory, there is significant variability regarding their implementation. All patients should expect to be given the best practice of care, regardless of where they live.

3. PUBLIC CONFIDENCE AND UNDERSTANDING OF NICE

3.1 Breakthrough Breast Cancer welcomes the move by NICE to run consultations on many of their processes, such as the technology appraisal process, clinical guideline development and interventional procedures appraisal process. This demonstrates a willingness to be efficient and inclusive.

3.2 It is very important that NICE continues to provide opportunities for the public, individual patients and stakeholder organisations to be involved in their work. Breakthrough welcomes the opportunities it has to involve staff and Breakthrough CAN members in the work of NICE. For example, a Breakthrough CAN member was chosen as a patient expert in the Single Technology Appraisal of Herceptin; a staff member was chosen as a patient expert in the Single Technology Appraisal of docetaxel; and a staff member was selected to be on the Guideline Development Group for the update of the Familial Breast Cancer guidelines.

3.3 Public confidence in the role of NICE is mixed. High profile debates over negative decisions by NICE (most recently demonstrated over the Alzheimer's treatments donepezil, rivastigmine and galantamine) and the variability of access to treatments,⁴⁵ services and standards of care strongly influences the public's opinion of NICE. Quotes from Breakthrough CAN members highlight a range of views:

"I think NICE have improved dramatically since their inception and there is more understanding in the media and elsewhere about their role." Breakthrough CAN member

"I think we only hear about the work of NICE when it hits the headlines." Breakthrough CAN member

"I think [NICE guidance] is too much based on cost-effectiveness." Breakthrough CAN member

⁴⁵ Richard M (2006). *Usage of cancer drugs approved by NICE: Report of Review undertaken by the National Cancer Director*. Department of Health: London.

3.4 Public confidence may be largely affected by a lack of understanding of the role of NICE. Whilst many people would agree with the core principle of NICE to reduce inequality in access to treatments and care, there is a lack of understanding of how NICE produces guidance and how it makes its decisions. This is illustrated by some quotes from Breakthrough CAN members:

“I don’t know enough about NICE.” Breakthrough CAN member

“The idea of NICE is good but I’m not sure how it works in practice.” Breakthrough CAN member

“NICE could do a better job of explaining their decisions—there might be very good reasons for their decisions but the media report them as a yes or no and it’s not that straightforward.” Breakthrough CAN member directly involved in the work of NICE

3.5 Public expectations of NICE and healthcare overall continue to rise as they become increasingly aware of both the role of NICE and the many new treatments that are being developed and licensed for use in the UK. Breakthrough believes NICE will face mounting pressure to produce guidance on an increasing number of treatments. As advances in technology result in more targeted and expensive treatments, NICE will face greater levels of objections to negative decisions which may appear to be driven by cost factors.

“We pay for our health during our working lives in National Insurance contributions—we are entitled to the drugs.” Breakthrough CAN member

“Misrepresentation in the media makes me angry as it raises expectations among patients and not always justifiably.” Breakthrough CAN member

3.6 Increased litigation and judicial reviews could be one of the more significant consequences NICE and PCTs will face.

4. THE EVALUATION PROCESS AND PUBLISHING OF GUIDANCE

4.1 There is currently a lack of clarity over how topics are selected for appraisal by NICE. For example, Herceptin for early stage breast cancer treatment was referred by the Secretary of State for Health, Patricia Hewitt, to a fast-track appraisal, following the announcement of significant clinical trial results in May 2005. If this had not happened, there would have been a significant delay in this important treatment being available to patients across the NHS. As the Prime Minister made clear at the time:

“The steps recently announced by my right hon Friend the Secretary of State for Health should mean that the drug [Herceptin] is available throughout the country as swiftly as possible. Because the matter arises as a result of the National Institute for Health and Clinical Excellence guidelines, we are looking at how we can speed up the process in cases where it particularly matters to people who may be desperately ill and who think there is a drug on the market that can help them. We all accept that at present the procedures are too slow. The idea of NICE is an excellent idea. It has a broad measure of support, but we need to make sure that its processes work more quickly so that what has happened in the case of this drug is not repeated.”

Prime Minister, The Rt Hon Tony Blair MP, 19 October 2005

4.2 The introduction of the Single Technology Appraisal (STA) process has undoubtedly provided a quicker, more efficient system for producing guidance recommendations on new treatments.

4.3 Breakthrough welcomes the recent amendment to the STA process which now allows all patient organisations to provide a statement regarding a new technology. Previously, it was felt that the new STA process significantly reduced the input from the patient perspective, only allowing a few individuals to provide their views. Such views may not have been truly representative of affected patient populations thus this recent change goes some way to address this issue. This is an issue that was recognised by both patient organisations and patients alike:

“I like the idea of the process being speeded up but don’t want this to happen without full participation and involvement of all interested parties.” Breakthrough CAN member

“I think it is important that patient representatives are fully conversant with all aspects of the illness and can represent all views not just their individual ones.” Breakthrough CAN member

4.4 Whilst the new appraisal process reduces the amount of bureaucracy, it is questionable whether NICE currently has the capacity and resources to cope with the increasing numbers of technologies being developed. NICE must be reactive to such increasing demands and ensure capacity is available to produce guidance promptly and appropriately.

“NICE seems to lack the resources to undertake the masses of work required to evaluate all possible future drugs.” Breakthrough CAN member

4.5 Furthermore, it is not clear whether NICE is sufficiently resourced with appropriate systems to deal with advances in treatments, many of which will cost significantly more than current available treatments thus the current cost thresholds applied by NICE may no longer be appropriate. Breakthrough is concerned

that if NICE does not review its current cost thresholds there is a danger that the NHS will not keep up-to-date with treatment advances and that patients in England and Wales will not be offered the most effective treatments for their conditions. For example, breast cancer patients in the UK have lower survival rates than many other countries in Europe⁴⁶ thus cannot afford to be denied the most effective treatments.

4.6 There is concern that the existence of different organisations and systems for producing guidance on new technologies and standards of care in the UK actually introduces a post-code lottery. The fact that organisations, such as the Scottish Medicines Consortium, the Scottish Intercollegiate Guidelines Network and the All Wales Medicines Strategy Group, are all producing guidance, and in different ways, causes confusion and sometimes also anger. There appears to be a lack of consistency on what guidance is prioritised, on what basis the guidance is produced and the length of the process to produce guidance.

“It is very wasteful and inefficient to have more than one organisation in the UK evaluating new drugs and, in comparison with the SMC, NICE seems to be much less efficient. This is not acceptable.”
Breakthrough CAN member

5. NICE’S DECISIONS

5.1 There is concern that the decisions made by NICE do not fully take into account quality of life issues for patients. The process by which decisions are made places greater weight on the evidence for survival benefits of treatment and care, than on improvements to quality of life. This is an issue of particular importance to cancer patients, particularly those with advanced, metastatic cancer. Patients with metastatic breast cancer typically have limited treatment options and, understandably, want access treatments and care that will give them the chance of an improved quality of life to spend more quality time with their friends and families. For these patients, the importance of quality of life cannot be underestimated. Breakthrough believes NICE should review their decision-making processes to take greater account of quality of life issues, and consider whether there is future scope to include the wider benefits to society of new technologies and care options, such as the longer term savings of investments, in their decision-making.

“In determining cost effectiveness it would seem important to consider future cost to the health service and other care services.” Breakthrough CAN member

“NICE should look to the future—life-saving drugs will eventually save money for the NHS in terms of long term care / hospital treatment etc.” Breakthrough CAN member

5.2 As a research charity, Breakthrough believes it is vital that proven results from clinical research are promptly translated into benefits for all clinically eligible patients. It is important that the NICE appraisal process is as efficient as possible so that patients may benefit quickly, by having the capacity to undertake the work ensuring that unnecessary delays are not introduced.

5.3 An example of where the NICE’s appraisal process may be delayed is the use of the system to appeal decisions. If an appeal to a decision of an STA is made, this can significantly delay the issuing of guidance to the NHS. While it is necessary that the right to appeal is maintained, it should be ensured that the appeal system is not used to obtain clarification or deliberately delay guidance.

5.4 The Final Appraisal Determination on Herceptin was appealed in July 2006 by Newbury and Community Primary Care Trust. The majority of the points involved in the appeal were actually regarding clarification of a number of statements within the guidance, rather than an outright objection to it. This could have been dealt with more effectively earlier in the appraisal process.

6. IMPLEMENTATION OF NICE GUIDANCE

6.1 Breakthrough Breast Cancer is concerned that guidance from NICE is not consistently implemented across the NHS. This results in disparities in access to treatments and the best standards of care, which have been shown to be clinically and cost effective. For example, Breakthrough is aware that there is wide variation in the use of Herceptin in the treatment of secondary breast cancer, as, in many places, it is not offered to all eligible patients who could benefit from it.⁴⁷

6.2 Currently, there appears to be little incentive to ensure guidance is implemented and there is a lack of penalty for non-implementation. This issue should be addressed as a priority by the Department of Health, NICE and the Healthcare Commission. One of the key principles of NICE is to ensure equality in access to the best standards of treatment and care—there is limited value to NICE’s guidance if it is not implemented consistently.

“NICE should have more authority in making people follow the guidelines.” Breakthrough CAN member

“A huge amount of time and expense goes into drawing together guidelines so implementation is very important.” Breakthrough CAN member directly involved in the work of NICE

⁴⁶ Coleman, MP (1999). Opinion: why the variation in breast cancer survival in Europe? *Breast Cancer Research 1*: 22–26.

⁴⁷ Richard M (2006). *Usage of cancer drugs approved by NICE: Report of Review undertaken by the National Cancer Director*. Department of Health: London.

6.3 For some services, there is wide variation in clinical practice as clinical guidance from NICE is not mandatory. Breakthrough is aware of variation in lymphoedema services for breast cancer patients despite NICE's *Improving Outcomes in Breast Cancer* (2002) guidance which stated that "networks should agree guidelines for identification and management of lymphoedema". The Lymphoedema Support Network, a national patient support group for this condition, has identified national deficits in service provision in the UK, with many parts of the country failing to offer any service. Where care is provided, it is delivered through acute specialist centres or palliative care centres, with few providing all elements of the required therapy.

6.3 Information provided to Breakthrough by breast care nurses from across the UK has identified instances where the value of specialist breast care nurses is being questioned, with some having to justify their roles within hospitals and/or carry out non-specialist duties, taking them away from caring for breast cancer patients. The value of specialist breast care nursing posts, and their benefits to patients and impact on clinical outcomes, is clearly identified in NICE's *Improving Outcomes in Breast Cancer* (2002) guidance. Breakthrough is disappointed that in some areas specialist nurse posts are under threat and believes that there needs to be a review of the implementation of NICE clinical and commissioning guidance and how it is prioritised within the NHS.

6.4 Women with significant risk of developing breast cancer because of their family history are entitled to annual mammography breast screening between the ages of 40–49 through a breast clinic. In addition, some women at high risk of developing breast cancer because of their family history may also be entitled to annual MRI screening from a young age. Women and healthcare professionals have told Breakthrough that they are struggling to access this "safety-net" screening as many PCTs are not commissioning the services.

"NICE guidance is one thing; it is another matter altogether implementing the guidelines at local level." Breakthrough CAN member

6.5 Breakthrough is concerned that many PCTs are unprepared for new guidance which can result in resistance towards, and the lack of implementation of, guidance. Better horizon-scanning is very important in ensuring that plans are in place to react to and implement new NICE guidance. NICE could play a greater role in the initiation and success of horizon-scanning within the NHS, which is likely to result in a smoother take-up of new technologies and improvement in standards of care through more consistent implementation of their guidance.

7. RECOMMENDATIONS FOR ACTION

7.1 NICE must continue to involve the public, patients and patient organisations in its work and the development of guidance.

7.2 NICE must ensure that it has sufficient capacity to provide thorough and prompt guidance within an environment of increasing numbers of technologies.

7.3 NICE must ensure that it has sufficient capacity to, and demonstrate how, it will respond to increasing public expectations and make appropriate decisions within an environment of increasingly advanced and expensive technologies.

7.4 Breakthrough urges NICE to review the current cost thresholds that are applied in cost effectiveness decisions, in the light of increasing numbers of advanced, expensive technologies.

7.5 NICE must place greater weight on quality of life issues and Breakthrough also urges NICE to take into account wider benefits to society and future savings benefits when making their decisions regarding new technologies.

7.6 Breakthrough believes that NICE should take a greater lead (alongside the Department of Health and Healthcare Commission) in ensuring implementation of their guidance within the NHS.

7.7 Breakthrough believes that NICE could take a greater lead on implementing effective horizon-scanning within the NHS, in order to ensure that PCTs are able to effectively plan their services to be able to implement new guidance quickly and appropriately.

7.8 NICE should ensure that the appeal system is used appropriately, ie to challenge recommendations rather than to achieve further clarity, which may include reviewing the STA system to allow for clarification at an earlier stage of the process.

Vicki Nash
Breakthrough Breast Cancer

March 2007

Evidence submitted by Bristol-Myers Squibb Pharmaceuticals Ltd (NICE 51)

ABOUT BMS

Bristol-Myers Squibb Pharmaceuticals Ltd (BMS) is a global research and development-based pharmaceutical company and one of the leading suppliers of both hospital and GP-prescribed medicines to the NHS. We develop and supply medicines for some of the NHS' highest priority treatment areas, including cancer, cardiovascular disease, severe mental illness and HIV and we are proud to have launched five new medicines into the UK in the last three years. Our business strategy is based around the development of innovative medicines in areas of greatest unmet medical need. Our medicines have been the subject of several NICE appraisals affording us significant experience of working with NICE, of its process and the impact of its guidance on patient care.

INTRODUCTION

We welcome the decision of the Health Select Committee to conduct an inquiry into NICE, given increasing public concern about the availability of medicines in the NHS. It is becoming clear that NICE is, in effect, operating as a "fourth hurdle" and that medicines must demonstrate not only the quality, safety and efficacy required by the licensing authorities, but also "cost-effectiveness", as defined by NICE, before they can become widely available to patients. The perception in much of the NHS—if not the legal actuality—is that the funding of medicines is contingent on them being "approved" by NICE. To some extent this may represent opportunistic behaviour by budget-holding primary care trusts constantly searching for financial economies. However, it is also indicative of the ambiguity of NICE's status which is central to the issues we have with it.

NICE was established with the objective of accelerating the uptake of effective new technologies and of reducing or eliminating geographical disparities in their use (so called "postcode prescribing"). It has made some, but only limited, progress towards meeting these objectives for those technologies it recommends. Even here, however, the uptake of NICE guidance is patchy and incentives for implementing "positive" guidance are weak.

Of even greater concern is that NICE would appear to have moved away from these objectives in more recent time. It now has an implicit, if not explicit, rationing function, where its recommendations on specific technologies stem directly from the question of what can be afforded, not what is best for patients. This, we believe, is not what Parliament intended, and we recommend that the Health Select Committee focuses its inquiry on the question of whether NICE has gone beyond its original remit in this way.

We believe it is time Parliament called NICE to account and the Health Select Committee inquiry is an excellent way of doing this. The inquiry is even more timely in light of the recent report by the Office of Fair Trading into the Pharmaceutical Price Regulation Scheme. The OFT proposes a central role for NICE in defining a medicine's value, as a critical input into determining the price the NHS will pay for that medicine. It is important that the Committee fully considers the significance of this proposal as it conducts the inquiry.

The OFT report is complex and far-reaching in its implications and it is too early to offer a full assessment of it at this stage. However, an initial observation is that while the principle of value-based pricing merits examination, the practicalities of how such a system will work are highly complex. In particular, we do not believe that NICE is ready and able to take on the enhanced role that the OFT envisages. In effect it would be asking NICE to run before it can walk, and consequently we believe the government should exercise great caution before moving in the direction the OFT proposes.

We recognise the Committee's observation, reflected in the inquiry remit, that NICE's decisions are increasingly being challenged and that public confidence in NICE is waning. We believe there are a number of reasons for this which we set out and discuss below.

The points highlighted in this submission are those that are of particular importance to Bristol-Myers Squibb. We are members of the ABPI and fully endorse the points made by the ABPI in its own submission to the enquiry, even if we do not specifically echo them below. In particular, we share the ABPI's concern about the consistency and quality of assessments carried out by the economic review groups (ERGs) as part of the STA process and about the lack of opportunity for companies to have dialogue with either the ERGs or the appraisal committee in the course of the review. Given the flaws in the NICE appeals process—also documented in the ABPI's submission and known to BMS through direct experience—anything that makes the process more inclusive, thereby helping to reduce the incidence of appeals, should be warmly embraced by NICE.

BMS COMMENTS

1. *The Role of NICE*

- Health technology assessment—the process of making judgements about the cost and clinical effectiveness of a medicine or medical technology—has an important part to play in informing choices made by doctors and patients. The stated purpose of NICE is to provide “national guidance” and BMS supports this role.
- Increasingly, however, the way in which NICE is being interpreted is to undermine choice since, if NICE recommends against a technology, then it is extremely difficult, if not impossible, for that product to receive funding by the NHS. In effect, the “choice” is being made by NICE, not by the doctor or patient.
- Moreover, a “yes” or “no” decision from NICE now centres around whether the technology is judged “cost-effective” against a “cost per QALY” threshold for which the maximum acceptable level is £30,000. There is also evidence of this threshold being driven closer to £20,000. This is not a cost-effectiveness threshold, since there is no law of health economics that says a technology suddenly becomes non cost-effective above a particular cost per QALY point (or cost-effective below it). It has become a de-facto affordability threshold, based on a judgement about what level of cost-effectiveness the NHS is prepared to pay for.
- In summary, therefore, NICE is making judgements about what products should or should not be paid for by the NHS (and therefore reach patients), based on considerations of affordability. This is neither NICE’s stated role (NICE, for example, refuse even to acknowledge that a threshold exists, though evidently it does), nor what Parliament envisaged. While NICE has a role in informing choice, to delegate choice to NICE in this way is anathema to broader government policy.

2. *The Accountability and Transparency of NICE*

- It is reasonable that an expert body such as NICE should carry out the technical function of assessing the clinical and cost-effectiveness of different medical interventions and making recommendations about their use in the NHS. It is not right however that NICE should be asked to make highly political decisions related to what the NHS can afford to provide for the population.
- As noted above, NICE currently uses a cost per QALY threshold approach to determine when it does or does not approve a treatment for use. This threshold has simply emerged: it has never been mandated through any political or democratic process. We believe this is wrong given that decisions about patients’ access to medicines revolve around this threshold-based judgement made by NICE. Such public policy decisions should be exposed to the full oxygen of public and political debate.
- Although NICE is supposed to assess both the cost and clinical effectiveness of medicines and medical technologies, in practice it is a product’s cost per QALY against threshold that determines the outcome. The balance of factors taken into account by NICE in appraising a technology is not made clear. Nor does the process acknowledge that assessing cost-effectiveness is an imprecise science, based on a variety of inputs and assumptions, and that for any product there is a range of plausible cost-effectiveness ratios. The manner by which NICE absorbs such imprecision yet is capable of making definitive and binding decisions about technologies is frequently unclear. This exposes the process to the suspicion that it is driven by subjective judgements (such as around affordability) rather than objective ones.
- It is critical for public confidence in NICE that there is proper transparency in all its processes. In particular, it should be much clearer how the threshold is determined and, crucially, that the Government, rather than NICE, takes full accountability for it.
- Many of these problems and concerns stem from the fact that NICE is not a truly independent body. It is part of the NHS, and therefore part of the organisation that has to fund its decisions. We believe this to be a conflict of interest that needs to be resolved if NICE is to command the confidence of the wider public.

3. *Cost-effectiveness and value*

- We have concerns that the appraisal methodology NICE employs does not properly consider a medicine’s full value to the patient, to the NHS and to society more broadly. It is in part because of this that NICE’s decisions are increasingly being challenged.
- NICE’s methodology is over-reliant on the cost per QALY as a measure of cost-effectiveness and, indeed, value. The QALY is in fact just one piece of evidence that should be considered as part of a full assessment of the value of a medicine.

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- Judgements about the value of a medicine to patients and the NHS should be taken on a broader basis, encompassing both the clinical benefits of the medicine as well as its cost-effectiveness. Factors that should be taken into account include, for example, whether the product fulfils a genuine unmet medical need, the availability of other treatments, the benefits that are of most importance to the patient and his or her carers and wider societal benefits and savings such as in social security costs.
 - We believe that the health technology assessment carried out by NICE should focus more on the additional clinical benefit to patients that the new medicine provides, and this should be given at least equal weight in forming the overall recommendation. A measurable assessment of the clinical benefit of the medicine separate to the cost per QALY assessment would add both clarity and balance to the process.
 - A potential model would be the French Amelioration du Service Medical Rendu, or ASMR, where the clinical benefit is expressed as a classification between 1 & 5, as follows:
 - 1 = major improvement, delivered to innovative product of significant therapeutic benefit,
 - 2 = important improvement, delivered to product of therapeutic benefit in terms of efficacy and/or reduction in side effect profile,
 - 3 = moderate improvement in terms of efficacy and/or reduction in side effect profile, delivered when already existing product, where equivalent pharmaceuticals exist,
 - 4 = minor improvement, and
 - 5 = no improvement
 - The problems associated with making definitive cost-effectiveness judgements on new medicines are exacerbated by the fact that the default mode for NICE is becoming an assessment of a product made at or around the time of launch. By definition, the full data required to form a rounded judgement of a product's full value are not available at this time: such data can only be gathered through extensive use of the product in a real-life setting. Long-term outcomes or survival data, for example, will not generally be available at this stage.
 - While we recognise the desire of the NHS to have guidance available close to when a new product is launched—a desire that, understandably, NICE wants to fulfil—it has to be recognised that all that can be produced at this early stage is precisely that—guidance. The problem with assessment at launch is that NICE is now making, in effect, once and for all value judgements about a new medicine at this stage. This is completely inappropriate, and has the effect of constructing a barrier to entry at launch that is damaging potentially both to patients and to incentives to innovate for the pharmaceutical industry.
 - The cost-effectiveness approach adopted by NICE takes almost no account of the fact that medicines designed to treat highly-specialised diseases will always be more expensive unit per unit because there is a much smaller patient base from which the company can recoup the costs of research and development. NICE has recognised the need for a different approach to cost per QALY analysis in the case of so-called “ultra-orphan” drugs (those affecting up to 1000 people in the UK). We believe that this needs to go further: if cost per QALYs are to play such a pivotal role (and, as we argue above, this is debatable) then at least there should be scope for adopting different thresholds for different products, depending on their type and patient base. The overall budgetary impact should be kept in mind in making these judgements.

4. *Assessment at launch*

- As set out above, we recognise the desire for NICE to issue guidance as close to launch as possible. We would point out however that there are real practical issues with proceeding too early, not least that the final licensed indication(s) is often not known until approximately two months prior to marketing authorisation. It is our experience that appraisals begun before this point cause significant problems for the manufacturer and can result in an unnecessary additional resource burden. We urge the Committee to call on NICE to be as flexible as possible in the timing of appraisals close to launch.

5. *Implementation of NICE guidance and patient access to medicines*

- When NICE has deemed that a treatment is cost-effective, the NHS is required to fund its availability to all appropriate patients. Unfortunately this is still very often not the case and many patients do not receive the best available treatments. There is significant variation in the availability of NICE approved medicines across the country.
- Anti-platelets are one example of this phenomenon. Anti-platelets, of which aspirin is the most widely used, help to prevent patients with heart disease suffering a further heart attack or stroke. As such they are an important tool in preventing ill-health and death from cardiovascular disease, a key priority for the NHS. Despite this, there is a six-fold variation in usage of anti-platelets

between PCTs nationally. This is a stark differential in prescribing of a proven and cost-effective class of treatments which have the potential to contribute to improved public health at a very reasonable cost.

- We therefore believe the government and the NHS must focus more on what needs to be done to ensure that NICE approved treatments are made widely available to patients. In particular, the Healthcare Commission should be more rigorous in its annual assessment of NHS organisations in reviewing performance in relation to NICE guidance implementation.

6. *Availability of medicines that have not been reviewed by NICE*

- The NHS is increasingly using absence of NICE guidance as a reason not to make medicines available to patients. In many instances, PCTs will not pay for medicines that have not been reviewed by NICE, regardless of the evidence supporting the value of the product. More often, particularly where a medicine is new to the market, bureaucratic hurdles are put in place to make it difficult for clinicians to prescribe it. The result is that patients are denied treatments that could be beneficial to them—often for considerable periods of time if an appraisal overruns, as is sometimes the case, or if NICE decides not to review a particular treatment.
- Medicines for conditions that are not government priorities are particularly likely to be refused funding. We are aware, for example, of patients with Hepatitis B, a serious and life-threatening condition, who have sought treatment with a new drug that has yet to be appraised by NICE and been told that their PCT will not pay for it.
- The Department of Health recently re-issued guidance making it clear that lack of NICE guidance was not an acceptable reason to refuse to fund a medicine. It remains to be seen whether the guidance will have any impact. The Department must monitor this situation closely and ensure that patients requiring treatment with non-NICE reviewed medicines are not discriminated against in this way.

Bristol-Myers Squibb Pharmaceuticals Ltd

March 2007

Evidence submitted by the British Association for Counselling and Psychotherapy (NICE 92)

EXECUTIVE SUMMARY

1. Psychological therapies are an important part of the delivery of health care within the NHS and the private sector. They are highly valued by patients who increasingly choose counselling and psychotherapy in preference to medication.

2. NICE guidelines now exist to support the delivery of psychological therapies across a range of mental health conditions, including depression and anxiety.

3. The NICE guideline development process is robust and transparent. NICE guidelines are based on evidence reviews, with systematic review and randomised controlled trial (RCT) evidence given most weight.

4. There are two disadvantages of maintaining this rigid hierarchy of evidence:

5. The first disadvantage relates to the lack of systematic review and RCT evidence for the psychological therapies:

6. Mental health research is seriously under-funded. RCTs are expensive, as are systematic reviews to synthesise RCT data. There is limited systematic review and RCT evidence for the efficacy of psychological therapies, with the exception of CBT for a range of conditions. Many psychological therapies remain unevaluated by RCT. Therefore NICE guidelines are based on a robust but very narrow evidence base.

7. BACP has concerns, therefore, about gaps in the evidence and in service recommendations based on a restricted evidence base. Reliance on a limited range of evidence based treatments may disadvantage patients through restricting patient choice for and access to a range of interventions and over-resource standard treatments that are not panaceas and will not suit all patients.

8. The second disadvantage relates to the downgrading of other types of research evidence, such as case studies and effectiveness studies, which are needed to assess not only whether a treatment works, but if and how it works in practice.

9. Studies that show that a therapy can work in the trial context must be complemented by other methodologies (such as audit and benchmarking) that can assure that their delivery in routine settings (such as the NHS) is still producing positive outcomes. It is important to assess not only whether a treatment works, but how it works in practice.

10. BACP recommends that NICE reviews its evidence evaluation process to admit a range of quantitative and qualitative evidence in the evaluation of psychological therapies, including highly controlled studies, case studies and effectiveness studies.

11. Besides the ways in which NICE's evaluation may disadvantage certain groups of patients, BACP has concerns about the implementation of NICE guidance:

12. There is concern that NICE guidelines for psychological therapies might be used as a basis for new commissioning strategies or for re-designing existing psychological therapies when the evidence underlying their recommendations does not support this.

13. Implementation of NICE guidance based on a narrow evidence base will severely limit treatment options for patients at a time when the Government is responding to public concern about lack of access to, and health inequities in, the provision of psychological therapies, and prioritising patient choice.

14. The concerns stated here are shared not only by BACP but also by psychological therapists in other professional bodies and by researchers in both academic and practice settings. This lack of confidence in the evaluation process in itself constitutes a challenge to the NICE decision making process.

AREA OF EXPERTISE

15. BACP is recognised by legislators, national and international organisations and the public, as the leading professional body and the voice of counselling and psychotherapy in the United Kingdom; with over 26,000 members working to the highest professional standards.

NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process

16. NICE guidelines are based on evidence reviews, with systematic review and RCT evidence given most weight. The guidelines use predetermined and systematic methods to identify and evaluate evidence relating to the specific condition in question. Where evidence is lacking, the guidelines incorporate statements and recommendations based upon consensus statements developed by the guideline development group.

17. NICE acknowledges that clinical guidelines have limitations and that "they are not a substitute for professional knowledge and clinical judgement. They can be limited in their usefulness and applicability by a number of different factors (including) the availability of high quality research evidence . . . (and) the generalisability of research findings" (1).

18. BACP applauds the transparency and rigour of the NICE evidence review process. However, we believe that the current NICE evaluation process, based on a rigid hierarchy of evidence, disadvantages the psychological therapies (and thus the patients receiving therapy) on several counts:

19. Mental health has long been under-researched and under funded. The lack of research funding for the psychological therapies compared with the funding available to evaluate pharmacological and other technologies means that there is limited RCT evidence for the efficacy of psychological therapies (2).

20. RCTs are able to indicate whether or not a therapy works and which therapy works best, as well as indicating when therapies are actually doing more harm than good. However, RCTs are expensive and there is limited RCT evidence for psychological therapies which means that many therapies are unevaluated.

21. Because NICE guidelines utilise a hierarchy of evidence that places systematic reviews and RCTs at the top, and because there are very few highly controlled trials of psychological therapies, NICE guidelines for psychological therapies make recommendations based on a very narrow evidence base.

22. BACP has concerns, therefore, about gaps in the evidence and in service recommendations based on a restricted evidence base. Reliance on a limited range of evidence based treatments may disadvantage patients through restricting patient choice for and access to a range of interventions and over-resource standard treatments that are not panaceas and will not suit all patients.

23. Because many therapies are not evaluated by RCT, they tend to be excluded from NICE guidelines, or, if they are included because based on consensus statements, they tend not to be recommended as first line treatments. NICE repeatedly states that "It is important to remember that the absence of empirical evidence for the effectiveness of a particular intervention is not the same as evidence for ineffectiveness" (1) but the current hierarchy of evidence inevitably excludes or downgrades non RCT evidence.

24. When seeking evidence of causal relationships, or unbiased comparisons of treatments, RCT methodology is likely to be the method of choice in most circumstances. However, even among those who accept the primacy of RCTs as a method of scientific evaluation, there are a number of criticisms of their applicability to routine service provision:

25. Psychological therapy does not lend itself easily to evaluation by RCT. The biomedical paradigm underlying much RCT evidence is reflected in the wide use of manualised treatments for patients with DSM based diagnoses. By contrast, most patients present in the NHS with wide-ranging difficulties such as marital problems, bereavement, problems associated with ill health and so on. Patients may be worried, anxious or depressed, they may have multiple problems; they do not always fit neatly into diagnostic categories.

26. Certain types of manualised (or manualisable) interventions, such as Cognitive Behavioural Therapy (CBT) or Interpersonal Therapy (IPT) lend themselves to evaluation by RCT. Other types of intervention (such as the commonly practiced integrative therapy) are less easily evaluated in trial settings. This means that there is a robust evidence base for certain types of interventions such as CBT and IPT, but there is less RCT evidence for other psychological therapies. No evidence of effectiveness is all too often construed as evidence of no effectiveness in a system that gives most weight to systematic review and RCT evidence. At the same time, over-reliance on evidence from RCTs which use strictly manualised treatments can lead to inappropriate assumptions about the effectiveness of a particular “brand name” therapy (3).

27. There is evidence to suggest that the quality of the therapist-patient relationship or therapeutic alliance is relevant to treatment efficacy (4). Trial evidence tends to focus on the type of treatment offered (eg, CBT or IPT) rather than the person giving it. By giving most weight to reviews and RCTs, guidelines may promote best technologies over best practitioners.

28. Psychological therapies are by definition relational therapies. The therapeutic alliance between therapist and patient is an important influencing variable in terms of outcome; it tends to be best captured by qualitative research and case studies.

29. Studies that show a therapy can work in the trial context must be complemented by other methodologies (such as audit and benchmarking) that can assure that their delivery in routine settings is still producing positive outcomes. For example, the “hourglass” model of treatment development has been described (5) in which highly controlled studies are relevant for only one portion of the development cycle, while less controlled methods (such as case studies and effectiveness studies) have crucial roles early and late in the development of the therapy respectively. The relationship between RCT based evidence and systematic data collection from routine settings (audit, benchmarking, quality evaluation) and the role of qualitative research need to be reviewed in order to improve the NICE evaluation process, and to make the ensuing guidelines applicable to the NHS.

Concerns about the Implementation of NICE Guidance and Corresponding Challenges to NICE Decisions

30. Current government initiatives have placed considerable emphasis on “patient choice”. However, there is an increasing focus on a single model of psychological therapy—cognitive-behavioural therapy (CBT)—because of its robust RCT evidence base. When other forms of psychological intervention have been compared with CBT in DH funded RCTs, findings have shown broad equivalence of outcomes, for example, in depression and anxiety in primary care (6). However, the weight of evidence for CBT has tended to mean that these therapies are overlooked.

31. The over reliance on CBT evidence has led to the identification of a shortage of CBT practitioners which requires additional funding to correct. This approach has generated artificial problems regarding resources (ie, practitioners) to deliver psychological therapies.

32. There is a growing debate within the area of the psychological therapies as to the contribution (ie effectiveness) of practitioners versus specific therapies. There has been research arguing for both sides of the case (7), although it is becoming clear that the effectiveness of practitioners may be of at least equal importance (8).

33. To date, RCTs have investigated technologies, rather than practitioner effects. The contribution and variability of practitioners is an important component which is currently being determined from analyses of large data sets collected from routine NHS mental health settings (9). But because this data has not been collected within an RCT, it is not included in the NICE hierarchy of evidence. Such a strategy places NICE at a distance from everyday practitioners and does not facilitate practitioners adopting and implementing NICE guidance.

CONCLUSION

34. BACP considers the instigation of NICE, with its rigorous and transparent hierarchy of evidence, to have been a major step forward in the development of evidence based guidelines for the psychological therapies within the NHS.

35. However, public confidence is waning in NICE guidance because its recommendations do not reflect NHS practice. Reliance on robust systematic review and RCT evidence currently leads to an over emphasis on certain brand name therapies (CBT, IPT) with resulting narrow recommendations which the practitioner in the NHS finds hard to equate with the complexity of problems with which patients present in routine NHS settings.

36. Given the diversity of human beings, we need to ensure that patient choice is a reality by funding research into psychological approaches other than CBT.

37. The relationship between RCT evidence and systematic data collection from routine settings (audit, benchmarking, quality evaluation) and the role of qualitative research need to be reviewed in order to improve the NICE evaluation process (and its hierarchy of evidence) so as to make NICE guidelines relevant and applicable to the NHS.

RECOMMENDATIONS

38. We recommend that the Government should set up a review of the evidence hierarchy which NICE relies on for its mental health guidelines, to investigate the impact of current criteria for evaluating research into psychological therapies and consequent clinical guidelines on patient choice, innovative services, and patient care.

39. Future guideline development groups set up by NICE for mental health guidelines should have a broader balance and cross-section of professional stake holders and peer reviewers to try to ensure researcher-allegiance bias does not distort the guideline development process. These appointments should be transparent and decided by elected representatives from the stake holder organisations.

40. NICE should publish the estimated costs of implementing mental health guidelines in terms of treating unmet need, delivering new psychological treatments, workforce and training implications and service redesign. These monies should be ring-fenced as additional investment provided via Strategic Health Authorities before clinical guidelines are issued.

41. Prior to NICE's review of its Depression and Anxiety guidelines in 2008, an evaluation of what impact they have had, and whether they are being implemented, should be undertaken by the Audit Commission. Where implementation is patchy or slow, a commissioning strategy should be included as part of the review process for clinical guidelines.

42. The Department of Health should work with NICE, the professional bodies in psychological therapies and the mental health charities, to agree a national research programme, which identifies the gaps in the evidence (across all the mental health guidelines), and priorities for research, and provide funding for these to be undertaken as an important part of the development and implementation programme for NICE guidelines.

43. NICE and the Department of Health should work with the professional bodies, with research departments for psychological therapies and with mental health research charities to establish an evaluation and audit infrastructure within NHS services which will enable ongoing improvements in practice, and better monitoring of whether clinical guidelines are having beneficial impacts on patient care.

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Nancy Rowland

British Association for Counselling and Psychotherapy

March 2007

Evidence submitted by the British Medical Association (NICE 95)

Before the formation of NICE, there was little in the way of widely circulated pan-professional evidence based guidance. Although our written submission raises significant problems with the operation of NICE, the concept remains a good one. This inquiry is timely as it affords the opportunity to reflect on ways to develop the institute.

Doctors in a wide-range of specialties have told us that a key flaw in the formulation of NICE guidance is the lack of involvement of front line clinicians in the evaluation of evidence and formulation of recommendations. GPs, in particular, have concerns around implementation. They feel disengaged from NICE because guidance is developed with acute care in mind and is divorced from their everyday reality. In some cases, for example “Improving Outcomes Guidance for Skin Cancers”, guidance goes against the grain of reform, in this case the aim of providing more minor surgery in primary care.

NICE decisions are increasingly being questioned and, partly as a consequence, public confidence is failing because cost containment is thought to be the primary concern. A growing awareness of the different availability of drugs across the UK’s national health services is adding to this as are the reports of financial challenges facing the English NHS. All these reasons make it likely that NICE and its work will become more politicised.

There is growing concern amongst hospital doctors that NICE is slow to produce guidance, particularly on the evaluation of new technologies. Patients and doctors are often clamouring to use new technologies long before NICE provides its advice. There have been several publicly exposed situations where NICE has yet to undertake an evaluation and in response to individual claims for guidance the Department of Health say this should be provided by PCTs in the interim. This lack of clarity makes the process unclear and frustrating for groups who are asking their doctor for a particular intervention. It also places a great deal of pressure on local decision makers who want better support from NICE and national policy makers.

We believe that NICE guidance should be more transparent about the evidence it draws upon and how this was interpreted. Guidance should more clearly rank the degree of authority evidence has and, by association, the authority of recommendations.

We are of the view that politicians generally and the government especially need to be more open about the financial challenges facing the NHS and provide political and financial support for NICE and the critical role it has to play in its analysis of clinical and cost effectiveness and recommendations for clinical practice.

1. The British Medical Association is an independent trade union and voluntary professional association which represents doctors from all branches of medicine all over the UK. It has a total membership of over 138,000.
2. In our written submission we raise a number of problems with the way NICE is working at present. However, before its existence there was little in the way of widely circulated pan-professional evidence based guidance, and though there are significant problems, the concept of NICE remains a good one.
3. This inquiry is timely as it affords the opportunity to reflect on ways to develop the institute.

On Reasons NICE’s Decisions Are Increasingly Challenged

4. Doctors from a wide range of specialties have told us that a key flaw in the formulation of NICE guidance is the lack of involvement of front line clinicians in their formulation.

5. General practitioners, in particular, feel that they are not fully recognised within NICE guidance. As the first port of call for patient care and with a broad range of skills, NICE seems divorced from the daily reality of specialist general practice. One GP used the phrase “ivory tower” to describe the gap between NICE and practice at local level. In secondary care too, hospital doctors feel that guidance is produced by academics and to improve, NICE needs to focus more on ways to help clinicians at the coalface improve the care of their patients by helping them to implement decisions, which are relevant to real world practice.

6. Doctors are sometimes put under pressure to ensure that NICE guidelines are implemented, but in some cases the guidance is not considered appropriate and there needs to be space for doctors to explain why, to feed back into NICE and aid the revision of guidelines. The following comment illustrates part of the problem:

“I recently challenged a respiratory physician over the NICE COPD guidelines. NICE think we in primary care should be monitoring, including spirometry, these patients up to four times a year. He could give me no evidence that this behaviour would improve outcomes. In my practice, 25–30% of my patients have CPD. How much time and resource would be wasted on this activity? And for what benefit?”

7. It would help clinicians if some of its material were not labelled “guidance” or even “best practice” when evidence is clearly inconclusive or weak. An acknowledgement that some areas need more evidence would improve the credibility of NICE. NICE reports should come with greater openness about the standard of evidence that has been used and the level of authority that should therefore be afforded to the review. Furthermore, it would help if the evidence on which NICE guidelines are drawn up was clearer. In particular, clarity could be achieved on how evidence was thought by making it public prior to guidelines being introduced to ensure that they are:

- (a) sufficiently robust;
- (b) are appropriate to everyday practice; and
- (c) aid a discussion of how they will be implemented.

On Public Confidence in the Institute

8. With the absence of any research it is difficult to know how the public feel about NICE. However, we feel confident that it will become better. This is because NICE will inevitably become further embroiled in debates about what the NHS can afford. Some have interpreted the recent report on public services—launched by Tony Blair and Gordon Brown—as a move toward the NHS setting out a core list of services the NHS will apply.⁴⁸ Of course, setting out what is available will involve decisions about what is not available.

9. If as many believe, the NHS will increasingly have to make difficult decisions about rationing, NICE will have to have the confidence of the public. This may be difficult and ultimately this process of setting priorities may have to be political, informed by the advice of experts.

10. NICE decisions are increasingly being challenged because of the perception that cost is an overriding issue. This is becoming increasingly apparent when the public and doctors believe that the evidence for effectiveness of any treatment is ultimately overshadowed by economic concerns. This will erode public and professional confidence in NICE.

11. One of the main difficulties for NICE is in trying to rationalise its difficult decisions on cost effectiveness. Who is to judge, for example, whether a certain period of additional survival in a terminal illness is cost effective, particularly if this is significant? For individuals and families—and the media that tell their story—any prolongation of life is seen as worth it. There will always be challenges in these circumstances.

12. Another dimension of public confidence—already being raised as a question in the Westminster Parliament—is increasing awareness of differences across the UK. In mid-March an English MP asked the Prime Minister “why only British taxpayers with a Scottish postcode” were able to access a drug for sufferers of lung cancer.

13. Even within England, there is a widespread perception of a postcode lottery and this also undermines public confidence in NICE.

14. A further reason for reduced confidence is that decisions are often not given with enough explanation or that offered explanation is not easy to follow. When NICE’s decisions are overturned then confidence sinks even lower.

On NICE’s Evaluation Process, and Whether Any Particular Groups Are Disadvantaged By The Process

15. Both hospital doctors and general practitioners express concerns that NICE’s evaluation groups are unrepresentative and lacking views of doctors at the coalface of practice whose working knowledge could be drawn upon. GPs feel particularly strongly that NICE guidance is produced, in the main, by secondary care doctors, who tend to be from highly specialist academic departments. There is a wish to see more front-line doctors represented on groups.

16. From a patient perspective, there is a concern that NICE does not have a strategy for undertaking race equality impact assessments on their guidelines. NICE needs to improve its process to ensure that its work has cross-cultural relevance.

On the Speed of Publishing Guidance

17. There is concern that NICE is slow to produce guidance, particularly on the evaluation of new technologies. There have been several publicly exposed anomalies where NICE has yet to undertake an evaluation and the Department of Health respond to questions by saying that local PCTs should make a judgement in the interim. These gaps make the process unclear, are frustrating for groups who are asking their doctor for a particular intervention and place a great deal of pressure on local decision makers who want better support from NICE and national policy makers. Patients and doctors are often clamouring to use new technologies long before NICE provides it advice.

18. We accept, however, that the work of NICE necessitates careful evaluation and a reasonable time to complete this. It might be possible to speed this activity with greater financial support that would enable NICE to employ more evaluators. It seems that the political prominence of priority setting is increasing, as is the rate of new technologies, not all of which can be afforded. At the same time, the government is expecting NICE to do more whilst not supporting this with resources.

⁴⁸ Nicholas Timmins. NHS may be restricted to core services. *Financial Times*: 19 March 2007; www.ft.com

On Comparisons With The Work of the Scottish Intercollegiate Guidelines Network (SIGN)

19. The main concern of hospital doctors is the very slow speed in publishing guidance. The advantage of the Scottish Medicines Consortium (SMC) is that it provides a much more rapid response based on clinical and cost effectiveness data. We understand that NICE has had discussions with the SMC and intends to adopt some of its procedures for single health technology appraisals. That said, the multiple health technology appraisals that NICE undertake are valuable and this process clearly takes longer to complete.

20. The Scottish Intercollegiate Guidelines Network (SIGN) has been an invaluable way of ensuring that peer reviewed high quality evidence is synthesised into clinical practice guidelines. Its guidelines are used and methodology respected. Crucially, it grades evidence appropriately according to international standards. This means that the recommendations can be accepted by clinical professionals and by NHS organisations.

21. A major weakness of SIGN guidelines, however, is that they have no data on cost effectiveness. It is expected that in future, SIGN guidelines—now under the umbrella of NHS Quality Improvement Scotland should contain cost effectiveness data alongside recommendations.

On the Implementation of NICE Guidance

22. The issue of implementing NICE guidance is a huge bone of contention for doctors.

23. Guidance can be confusing and frustrating where it goes against the grain of general policy. At present, for example, an aim of the reform programme is to provide more care outside of hospital and into community settings. NICE guidance can be a major deterrent to this aim. Most recently, the NICE guidance on Improving Outcomes Guidance for Skin Cancers has been criticised for its potential to prevent minor surgery in primary care, if implemented as directed. A GP commented that:

“I carry out about 100 minor surgical procedures within my practice per year. My audit last year showed I excised six BCCs. To be able to continue to provide this service to my patients I will have to:

- (i) become an accredited surgeon;*
- (ii) carry out 40 surgical interventions for expected skin cancer per year;*
- (iii) maintain a log book;*
- (iv) perform an annual audit of excision margins etc;*
- (v) attend a skin course every two years;*
- (vi) attend one session per year of training with a consultant;*
- (vii) attend a minimum of four local skin multidisciplinary team meetings per year;*

So in effect this will stop all GPs performing this surgery unless they are GPs with special interests. The patients will have to travel further and cost the NHS more, for what gain?”

24. As stated, GPs are concerned that the secondary care slant within NICE guidance—and a failure to translate it to general practice—makes it difficult to implement NICE guidance in primary care. Because GPs are “gatekeepers” of NHS resources and navigators for patients, they are concerned with commissioning care and referring patients to appropriate services. There is a view within general practice that compelling NICE guidance on PCTs does not always lead to appropriate behaviour.

“The whole exercise has been a colossal waste of money and the best thing to do with NICE guidance is to use what is useful. It would be very helpful if the Select Committee were to recommend that NICE guidance should revert to the status of guidance rather than having protected status as holy writ, since it is inhibiting progress and leading to waste.”

British Medical Association

March 2007

Evidence submitted by the British Society for Rheumatology (NICE 53)

EXECUTIVE SUMMARY

1. The British Society for Rheumatology (BSR) is a medical society committed to advancing knowledge and practice in the field of rheumatology. We aim to improve awareness and understanding of arthritis and other musculoskeletal conditions and work at national and local level to promote high quality standards of care for people with these conditions. We have around 1,400 members in the UK and overseas; the majority of these are consultant and trainee rheumatologists. BSR also has a number of members who are allied health professionals, primary care workers, scientists and others working in the field of Rheumatology.

2. As an organisation BSR has participated in over 25 NICE technology appraisals.

3. Submissions to NICE, by all stakeholders, are becoming more detailed and sophisticated.
4. Scepticism is growing about the health economic analysis that is used by NICE.
5. The lack of accessibility to the analyses is unhelpful.
6. NICE health economics focus on the costs to the NHS without taking societal and employment costs into account. This skews the focus of the analysis from the perception of patients and their carers.
7. Much of health economic analysis is beyond the understanding of the general public (and many professionals), and this raises the suspicion that NICE has a purely rationing function.
8. Stakeholders such as BSR and patient representative organisations do not have the resources or the manpower to mount several appraisals simultaneously.
9. Because of the thoroughness of the evidence considered, the number of stakeholders even in single technology appraisals, and the appeals process, the speed of publishing guidance is very slow.
10. Because the process is slow, and new evidence is emerging all the time, it seems perverse that NICE will not consider new evidence that is pertinent to the issues at hand.
11. SIGN and NICE duplicate a great deal of work. It would be logical to look at ways avoiding unnecessary duplication and the sharing of evidence and therefore speeding up the process.
12. NICE has not eliminated postcode prescribing or poor implementation of NICE guidance.

Why are NICE's decisions increasingly being challenged?

13. Stakeholders are increasingly sophisticated in their submissions, improving their data, and performing their own health economic analyses. It is no longer just the pharmaceutical industry that can mount robust defences of the cost-effectiveness of their drugs. For example, BSR established a Biologics Register to collect data on patients with rheumatoid arthritis. This was done with the encouragement of NICE as it is a useful tool to support their guidance. The Biologics Register has enabled the BSR to commission an independent health economic analysis of the cost effectiveness of anti-TNF² therapy in rheumatoid arthritis (performed in Sheffield⁴⁹).
14. The results demonstrated incremental cost efficiency ratios that were substantially lower than those of the Birmingham Assessment Group. This appears to be a recurrent theme that generates scepticism about the process. Health economic analyses commissioned from Assessment Groups are invariably more expensive than most other analyses, and lack transparency^{50, 51}.
15. The lack of accessibility of these analyses has been highlighted as a serious problem.⁵² This is the principal reason cited by those seeking a judicial review on the NICE decision on drugs for Alzheimer's disease.⁵³ The Assessment Group has access to other economic analyses at the start of an appraisal, but other stakeholders do not have reciprocal access to their work, which is unjust³.
16. Currently the BSR is engaged in the appraisal process for anti-TNF drugs in ankylosing spondylitis (AS). The Liverpool Assessment group has generated a health economic model with which the BSR has profound difficulties, with assumptions about the disease that do not bear any relationship to the disease as we recognise it. However, the lack of transparency has made their economic modelling impenetrable. Because health economics is the central pillar of technology appraisals, the unsatisfactory accessibility of the Assessment groups' work will continue to fuel challenges to decisions. It is at least a positive step that the AS health economic model has now been referred to the Decisions Support Unit for further assessment.
17. Because re-appraisals may not take place for three to four years (or even longer in the case of guidelines), stakeholders who feel that appraisals or guidelines are incorrect will feel obliged to put a great deal of effort into trying to ensure contentious elements are modified. This is in an attempt to avoid patients being denied access to appropriate treatment in the intervening years.

⁴⁹ Bansback NJ *et al.* The NICE re-appraisal of biologics in 2005: what rheumatologists need to know. *Rheumatology* 2005;44:3–4.

⁵⁰ Chauhan D *et al.* Exploration of the difference in results of economic submissions to the National Institute of Clinical Excellence by manufacturers and assessment groups. *Int J Technol Assess Health Care* 2007;23:96–100.

⁵¹ Miners A *et al.* Comparing estimates of cost effectiveness submitted to the National Institute for Clinical Excellence (NICE) by different organisations: retrospective study. *BMJ* 2005;330:64

⁵² Stirling B *et al.* Seeing the NICE side of cost-effectiveness analysis: a qualitative investigation of the use of CEA in NICE technology appraisals. *Health Econ* 2007;16:179–93.

⁵³ Dyer C. NICE faces legal challenge over restriction on dementia drugs. *BMJ* 2006;333:1085.

18. NICE health economics focus on the costs to the NHS without taking societal costs into account. The cost to the state of social services care, invalidity benefit and loss of tax revenue from a person of working age who has had to give up their employment must be considered, otherwise the focus of the analysis is skewed from the perception of patients and their carers.

Is public confidence in the Institute waning?

19. Much of health economic analysis is beyond the understanding of the general public (and many professionals). However the decisions as reported always list the cost-benefit analysis as a key driver, and this raises the suspicion that NICE has a purely rationing function.

20. Members of the press have raised populist arguments criticising the decisions of NICE (eg Clare Rayner and Thomas Stuttford), and patient representative bodies protest against NICE decisions. Seeing angry patients and their carers carrying condemnatory placards and handing in large petitions leaves a powerful emotional image. The possibility that the Alzheimer's society may mount a legal challenge to the NICE decision on availability of drugs for this condition results in bad publicity for the Institute⁵.

21. NICE claims not to have a cut-off for costs per QALY in the decision-making process, but its decisions point clearly to a ceiling for an incremental cost effectiveness ratio of £30,000/QALY. Above this a drug will only be supported if it is innovative, if there are particular features of the condition and population receiving the technology, and sometimes with reference to wider societal costs and benefits.⁵⁴ It is unclear how this figure was reached, which spawns the suspicion that it is arbitrary. It has been argued that deciding affordability is not a role of NICE in setting a threshold above which a technology will not be accepted, and this should be a role for parliament.⁵⁵

22. Decisions mean that some drugs may be less available to NHS patients than they are in other countries, inviting the public to query why this is the case. For example, NICE eligibility criteria for anti-TNF α drugs for rheumatoid arthritis are pitched at a level that means that far fewer patients have access to these drugs than is the case in other European countries and the US.⁵⁶ For example, a recent survey showed that 47.9% of Norwegian and 41.3% of Danish rheumatoid arthritis patients currently on anti-TNF would not meet the NICE criteria.⁵⁷ It is also true that some drugs rejected by NICE have been approved in Scotland.

23. Although patient representatives are invited to Appraisal Committee meetings, in our experience their presence is cosmetic, and does not influence the committee's final decisions.

24. Although NICE claims to be independent,⁵⁸ there are clear examples where it appears that there has been political influence (eg the intervention of the Health Secretary to fast-track the assessment of Herceptin after a politically embarrassing court case, and B-interferon where the government intervened with a risk sharing special purpose scheme with the drug company⁵⁹). This raises the suspicion among healthcare professionals that political interference might take place at other levels of the process, despite the reassurances.

25. Because of the delay between initiating a technology appraisal and the final determination, patterns of treatment of uncertain cost effectiveness can become established. The longer they persist the harder they become to reverse. For example, some patients for whom biologic agents have been prescribed for ankylosing spondylitis, and who have done very well, may be denied ongoing access to their treatment if the Final Appraisal Determination bears any resemblance to the Appraisal Consultation document. Understandably, the withdrawal of effective therapy will be very unpopular with these patients and their clinicians and will undoubtedly result in local political pressure and adverse publicity.^{60, 61}

26. The general public may not be aware of the strategy that NICE has to explain its decisions and processes. Much of the strategy is laid out on their website, however this has a limited audience. As a consequence the process can have an unnecessary air of mystery which does little to give confidence to the wider public. NICE may engage with patients' representative groups, but the wider public gets its information mainly from the media, and then only on issues which have grabbed the headlines.

⁵⁴ National Institute for Clinical Excellence. Guide to the methods of the technology appraisal. London: NICE, 2004.

⁵⁵ Culyer A *et al.* Searching for a threshold, not setting one: the role of the National Institute for Health and Clinical Excellence. *J Health Services Research & Policy* 2007;12:56.

⁵⁶ Deighton CM *et al.* Updating the British Society for Rheumatology guidelines for anti-tumour necrosis factor therapy in adult rheumatoid arthritis (again). *Rheumatology* 2006;45:649–52.

⁵⁷ Hjardem E *et al.* Prescription practice of biological drugs in rheumatoid arthritis during the first three years of post-marketing use in Denmark and Norway: criteria are becoming less stringent. *Ann Rheum Dis* 2005;64:1220–3.

⁵⁸ Rawlins MD. Five NICE years. *Lancet* 2005;365:905–9.

⁵⁹ Department of Health. Cost effective provision of disease modifying therapies for people with multiple sclerosis. *Health Service Circular HSC* 2002/004.

⁶⁰ Gadsby K, Deighton C. Characteristics and treatment responses of patients satisfying the BSR guidelines for anti-TNF in ankylosing spondylitis. *Rheumatology* 2007;46:439–41.

⁶¹ Smith N *et al.* The potential impact of NICE guidelines on anti-TNF in ankylosing spondylitis. *Rheumatology* (in press).

The NICE Evaluation Process

27. Stakeholders such as BSR and patient representative organisations do not have the resources or the manpower to mount several appraisals simultaneously. These processes are incredibly time-consuming for all concerned.

28. Any individual or organisation that does not have grounding in health economics will find the arguments very difficult to follow.

29. Smaller organisations are effectively excluded from processes if they rely on volunteers and have no paid staff.

The Speed of Publishing Guidance

30. Because of the thoroughness of the evidence considered, the number of stakeholders even in single technology appraisals, and the appeals process, the speed of publishing guidance is very slow. For example, the NICE re-appraisal of anti-TNF was started in October 2004 with the consultation on the draft scope. The appeal will be heard in early April 2007. This means that by time the Guidelines are published, over two and a half years will have passed.

The Appeal System

31. Because the process is slow, and new evidence is emerging all the time, it seems perverse that NICE will not consider new evidence that is pertinent to the issues at hand. In the two and a half years of waiting for the NICE re-appraisal of anti-TNF therapy a great deal of new evidence has emerged that could have informed the process.

Comparison with the Work of SIGN

32. SIGN are considerably quicker at publishing guidelines. SIGN and NICE duplicate a great deal of work. It would be logical to look at ways of avoiding unnecessary duplication and the sharing of evidence and therefore speeding up the process, especially as in some instances the two bodies have reached contradictory conclusions.

The Implementation of NICE Guidance

33. NICE guidance is poorly implemented. This remains a key problem for BSR. A survey of rheumatologists revealed that 46% had limited access for their eligible RA patients to anti-TNF α four years after the initial NICE guidelines, with funding issues being the main reasons for lack of compliance from their PCTs.⁶² Although implementation of appraisals and guidelines is not a direct responsibility of NICE, the authority and purpose of NICE is undermined if its work is ignored or funding of approved products is unobtainable.

34. In 2005 (following the publication of NICE guidance on the topic) BSR, working with the Arthritis and Musculoskeletal Alliance (ARMA), commissioned a survey of 148 consultant rheumatologists. They were asked whether they were able to prescribe anti-TNF α therapy to all rheumatoid arthritis patients they identified, in accordance with NICE guidance, and if not what was the main barrier to prescription. 31% of rheumatologists were unable to prescribe for all patients they identified, with most saying that funding was the main barrier to prescription. The results showed that no improvement had been made since the same survey was undertaken in 2003 (before NICE guidance).

35. There are implementation problems with all guidelines that are not unique to NICE. A study of the implementation of NICE guidance came to the conclusion that NICE guidance is more likely to be implemented where “there is strong professional support, a stable and convincing evidence base, and no increased or unfounded costs, in organisations that have good systems for tracking guidance implementation and where the professionals involved are not isolated⁶³”. We are sure that the same could be concluded about the implementation of any guidelines. If guidelines court controversy, their uptake will be patchy. If opinion leaders, professional bodies and associations are critical of guidance it is unlikely to be accepted.

36. Many of the problems associated with poor implementation are often caused by a lack of ownership. There is still confusion between local and national powers, and despite a number of attempts to resolve these issues the problems still persists. A clear implementation strategy would help this.

⁶² Kay LJ *et al.* UK consultant rheumatologists' access to biological agents and views on the BSR Biologics Register. *Rheumatology* 2006;45:1376-9.

⁶³ Sheldon TA *et al.* What's the evidence that NICE guidance has been implemented? Results from a national evaluation using time series analysis, audit of patients' notes, and interviews. *BMJ* 2004;329:999.

37. NICE has a tendency to focus on new drugs that add to the budgetary demands of funding authorities. If they also assessed older drugs and technologies for which there was no good evidence to support their perpetuation, the release of funds might make acceptance of new drugs and technologies more palatable⁶⁴. Canvassing the opinions of NHS staff on appropriate topics for consideration by NICE might increase the chances of cost-saving initiatives being considered, increase the ownership of the process for NHS workers, and increase implementation of guidance.

British Society for Rheumatology

March 2007

Evidence submitted by Cancerbackup (NICE 42)

1. EXECUTIVE SUMMARY

1.1 Cancerbackup is the leading national charity providing information, understanding and support to people affected by cancer. The charity's specialist cancer nurses answer more than 60,000 enquiries a year from patients and carers on all aspects of cancer and its treatment. Cancerbackup's services include a telephone helpline, a wide range of booklets and factsheets, two award-winning websites and a network of local information centres. In addition to providing information and support, Cancerbackup works to promote patient-centred services and equitable access to high quality treatment, information and support for everyone affected by cancer.

1.2 Cancerbackup has long supported the principle of a body such as NICE. In a complex health world there is a need for an independent body to assess the cost effectiveness of healthcare. During the past year NICE has introduced the new Single Technology Appraisal process, a new implementation team and Government has issued the Best Practice Guidelines, updating and clarifying Health Service Circular 1999/176. Cancerbackup warmly welcomes these moves and believes that many more patients will benefit as a result.

1.3 However, it remains the case that the UK lags behind much of the rest of Europe:⁶⁵ we spend less than other countries on cancer treatments, and we are slower to provide them on the NHS. These delays and barriers to treatment mean that for many people with cancer treatments are not available in time to help them.

1.4 Since the inception of NICE Cancerbackup has campaigned to develop the NICE process and improve the implementation of guidance produced. We strongly believe that as a patient organisation our role in relation to NICE is three-pronged:

- to ensure the views of people living with cancer are represented in NICE technology appraisals and guideline development;
- to ensure that the processes NICE undertakes consider the needs and views of all people living with cancer their families and friends fully; and
- to ensure that NICE guidance on cancer is implemented across the NHS.

2. *Why NICE's Decisions are Increasingly Being Challenged?*

2.1 Throughout the cancer community there is a widespread sense of difficulty in accessing treatments for people with cancer. We acknowledge that not all cancer treatments will be approved, or even assessed, by NICE. However there is often a consensus amongst clinicians, patients and patient groups that specific treatments are particularly important for people with cancer and should be approved. It is in these instances that Cancerbackup would challenge a NICE decision.

2.2 Cancer treatments face specific issues which are not common to other disease areas.

- Treatments are frequently developed to tackle late stage cancers before they are developed for early stages of the same disease. In these late indications treatments often give small, incremental survival and/or quality of life benefits to patients. Whilst these benefits are hugely valuable to people with cancer, many of these treatments prove non cost-effective under the NICE Technology Appraisal processes.
- Quality of life issues can be specific to cancer treatments and not score highly within the NICE process. The impact of issues such as the oral administration of treatment in place of IV administration, chemotherapy induced fatigue and hair loss of patients undergoing cancer treatment and often in their final weeks of life are frequently undervalued.

⁶⁴ Maynard A *et al.* Challenges for the National Institute for Clinical Excellence. *BMJ* 2004;227-9.

⁶⁵ Nils Wilking and Bengt Jonsson (2005): *A Pan-European Comparison Regarding Patient Access to Cancer Drugs.*

- Cancer treatments are becoming increasingly targeted and are therefore effective for smaller groups of patients. However the development costs for such treatments remain the same as, and may in fact be higher than, those for disease areas with larger patient numbers. The adherence by NICE to a strict QALY limit means that these treatments are seen as not cost effective, despite the obvious benefits to people with cancer and the low overall NHS cost.

2.3 Whilst we understand the argument that in order to ensure equity across healthcare all treatments should be considered by the same process we feel that there is a strong case for a cancer specific work strand within NICE. See paragraph 4.6 for more information.

3. *Whether Public Confidence in the Institute is Waning, and if so Why?*

3.1 It is not public confidence in NICE that is waning so much as confidence in the ability of the NHS as a whole to provide gold standard and internationally comparable cancer care. When NICE appears to get a decision “wrong” (as mentioned above in paragraph 2.1) this undermines confidence in the NHS. Public confidence in the NHS is damaged further when treatments are available in the EU and even Scotland but not in England and Wales.

3.2 A recent MORI poll⁶⁶ carried out for Cancerbackup showed that nine in 10 British adults agreed that all groups in society should have equal access to cancer care, regardless of their age, gender, or walk of life; proving that the public values equity in cancer care. Importantly this statistic did not vary significantly across age groups.

3.3 Variations in the availability of treatments around the UK creates uncertainty about the level of cancer care the NHS would provide. The same poll also found that only seven in 10 British adults were confident that the NHS would provide good cancer care if they had cancer compared to nine in 10 people who have had cancer in the past five years.

3.4 A number of factors could support public confidence in NICE and NHS cancer care. In particular, promoting greater understanding of the role of NICE, changes to the evaluation process and above all a greater focus within the NHS on the implementation of guidance would all benefit the Institute’s public standing.

4. *NICE’s Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process*

4.1 Cancerbackup participates in NICE to ensure that the views of people living with cancer their families and friends are considered. We recognise that NICE’s evaluation processes are rigorous however we are particularly concerned by certain aspects of the technology appraisal process; in particular:

- how much weight is placed on the views of patients and patient groups;
- how QALYs are formulated;
- the formulation of assessment reports by the Evaluation Review Groups (ERGs);
- how orphan drugs and orphan disease areas are appraised;
- and how cancer treatments as a whole can best be appraised.

4.2 *Patient views*

4.2.1 As a patient organisation there is a concern regarding what evidence we can usefully add to the NICE process and how much this evidence is actually considered. The focus on cost per Quality Adjusted Life Year (QALY), statistical evidence and data from the manufacturers leaves little room for consideration of patient views. For example a recent Final Appraisal Determination stated:

“The Committee noted the clinical and patient experts’ views that [X] is a potential breakthrough for patients for whom no other treatment is available”,⁶⁷ before then issuing a negative decision on the treatment with little, apparent, consideration of the patient perspective.

4.2.2 The views of people with cancer and patient organisations must be fully considered and weighted within the appraisal process.

⁶⁶ *Cancer—A Public priority? Attitudes towards cancer treatment in Britain*. Research Study conducted for Cancerbackup, Ipsos MORI, August 2006.

⁶⁷ *Final Appraisal Determination, Erlotinib for the treatment of non-small-cell lung cancer*, NICE February 2007.

4.3 QALY

4.3.1 The NICE evaluation process focuses heavily on the cost per QALY of new treatments. We are concerned that the figures that make up the QALY do not include, or sufficiently weight, issues that are crucial to people with cancer.

4.3.2 We would very much encourage the Committee to probe further the assessment of the cost per QALY and question whether it fully considers:

- the impact of the treatment on quality of life;
- the value society places on symptom management in the last weeks/months of life;
- whether QALYs fully consider the costs to the wider NHS—with a long term perspective and across budget silos; and
- and whether QALYs should include wider societal costs such as the ability of someone with cancer to continue in employment or to care for their children?

4.4 Evaluation Review Groups

4.4.1 The NICE appraisal process relies heavily upon reports from the Evaluation Review Groups, especially in the case of Single Technology Appraisals (STAs). There are seven ERGs based within universities across the UK.

4.4.2 We are concerned that the conclusions these groups come to, the methods they use, and often therefore the results of an appraisal, vary between the ERGs. We would very much encourage the Health Select Committee to explore this stage of the process.

4.5 Orphan drugs and diseases

4.5.1 Cancerbackup is concerned that drugs designated as orphan products by the EMEA are unlikely to receive NICE approval if the same appraisal process and cost effectiveness threshold applies as for other treatments. NICE examined this issue in 2005 with its Citizens Council⁶⁸ and published draft recommendations in 2006.⁶⁹ NICE decided to divide orphan drugs into two categories:

- Orphan drugs—conditions with a prevalence of less than five per 10,000 of the population.
- Ultra-orphan drugs—conditions with a UK prevalence of less than one in 50,000.

4.5.2 NICE recommended that separate decision rules and a new a higher QALY threshold, up to £300,000 per QALY, would be needed to enable it to assess ultra-orphan drugs.

4.5.3 Cancerbackup believes that the EMEA definition of orphan drugs should be adopted and that a new process is needed to assess all orphan products. Cancerbackup believes this separate appraisal procedure should also cover treatment for rare cancers where the treatment is suitable for less than 5 per 10,000 of the population but where the manufacturer did not apply for orphan drug status at the time of licensing.

4.6 Cancer Specific Workstream

4.6.1 Cancerbackup believes that there are strong justifications for a cancer specific workstream within NICE. Assessing cancer treatments raises a very specific set of issues (as laid out in paragraph 2.2 above) and there are a large number of cancer treatments currently going through, or shortly due to start, the licensing process.

4.6.2 A cancer specific workstream could continue the model of the cancer specific Consideration Panel. It could ensure that those experts carrying out NICE appraisals on treatments for cancer fully understand cancer, the issues for people living with cancer and the specific set of issues associated with this condition. If this is to be successful it would be necessary to allocate sufficient resources to NICE for it to carry out its role successfully.

5. The Speed of Publishing Guidance

5.1 Throughout 2005 Cancerbackup campaigned to speed up the NICE technology appraisal process; naming 23 cancer drugs which were being held up in the system as a result of delays inherent in the way technologies were appraised. These delays meant that many cancer patients would be waiting for up to four years for new treatments to become routinely available on the NHS. For many, the delays meant that the treatments would not be available in time to help them.

⁶⁸ NICE Citizens Council Report: *Ultra Orphan Drugs*, November 2004.

⁶⁹ NICE: *Appraising Orphan Drugs*, March 2006.

5.2 The new Single Technology Appraisal (STA) process introduced at the end of 2005 has seen a considerable improvement in the time taken for treatments to pass through the NICE appraisal process. The new Consideration Panels for referring treatments to NICE are now looking at treatments and procedures far ahead of licensing and supporting a faster NICE process. We welcome this.

5.3 However of the eleven cancer treatments which have gone, or are in the process of going, through the NICE STA process six have received negative decisions⁷⁰ many due to a lack of evidence or cost effectiveness issues. If NICE is to continue to appraise new cancer treatments quickly we hope it will understand that data is often immature at license stage and cost effectiveness data may be best built up whilst the treatment is used within the NHS. Risk sharing agreements and early access agreements may need to be entered into in order to enable speedy use of new treatments within the NHS.

6. *The Implementation of NICE Guidance, both Technology Appraisals and Clinical Guidelines*

6.1 Cancerbackup is seriously concerned with the continuing problems regarding the implementation of NICE guidance. We believe that much greater emphasis should be given to ensuring NICE guidance is implemented.

6.2 We know from the recent report⁷¹ by the National Cancer Director that whilst the uptake of cancer drugs which have been approved by NICE is improving it varies by 2.2–3.3 fold across the country. Cancerbackup believes that an annual audit on the implementation of NICE guidance and support for those Trusts with a slow uptake of guidance is needed to reduce problems of postcode prescribing.

6.3 The Department of Health should set aside a pot of money as an “Innovation Fund”. This Fund should be available to fund the use of new cancer treatments which get their licence and/or NICE guidance part way through the financial year. This would ensure that new, innovative, treatments are made widely available across England and Wales as soon as possible. It would also support the implementation of NICE guidance in the first crucial few months.

6.4 The recent development by NICE of new commissioning tools and databases to aid implementation and the establishment of local representatives to explain guidance are to be welcomed. However the implementation of NICE guidance forms part of the Healthcare Commission’s assessment process and whilst Technology Appraisals are part of the Healthcare Commission’s Core Standards NICE Guidelines are only Developmental Standards.

6.5 NICE’s remit should be extended to include responsibility to work with the Healthcare Commission to promote and monitor implementation of NICE guidance. If this is to be successful it would be necessary to allocate sufficient resources to NICE for it to carry out its role successfully.

7. RECOMMENDATIONS

7.1 NICE needs to promote greater understanding of its role and processes.

7.2 The views of people with cancer and patient organisations must be fully considered and weighted within the appraisal process.

7.3 We would very much encourage the Committee to probe further the assessment of the cost per QALY.

7.4 We would very much encourage the Committee to explore the methods and conclusions of the ERGs.

7.5 The EMEA definition of orphan drugs should be adopted and a new process set up to assess all orphan products and treatments for rare cancers where the treatment is suitable for less than five per 10,000 of the population but where the manufacturer did not apply for orphan drug status at the time of licensing.

7.6 A cancer specific workstream should be set up within NICE to consider cancer treatments. If this is to be successful it would be necessary to allocate sufficient resources to NICE for it to carry out its role successfully.

7.7 To support positive results from the new STA process NICE must understand that clinical data is often immature at license stage and cost effectiveness data may be best built up whilst the treatment is used within the NHS. The use of risk sharing agreements and early access agreements to enable speedy use of new treatments within the NHS should be considered.

⁷⁰ In some cases this is not yet the final decision or is subject to appeal.

⁷¹ *Usage of cancer drugs approved by NICE. Report of a Review undertaken by the National Clinical Director, Gateway number 7124, 20 September 2006.*

7.8 The Department of Health should set up an “Innovation Fund” to fund the use of new cancer treatments which get their licence and/or NICE guidance part way through the financial year.

7.9 NICE’s remit should be extended to include responsibility to work with the Healthcare Commission to promote and monitor implementation of NICE guidance. If this is to be successful it would be necessary to allocate sufficient resources to NICE for it to carry out its role successfully.

Joanne Rule

Chief Executive, Cancerbackup

March 2007

Evidence submitted by Cancer Research UK (NICE 67)

1. SUMMARY

1.1 Cancer Research UK welcomes this timely inquiry and the opportunity to be involved in this debate. Cancer Research UK believes that the current approach to NICE and NHS access to anti-cancer treatments requires urgent review.

1.2 Cancer Research UK would be very pleased to provide oral evidence to this inquiry as it progresses.

1.3 This inquiry is particularly important for cancer. There are an increasing number of potential new anti-cancer treatments coming through the research pipeline. Combined with increasing public pressure for their provision by the NHS, this means that if cancer patients are not to be disadvantaged the framework within which NICE operates needs to be better defined.

1.4 It is of paramount importance to note however, that it is the combined effect of the way in which NICE operates alongside the Pharmaceutical Price Regulation Scheme (PPRS) that particularly disadvantages cancer patients in the UK.

1.5 It is vital that the quality of NICE appraisals is of a consistently high standard. To this end, reform is needed to address:

- The use of appropriate expertise on appraisal committees;
- The consistency and transparency with which appraisals consider quality of life measures;
- Cost considerations, such as whether calculated cost to patients covers solely the cost of the drug or includes the total cost of treatment;
- The extent to which appraisals take account of indirect treatment costs and savings; and
- The transparency of the appeal process, and whether this is conducted by an appropriately representative body.

1.6 Much has been made of the role that NICE could play in the future development and availability of treatments in the NHS. We would like to see NICE, the Government and the pharmaceutical and biotechnology industries working closely together with independent expert organisations, such as Cancer Research UK, to further develop these emerging ideas.

1.7 We note that the previous Health Select Committee inquiry into NICE in 2003 produced a number of laudable recommendations for how NICE might improve involvement, transparency and external perception of the organisation. We note that while a number of these recommendations have been taken forward, others have not. We would welcome, as part of this inquiry, a review of all these recommendations within the current climate.

2. BACKGROUND

2.1 As the major non-commercial cancer research funder in the UK, and as a charity directly supported by one in 10 people in the UK, Cancer Research UK is a unique and important stakeholder in this debate. Our focus, as always, is in achieving the best possible health outcomes for patients with all forms of cancer.

2.2 We fully understand and support the role that NICE plays in providing guidance to clinicians and the NHS both on clinical effectiveness, and on whether a new medicine constitutes value for money for the NHS. The number of innovative new anti-cancer therapies being approved puts pressure on NICE and on the NHS to make these therapies available to patients.

2.3 Our rapidly increasing level of understanding of how cancer develops has led to a new era of development of new anti-cancer therapies. A new generation of cancer therapies, targeted at the specific abnormalities found in cancer, are already becoming available. There are currently over 1,000 anti-cancer therapies in development. The whole pharmaceutical industry is investing heavily in oncology.

2.4 It is recognised that many of the newer treatments are being priced at levels much higher than historical averages. This, coupled with growing cancer incidence and expected lower levels of funding for the NHS, looks set to place strain on the NHS budget. This strain will also increase through future best practice using combinations of the newer, more expensive treatments.

2.5 We fear that the current NICE and PPRS processes work in conjunction to systematically undermine the adoption of new cancer treatments in the NHS. In areas where there are few or no competitor treatments the profit-cap system of PPRS actively encourages treatments to be priced as high as possible. These therapies will generally be those in areas of unmet medical need, such as cancer. Conversely in those addressing diseases for which a wealth of treatments options exists, such as cardiovascular disease, the PPRS encourages companies to set prices at suitably competitive levels. This problem is exacerbated by the current NICE process, which judges treatments according to the price set by manufacturers. The result is that expensive cancer treatments in areas of highest unmet medical need are therefore unlikely to receive NICE approval.

2.6 Furthermore, clinical development of the majority of new drugs is conducted in the end stage of the disease. This is due both to the often high toxicity of new cancer therapies, and the nature of disease, which means that proven treatments are used in the first stages of disease to prolong life, with newer-unproven treatments only resorted to when all other options fail. However, when setting the price of these treatments, manufacturers are aware that further research in an active clinical setting is likely to uncover suitable populations of patients at an earlier stage of their disease. This will naturally be a much larger market, and one where value for money is higher. Under the current PPRS, price negotiations with the Department of Health only ever result in a decrease in price. The manufacturers will therefore initially set as high a price as possible for their new therapy. When NICE then come to appraise such a treatment, they will necessarily find it too expensive in the population for which data are available, and in which marketing authorisation has been gained.

2.7 We are keen that solutions are found to these problems and we want to work with Government and the pharmaceutical industry to do this. The UK is a world-leader in the discovery and development of new anti-cancer treatments, but is perceived as being backward in the use of these new medicines. This is surely an untenable situation.

2.8 Our response to the specific areas raised by the Committee and the future role of NICE in the pricing and development of new treatments are below.

3. *Why NICE's Decisions are Increasingly Being Challenged*

3.1 As exciting new treatments are approved by regulatory agencies for use, it is inevitable that patients will expect access to them. We have already seen individual campaigns to lobby NICE and the Department of Health for specific anti-cancer medicines to be funded by the NHS. We expect that an increasing number of NICE decisions will be afforded a high media profile, particularly when the decision is negative.

3.2 This confusion is not helped by uncertainty among the health community (both professionals and patients) around the method by which NICE appraisal committees calculate whether a drug is cost effective. This is particularly true for the application of the "willingness to pay" threshold, which is generally accepted to be around £30,000 per QALY.⁷² Transparent public discussion around the threshold figure and its appropriateness is important and required.

3.3 The public should know where the £30,000 figure came from and why it is set at that level. We urge the Committee to recommend that Government enter a debate with stakeholders about what threshold is appropriate for a country such as the UK and for the NHS in the future.

4. *Whether Public Confidence in the Institute is Waning, and If So Why?*

4.1 Recent media coverage on NICE and its decisions suggests that public confidence in the Institute is not high. We believe that much of this is due to a misunderstanding of NICE's role in the process of making NHS treatments available to patients.

4.2 As a UK funder, we also consider it central to our role to ensure that the new and more effective treatments, all of which result from research, are accessible to cancer patients in the whole of the UK. There is a fear that the public's response to negative NICE decisions may develop into a lack of faith that medical research and medical research charities' advances are delivered to patients.

4.3 Indeed, the public may question the value of donating to cancer research if the resulting discoveries are then deemed too expensive for UK NHS patients to receive. Were this situation to worsen, it would obviously be very serious not only for medical research charities but also for the whole of biomedical research with its associated economic benefits in the UK.

⁷² Cost per quality adjusted life year.

5. *NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process*

5.1 A greater number of more expensive anti-cancer treatments are gaining UK marketing approval. Combined with the increasing public scrutiny of NICE's decisions, it is increasingly important for Government to assess the evidence for the cost-effectiveness threshold and how it is determined by NICE.

5.2 We welcome recent moves by NICE to improve the transparency of its processes, but believe that more should be done. This is particularly important in terms of the weight and consideration given to quality of life evidence considered in NICE appraisals, especially where data from clinical trials are lacking at the time of appraisal.

5.3 We also believe that there are circumstances where it is appropriate that exceptions to NICE's cost-effectiveness rules should be made. Examples of this include orphan indications for which there is a therapeutic void. It is important that the Government considers how flexibility may be built into the current process to address this need.

5.4 We welcome recent moves by NICE to actively pursue disinvestment in older, potentially poorly effective treatments, to free up resources for new treatments in the NHS. However, NICE must be adequately resourced to undertake these tasks.

5.5 It is currently unclear how dates for future review of NICE guidance and appraisals are set. It is important that review is not set for a somewhat arbitrary future date but should be undertaken when the specified additional information becomes available.

6. *The Speed of Publishing Guidance*

6.1 While the NICE approval process must be deliberative and consultative it must not unduly delay patients getting access to the best treatments. In the case of some new anti-cancer therapies, it is clear that beneficial treatments are not getting to patients as swiftly as they ought.

6.2 We welcome the introduction of NICE's Single Technology Appraisal process, which has been shown to be faster and effective. However, it is important that the existence of such a process does not disadvantage drugs being appraised by NICE not selected for this process.

6.3 It is also important that drugs are referred to NICE in a timely manner, and at an appropriate time in their development. For new treatments this will need, at least, to be brought in line with the time of successful application for Marketing Authorisation.

7. *The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines*

7.1 It is widely recognised that, despite a positive NICE appraisal, situations still exist where PCTs do not make an approved drug quickly available to their patients. The "postcode lottery" remains real.

7.2 It is important to recognise that while the current legislation states that NICE approved treatments should be made available within three months, PCTs are required to find funding for these treatments from their existing budgets. It may be that a separate ring-fenced budget is required to ensure new treatments approved within a financial year are made available to patients.

7.3 While the recommendations of NICE clinical guidelines are necessarily not mandatory we would like to see more emphasis on consideration of these recommendations at the local level. We would like to see it made a condition of the Healthcare Commission "Annual Health Check" that PCTs record how recommendations of emerging NICE guidelines have been considered and incorporated into future decisions.

8. *NICE's Role in Encouraging Future Research Activity*

8.1 Currently, when a negative announcement is made by NICE on a particular drug, there is no mandatory next step in terms of further research. We need, collectively, to be able to turn negative NICE decisions into positive action.

8.2 We believe that where a need for further research is identified by NICE, Government, the research community and industry should commit collectively to ensuring that appropriate further research is conducted to identify possible specific applications for the drug. In the case of cancer treatments, Cancer Research UK would be more than willing to facilitate this research.

8.3 We endorse the need highlighted in the Cooksey Review of UK Health Research Funding to identify resource to support NICE's research recommendations. We believe that a separate funding stream for NICE dedicated to taking these research recommendations forward would be the most appropriate solution.

8.4 There is also a need to establish formal arrangements between NICE, the NHS and the commercial sector to ensure that the output of research can be fed more systematically back in to the NICE review process and inform future recommendations.

9. NICE's Role in Setting Drug Prices for the NHS

9.1 Fundamental to the issue of access to medicines is the price set for them and Government's role in influencing those prices. We welcome the recent report from the Office of Fair Trading (OFT) recommending future reform of the Pharmaceutical Price Regulation Scheme. It is important that the difference between the cost of production and price of treatments is appreciated and carefully considered.

9.2 The current pricing mechanism disproportionately disadvantages new cancer treatments, because they often address an unmet need and often carry a higher price than other treatments. The conclusion of the OFT that there are several medicines for which the cost to the NHS significantly "outweighs their benefit to patients" and proposals that the current "profit-cap- and price-cut" scheme be replaced by a value-based pricing scheme clearly opens up an opportunity for the involvement of NICE. We would welcome further discussion about the role of NICE in future drug pricing.

9.3 We would fully endorse the introduction of conditional approvals by NICE. We consider it completely appropriate that NICE have a role in establishing the price the NHS is prepared to pay for particular treatments. The appraisal process would thus look at how effective NICE considers the drug to be, in comparison to other treatment options available. Then, rather than simply rejecting a new treatment based on a price set by the manufacturer, NICE should make recommendations on what an acceptable price would be for the treatment until new data is available that might justify a higher price.

9.4 We believe that a new system with a greater role for NICE would not disadvantage manufacturers as it would include flexibility for future changes in drug prices as more data become available.

10. NICE's Role in the Drug Development Pathway

10.1 We believe that positive action is needed to address current disincentives to development and innovation in the UK. A culture of cautiousness in adopting new technologies in the NHS and limitations set by the necessity for new technologies to be approved for use in the NHS act to restrict or delay access by patients to appropriate treatments.

10.2 We support recent discussion on how NICE can be integrated earlier in the process of drug development. However, we are concerned that these proposals are unlikely to work in practice. The UK constitutes only 3% of the global market for pharmaceuticals and is slow in adopting new treatments. It is highly unlikely therefore that companies would reconfigure their global clinical trials strategy around UK considerations.

10.3 Notwithstanding this, we do believe that companies should be encouraged to involve NICE in the process of drug development. A dialogue between NICE and companies, similar to that which already takes place with the Food and Drug Administration in the USA and the EMEA in Europe prior to finalising the design of clinical trials, would be very helpful.

10.4 A more open and permissive approach to the pharmaceutical and biotechnology industry to foster closer working relationships and intelligence sharing is likely to have long-term benefits in this area. It is important that changes to the drug development process are established with the involvement of all major funders of research, including charities, across the UK.

Cancer Research UK

March 2007

Evidence submitted by the Roy Castle Lung Cancer Foundation (NICE 24)

EXECUTIVE SUMMARY

RCLCF has engaged with NICE as a Patient Group, in both the NICE Technology Appraisal Process and in the Clinical Guideline Process:

- NICE decisions are increasingly being challenged, as many of their negative appraisals are deemed grossly unfair.
- Public confidence in NICE is waning.
- The opinions of Patient Groups do not appear to have weight within the process. Technology Appraisals are heavily influenced by health economists.
- The NICE appraisal process is far too long. Patients with life threatening and debilitating illnesses do not have time to wait. Until a positive NICE appraisal, there are considerable barriers to patients receiving new technologies.
- Having separate NICE and SIGN guideline writing processes represent a waste of resource. However, collaboration in literature review, as in the Lung Cancer Guideline, was unsuccessful.

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- NICE Technology Appraisals tend to be implemented. However, only some recommendations in Clinical Guidelines are acted on.

BACKGROUND

The Roy Castle Lung Cancer Foundation (RCLCF)

The Foundation is a UK wide charity, dedicated to the defeat of lung cancer. It funds basic science research, tobacco control initiatives and work in lung cancer patient information, support and advocacy. The Foundation, through its network of lung cancer patient groups, its information helpline, its Patient Advisory Board and Annual Patient Meeting, has the ability to collect the views of lung cancer patients. Ensuring equitable access to best treatment is of clear and obvious importance.

RCLCF and NICE

RCLCF has had contact with NICE, since the Institute was created. As a charity, reflecting the views of its lung cancer patient group, the Foundation has acted as a formal consultee in the NICE Health Technology Appraisal Process (submitting comment and attending two technology Appraisal Committee meetings, in 2001 and 2007) and also in the Guideline Development process. During the development of the NICE Guideline for the Diagnosis and Management of Lung Cancer, RCLCF's Medical Director chaired the Guideline Development Group. This three year process, including collaboration with the SIGN group, gives her a fairly unique perspective.

Why NICE's Decisions are Increasingly Being Challenged

1. Patients and their families are increasingly aware that the NHS, because of financial constraints, does not always provide the best treatment and care possible. For individuals, this is important. With widespread use of the internet and health information in the media, it is easy for patients and patient groups to find out what new technologies are widely available elsewhere. When NICE, then, make a decision contrary to this, patients will be aware of the unfairness. Also, with the Scottish Medicines Consortium making much speedier technology decisions, any time that SMC and NICE decisions are different, it will be deemed to be grossly unfair.

Whether Public Confidence in NICE is Waning

2. Yes. Without doubt, public confidence is waning. Recent high profile rejections by NICE, for technology in debilitating and life threatening illnesses, have been deemed to be unfair. There appears a lack of understanding by NICE, of the importance to individuals, of relatively small improvements in quality of life and control of symptoms.

NICE's Evaluation Process and Whether any Groups are Disadvantaged

3. It is our observation, given recent experience in the NICE Technology Appraisal Process, that although NICE asks Patient Groups and Clinical Experts for submission and advice, their focus appears to be on the Health Economic Assessment alone. Even when clinician and patient experts, are convinced of the benefits of a given technology, they are apparently ignored, if the findings of the Evidence Review Group differ. As a patient group engaged in the process, we are not convinced that our contribution is given weight.

The Speed of Publishing Guidance

Technology appraisals

4. There is no doubt that the established process was far too long. In diseases, such as lung cancer, where the median survival from diagnosis to death is only six months, patients do not have time to wait for new technology. As examples, NICE have recently appraised Pemetrexed and Erlotinib for advanced lung cancer. Part way through the process it was switched to the Single Technology Appraisal system. Despite this, EMEA approval was given for Pemetrexed in November 2004, with the guidance being issued in February 2007. For Erlotinib, EMEA approval was granted in September 2005, with the NICE guidance issues in March 2007. These timelines are far too long. It will be interesting to see what impact the Single Technology Appraisal process will have. We do, however, have concerns that the STA process will lead to a rejection of increasing numbers of technologies, recommending review of the guidance in one year. This will, of course, create delay for patients.

Clinical guidelines

5. The Clinical Guideline for Lung Cancer Diagnosis and Treatment took three years from scoping to publication. The “cut off” date for the research review was one year before the publication. This meant that the guideline was already out of date at the time it was published. This process is far too long and, given the rolling nature of research evidence, updating after two years is too long to wait for review.

The Appeal System

6. To date, we have no closely involved experience of the Appeal System. However, at the time of writing this submission, we are in the process of submitting Grounds for Appeal on the recently rejected Erlotinib review. It is somewhat ironic that, despite the length of the Technology Appraisal Process, we are required to lodge grounds for appeal within a mere 14 days of the decision. This, we find, to be a very short turn around, given the serious nature, to our patient group, of the situation.

Comparison with SIGN

7. At the same time as NICE was developing Guidance for Lung Cancer Diagnosis and Treatment, SIGN were updating its Lung Cancer Guideline. As the chair of the NICE development group, I observed the following:

- In the NICE process, literature review and assessment of research papers are done by professional reviewers. In the SIGN process, the review is done by reviewers, but the assessment of papers is done by clinicians, in their spare time. This, I would suggest, adds clinical bias to the process and is a poor use of clinician time. It is my personal observation, that the NICE process is more independent and does work.
- Collaboration was agreed in the literature review of the two lung cancer processes. SIGN undertook one third of the literature review for both processes, NICE one third for both processes and the final third, each undertook separately. This seemed reasonable in principle, however, was completely unsatisfactory for both groups.
 - As the two Guideline Development Groups had developed separate Guideline Scopes, there were some areas, felt key by the group, which were not covered by the others reviewers. This caused much complication.
 - During the process, the SIGN group had resource and personnel issues, which meant their timescales drifted massively. This had a delaying effect on the NICE process.
- Having two separate processes, reviewing the same scientific literature, is a massive waste of resource. However, collaboration in the literature review, as carried out in this case, was unsuccessful.

*The Implementation of NICE Guidance, Which is Acted on**Technology appraisals*

8. It is clear that much attention is paid to these. Indeed, there is considerable difficulty for many patients and clinicians, in accessing new medicines (our experience is, obviously with anti-cancer medicines), until they have been approved by NICE. On approval, our experience suggests that this guidance is, in the main, implemented.

Clinical guidelines

9. Having had published guidance for Diagnosing and Managing Lung Cancer since February 2005, it is clear that many recommendations have not been implemented. For example, a key recommendation was that patients are able to access specialist lung cancer nurses, throughout their patient journey. Despite this, it is clear, that in some Trusts, such nurses are viewed as a “frill” and with current financial pressures, some lung cancer specialist nurse posts have been under threat, whereas others have been required to work shifts on general wards, reducing their lung cancer patient commitment.

10. That said, the recommendations, within the Clinical Guidelines, have given clinicians and patients a supporting tool, when negotiating service provision. Good examples from the lung cancer guideline are the provision of second line chemotherapy in advanced non small cell lung cancer and the provision of PET scanners.

Dr Jesme Fox
The Roy Castle Lung Cancer Foundation

March 2007

Evidence submitted by the Continence Foundation (NICE 23)

The Continence Foundation is a small UK-wide charity concerned with bladder and bowel control problems in adults. Our membership includes members of the public as well as a wide range of health professionals (clinicians, GPs, nurses, therapists etc) The involvement of the charity with NICE is substantial:

- Work has been carried out on two Guidelines in the continence field since 2003: one on urinary incontinence in women was published in October 2006 and another on faecal incontinence is due for launch in June 2007. We have been involved in a long campaign for a guideline concerning male continence problems, and other groups excluded from the urinary incontinence scope.
- Technology Appraisals in this area have been concerned with surgical procedures. A suggestion was made concerning a TA on a drug but this was not followed through.
- Interventional Procedures in this clinical area are regularly considered.
- As current Chair of the Patients Involved in NICE (PIN) Group, the Director of the Continence Foundation, Dr Judith Wardle, is in regular contact with many other organisations representing patients and also with the Patient and Public Involvement Unit of NICE.
- Our recommendations appear at the end of this submission.

Why NICE's Decisions are Increasingly Being Challenged

1. NICE guidance has been challenged since it began work in 1999: some people will remember, for instance, the challenge regarding the guidance on beta interferon. What has changed is the increasing profile of such challenges, which in turn encourages more individuals, as well as patient groups, to challenge decisions. There is also more willingness by clinicians to challenge decisions.

1.1. Some of the increase may be attributable to changing attitudes: a more combative approach to official decisions of any kind. This is compounded by the attitude of the media which likes to publicise stories about an individual mounting a challenge, and sometimes does this without any attempt to understand the complexities of the clinical recommendations: which individuals can benefit from a treatment, whether evidence is as yet insufficient to make definite recommendations etc. But challenges are also being made because of loss of confidence that NICE's decisions are unbiased: see comments in the next section.

Whether Public Confidence in the Institute is Waning, and if so Why

2. Public confidence in NICE decisions is waning as part of general attitudes to what is happening in the NHS. There is a perception that decisions in the NHS, both nationally and at PCT level are being driven far more by cost than by clinical effectiveness. People see that individual PCTs are indeed cutting services without sufficient consideration for the long-term consequences. Therefore, they see NICE as part of that process, so that NICE is blamed for the refusal of treatment to individual patients, even where it is the PCT Board and not the NICE guidance that is behind that refusal.

2.1 NICE is regarded as insufficiently independent. Politicians actually had an even greater influence until recently over which topics were considered by NICE, since NICE is now allowed to make its own selections of which topics to propose. However, the decision about which topics go forward and the precise wording of those topics chosen for Guidelines, still lies with "the minister". This means that organisations, whether clinicians or patient groups, are unable to get any information about why a particular topic and the client groups to be covered were chosen, or to challenge those decisions. Indeed, it is impossible to find out whether ministers have ever refused to let a topic go forward. There is a widespread belief that some guidelines have been created because of high profile adverse events that were seen to be politically damaging. However, the lack of transparency about the process of deciding which guidelines should proceed means that it is impossible to know whether this belief is well-founded.

NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process

3. As stated above, there is a lack of transparency about which topics are chosen for evaluation.

3.1 Although individuals and organisations may now suggest topics for evaluation, there seems to be no mechanism for providing feedback to the people who made the suggestion regarding whether it has been accepted into the process and its progress through the system. It is essential that this is rectified if trust in NICE is to be restored. See final section of this submission, regarding problems of communication with NICE.

3.2 It is difficult for lay people from whatever background to participate in NICE evaluation processes. Even where the Interventional Procedures team of the PPI Unit supplies a lay explanation of the procedure, that is little help with understanding the document sent out for consultation. Lay members of a Guideline Development Group may have real difficulty with long tables of evidence presented, unless the staff from the collaborating centre supply verbal explanations of what particular studies claim to prove and any flaws in the study design. While some collaborating centre staff are very conscious of the mixed nature of a guideline development group, others need training in communication skills.

3.3 Where lay people are members of a Guideline Development Group, they can be made to feel sidelined by the attitude of the clinical members of the committee. In some cases, the clinicians concerned may not even realise how dismissive they are being about “non-expert” comments. The extent to which lay members feel welcomed seems to vary according to which collaborating centre has the lead: this needs to be investigated. The PPI unit offers training to lay participants to enable them to participate in NICE processes, but there is no training offered to health professionals in how to work with lay people.

3.4 Health economists seem to find it particularly difficult to present their work in a form that is intelligible to the non-specialist. It is, therefore, very difficult for a lay participant to challenge the economic evidence.

3.5 Regardless of the comments above, the Continnence Foundation recognises that NICE’s international reputation for producing guidance based on detailed, unbiased consideration of the evidence is richly deserved.

3.6 Perhaps, NICE’s communication team needs to do more to publicise to the general media just how much work goes into each document produced.

3.7 There should also be greater emphasis on how NICE responds to stakeholder comments: all comments made about a draft guideline (except for a few that are “commercial in confidence”) and the responses to those comments from the Guideline Development Group, indicating whether the final version has changed as a result, are made available when the final version of the guideline is published. However, only someone aware that these documents can be found in the “Development History” of a guideline, would think to look. If stakeholder comments were more prominent, the public would have more confidence that NICE is being transparent about how it responds to pressure groups of all kinds, including manufacturers. Also, NICE should discourage manufacturers from marking their comments “in confidence”: we have seen comments so designated that would not reveal anything that could affect the manufacturer’s business.

3.8 There is concern that staff of NICE central office edit some of the recommendations made by guideline development groups: this can dilute the clinical value of the message.

The Speed of Publishing Guidance

4. Since NICE has only recently changed its timetables for producing guidance—both Guidelines and Technology Appraisals—we feel the shorter timetables should be allowed to bed down before any further changes are suggested.

The Appeal System

5. We have no experience of this.

Comparison with the Work of SIGN

6. Our only experience of the work of SIGN is the guideline on “Management of Urinary Incontinence in Primary Care.” SIGN does not publish the evidence for guidelines in the great detail provided by NICE—we assume that the literature review, however, is equally thorough.

6.1 It seems to have greater acceptance by both health professionals and the public for the guidelines. This may be because they collect evidence at an early stage from patient and carer groups about the issues they would like to see addressed. The recommendations in the guideline on urinary incontinence are presented in clear language, giving both the implications for practice and what the recommendations mean for patients.

6.2 We also note that the average time line for production of guidelines is shorter than for NICE.

The Implementation of NICE Guidance

7. The process of producing guidance for implementation is flawed. During the period when consultation is taking place on a draft guideline, an implementation group is convened. We have no way of knowing how the decision is taken about who to invite to join that group. The implementation group is supposed to help NICE’s implementation team to produce documents to aid implementation, but they are doing this without knowing whether there will be significant changes to recommendations as a result of the consultation. This gives the impression that very little is likely to change. The implementation team seek assistance from other

people suggested by the implementation group and then produce drafts of slides to aid implementation and members of the group may comment. The next anyone sees of those slides is when they are published with the final guideline, with no attempt made to explain any changes. The slides and the economic report are very selective about which aspects of the full guideline are focussed on. In the case of the guideline on urinary incontinence in women, a recommendation for the use of a non-proprietary form of a drug (which has side-effects which are poorly tolerated) formed part of the initial costing. The recommendation was clearly made on cost grounds, not on clinical effectiveness, but it was omitted from the final version of the costing report on the grounds that it would have “a minimal budget impact nationally”. This sent out mixed messages to those who might implement the guidelines regarding whether the recommendations were to be treated seriously or not. NICE currently has no ongoing relationship with the members of the implementation group after the publication of the guideline concerned.

7.1 Monitoring of implementation is provided by the Healthcare Commission, but Trusts are only asked a general question about whether they are implementing NICE guidance: there is no specific information about particular guidance. Detailed evidence about failure to implement is generally provided by patient organisations, with help from individual clinicians who feel they are not being allowed to give their patients optimal treatment because their local Trust is not prepared to fund it. Patient organisations would prefer to work with NICE to monitor implementation of guidance—especially where they agree with that guidance. However, there is no mechanism for NICE to support that work. We appreciate that NICE does not have the manpower to monitor all individual guidance. However, we believe that a mechanism needs to be found to monitor a selection of individual guidance, perhaps on the basis of suggestions by either patient or professional groups.

7.2 For monitoring of implementation to work, recommendations in guidelines need, as far as possible, to have auditable outcomes. This needs to be made clear to guideline development groups at an early stage.

Additional Comment on Communication with NICE

8. The Continence Foundation has made an official complaint to NICE about repeated failures of communication. The Foundation has not been able to find out why a guideline topic on urinary incontinence was restricted to women, even though a significant number of stakeholders said, during the consultation on the Scope that it should cover both sexes—NICE would not tell us how many of the stakeholders said this. Subsequently the Foundation has worked with other charities and the British Association for Urological Surgeons (BAUS) to persuade NICE to start the process for a guideline on urinary incontinence in men (and also people with neurological conditions, who were also excluded from the first guideline). After our initial discussions, voluntary feedback from NICE was non-existent. Requests to specific individuals for information on progress were met with promises to report back, but the promises were not fulfilled. At one point, the Foundation and BAUS put in a detailed submission to support the topic. We are now in a situation where there are not one but two guidelines somewhere in the system and no-one seems able to explain why the topic was split in two. There are staff and clinical advisors to NICE now working on moving the guidelines forward, including one neurological conditions; but what concerns us most is that no-one at NICE seems to want to identify the lessons to be learnt from what has gone wrong.

8.1 The Continence Foundation would be willing to share with the Health Committee the text of its complaint to NICE and the inadequate reply received, but would prefer the material to remain confidential, since we are hoping eventually to resolve the matter with NICE.

Recommendations

- Remove the political influence from topic selection, or if that is not accepted, be open about which decisions on topics have been influenced by ministers.
- Where an individual or group has proposed a topic, feedback should be provided on whether it has been accepted and if so, on its progress.
- Training should be given to staff of collaborating centres on how to present evidence to groups that include lay representatives.
- Training should be given to health professionals on working in groups with lay representatives: SIGN already does this.
- Stakeholder comments on draft guidelines and the guideline development group replies should be made more prominent on the NICE website. This would give the public more confidence that NICE is operating transparently.
- NICE should discourage manufacturers from designating their comments “in confidence” when they do not contain any commercially sensitive information.
- NICE should adopt from SIGN the practice of asking patient and carer groups in advance what issues they would like addressed in a guideline: the groups consulted would be wider than those actually represented on the guideline development group.

- NICE should clarify how the members of an implementation group for a guideline are chosen. They should work more closely with that group on developing the implementation documents, and continue to liaise with them after publication of the guideline to encourage and monitor implementation.
- A mechanism should be found to monitor a selection of individual items of guidance, perhaps on the basis of suggestions by patient or professional groups.

Dr Judith Wardle
Director, Continence Foundation

March 2007

Evidence submitted by the Cystic Fibrosis Trust (NICE 43)

Executive Summary

The Cystic Fibrosis Trust wishes to put its experience of NICE before the Health Select Committee for the following reasons:

1. Since the launch of NICE, the Cystic Fibrosis Trust has worked constructively with them to try and improve the care of those with Cystic Fibrosis.
2. We are becoming increasingly frustrated by the lack of output, lack of adequate communication as to why this is, and concern that for a condition affecting a relatively modest number of people, the Government is reluctant to set targets or standards which often lead to sub-optimal care.
3. In this context, we feel that those with Cystic Fibrosis are a disadvantaged group. There are no nationally agreed clinical guidelines which those offering CF care have to meet.

Background

The Cystic Fibrosis Trust have actively engaged with NICE on a number of its initiatives. These include:

- the consultation process on living donor lung transplantation;
- the use of IVs at home;
- breast feeding; and
- the use of a particular antibiotic, TOBI.

However, our concern focuses on the lack of clarity as to where our detailed application for a clinical guideline for all aspects of the care of children and adults with Cystic Fibrosis to be developed by NICE has gone.

Detailed Case

Having contacted NICE in 2002 to better understand how topics were selected for consideration by NICE, we were informed that there was to be an imminent web-based consultation and applications could be made by individuals or patient groups for a particular technology appraisal or a clinical guideline. The announcement was, in fact, made just before Christmas 2002. The Cystic Fibrosis Trust worked very hard over the Christmas and New Year period and submitted an application on 29 January 2003 for a clinical guideline. A copy of this application is attached.

We then waited to hear how the application had been received and whether it would be reviewed. We heard nothing until May 2004, one year and four months after our application had been sent in. We were very pleased to receive an e-mail which stated that we had successfully gone through the first tier of the sifting process, a committee appropriately called the Topic Sift Committee, and we were now going to be referred to the Advisory Committee for topic selection. We were pleased to hear that an eminent CF Consultant, Dr Diana Bilton of Papworth Hospital, had been appointed as a medical adviser to this committee. The Cystic Fibrosis Trust was asked to comment on the briefing notes for this committee, which we did in June 2004 (copy attached).

We then heard, in December 2004, from two or three CF Consultants who had been asked to attend a meeting to discuss this report. They were given virtually no notice and were very concerned that at such short notice they were unable to attend.

At a similar time, the Cystic Fibrosis Trust was invited to attend and indeed to lead a workshop organised by NICE on the pilot study which had resulted in the web-based application and the processes being considered for its expansion. We were told at that stage that we were invited as a successful applicant of the

process, which we were very pleased to hear, but this was the first news we had that we were indeed a successful applicant. The Cystic Fibrosis Trust attended the workshop and learnt a great deal more about the process.

Then all went quiet once more. We heard nothing in 2005, and in spite of frequent requests for information from NICE were unable to get any feedback as to what was happening to our application. We decided to attend the NICE Conference in December 2005 with the specific objective of finding the status of our application and where it was in the system. Three of us from the Cystic Fibrosis Trust attended—Rosie Barnes (Chief Executive), Cara Doran (Expert Patient Adviser) and Jacqueline Ali (Publications Officer). We spoke to the Chairman of NICE as well as a number of key individuals, and nobody was able to give us any information about what had happened to our application. However, we were promised feedback from the Planning & Resources Director, Andrea Sutcliffe. We followed the Conference with a letter to Andrea Sutcliffe and to Professor Sir Michael Rawlins, and wrote again to Sir Michael on 3 February 2006. We received a reply dated 24 February 2006 informing us that our proposal had been considered by the Joint Planning Group and would be considered again at their next meeting in March 2006, after which Andrea Sutcliffe would write and let us know any decisions taken.

Again, we heard nothing and in spite of frequent checking of the website, could find no reference to our application.

We subsequently learnt that Dr Jayne Spink, who whom we had had a good working relationship at the Gene Therapy Advisory Committee, had transferred to NICE as Associate Director in the Centre for Clinical Practice. We dropped her a line to see if she could check on the whereabouts of our application. She replied to let us know that she had spoken to Professor Sir Michael Rawlins, who would contact us to let us know what the current position was. This was in June 2006.

We are now in March 2007 and, as far as we can tell, are no nearer getting a clinical guideline. We would be delighted to hear that this is not the case. However, having worked very hard on behalf of a vulnerable patient group over the Christmas and New Year of 2002–03, it does seem unreasonable that we still have no idea whether our proposal has been accepted and whether we are going to get a guideline for the care of Cystic Fibrosis patients.

We do not think this would be a particularly onerous task, as the Cystic Fibrosis Trust has well-developed guidelines which were broadly accepted by the Department of Health as part of the series of National Definition Sets which were drawn up by the Health Regions before they were abolished. The National Definition Set for Cystic Fibrosis (Number 10) is appended to this report. It has no particular status within the NHS or the Department of Health as it was a regional document, but does illustrate the fact that some work has been done on this in the past which resulted in a reasonably satisfactory outcome.

We have no idea whether our guideline is still in the system at all and is either bogged down somewhere within NICE or at Ministerial level, or has been dropped or abandoned.

Why We Are so Concerned

Apart from the fact that the Cystic Fibrosis Trust is frustrated, having worked hard and consulted widely to produce the submission in January 2003, and having come up against a complete opaqueness and lack of clarity as to the subsequent process, we are particularly concerned that a very vulnerable group of patients is not protected by any national standard, either a Government target or a NICE guidance. Although Ministers and officials within the Department of Health state that this is not a barrier to good care, the reality within the harsh economic climate of the current NHS is very different. PCTs and hospital trusts do what they have to do to achieve Government targets and to meet NICE guidelines, leaving precious little resource, either in time or money, to make adequate provision for conditions for which their performance will not be measured. Some CF patients are looked after well in spite of this situation, but many are getting mediocre or sub-optimal care. In addition, the high standard of service which has been provided by specialist consultants, specialist nurses, specialist physiotherapists and specialist dietitians in the past is being threatened. The new generation of clinicians is less likely to work the very long hours to provide a comprehensive service, but will complete the hours they are contracted to work. In addition, many hospital trusts are looking to cut back dramatically on Specialist nurses, physiotherapists and dietitians who are absolutely key to proper CF care. Without some form of protection, either via a Government target or a NICE guideline, it is hard to see how the current service will be adequately protected, never mind how it will be developed and expanded to meet the changing needs of CF patients as they live longer and new treatments become available.

One Hopeful Sign

Separately, the Cystic Fibrosis Trust responded to Lord Warner's review of specialised conditions, of which Cystic Fibrosis is one. Professor Sir David Carter's report was extremely helpful. The process was open, transparent and relatively speedy, and Lord Warner's resulting recommendations were very encouraging. We do hope that the arrangements for commissioning CF care, in England at least, will improve as a result of these recommendations if they are properly implemented.

The future care of CF patients does need to be secured, and the combination of a NICE guideline for the clinical care of those with CF and a properly implemented specialist services commissioning process under the banner of the Strategic Health Authorities would be a good start.

Rosie Barnes
Cystic Fibrosis Trust

March 2007

Evidence submitted by Deltex Medical (NICE 87)

SUMMARY

- Deltex Medical produce an innovative medical device called the CardioQ which accurately monitors changes in blood flow during surgery. Numerous independent clinical studies have shown that the CardioQ reduces the number and severity of post-operative complications leading to reduced hospital stays.
- NICE's Interventional Procedure Programme (IPP) has declared the CardioQ technology "standard clinical practice" yet this has done little if anything to encourage uptake.
- NICE has not undertaken any technology appraisal of the CardioQ and has no plans to do so. However, NHS management often use the absence of such an appraisal to justify its refusal to invest in the technology.
- As a result 49 out of 50 NHS patients undergoing major surgery are being denied potentially life saving technology which has the proven potential to save the NHS over £400 million a year.
- The NICE appraisal process for new technologies must be altered so that "no-brainer" technologies are not disadvantaged simply because they have proven economic as well as clinical benefit.

INTRODUCTION: ABOUT DELTEX MEDICAL AND CARDIOQ

1. Deltex Medical is a small innovative British Healthcare company which has developed a device, the "CardioQ" Oesophageal Doppler monitor (ODM), to accurately monitor blood flow during surgery and in critical care. Reduced circulating blood volume is known as hypovolemia, which leads to insufficient oxygen being delivered to the organs, causing medical complications including peripheral and major organ failure resulting in longer hospital stays and in some cases death. Using the CardioQ allows the clinical team to better manage the patient during this time (haemodynamic optimisation), reducing complications and mortality.

2. Clinical evidence has shown that there are approximately 1 million NHS patients each year who would derive a clear clinical benefit from haemodynamic optimisation. If lengths of hospital stay for these patients were reduced by two days each, the NHS would free up about 5,500 beds, with a saving of at least £350 million a year. Were NHS managers to embrace the CardioQ technology and work with their clinical colleagues towards implementing it effectively they would significantly improve the experience of hundreds of thousands of their patients undergoing operations. By freeing up hospital beds they could choose whether to treat more patients, close beds or redeploy resources to meet local priorities.

3. In 2004 managers and doctors at the Medway Maritime NHS Trust worked together to audit the impact of the CardioQ in over 200 operations in a four month. They found that CardioQ reduced the average length of patient stay after surgery by over three days for the broad range of moderate and major risk surgery where it was used. This equated to an approximate saving of £800 per patient, and a realised saving of £1 million a year for the Trust in its first phase implementation. Chief Executive of the Trust Andy Horne underlined the effectiveness of CardioQ commenting : "We have used the CardioQ in around 200 operations over the last four months and had very good results. It has improved the quality of care for patients as they are healthier when they leave theatre, need less post-operative care and get home quicker."

4. In May 2006 the Royal Alexandra hospital in Paisley used CardioQ in a study of thirty patients who underwent major colorectal surgery. The result was a 20% reduction in the average length of post operative hospital bed stay and a saving of over £1,000 per patient.

5. In August 2006 the British Journal of Surgery published the results of a major new randomised controlled clinical trial of the CardioQ during surgery. The study on bowel surgery patients at the Freeman hospital in Newcastle-Upon-Tyne was funded by the Royal College of Surgeons and was the seventh high quality CardioQ outcome study to be published in a leading peer-reviewed journal. It demonstrated that in those patients whose circulating blood volume was optimised using the CardioQ, serious post-operative complications, emergency post-operative admissions to critical care units and emergency readmissions to hospital were almost entirely eliminated. The study found that CardioQ patients were also fit to go home three days earlier than non-CardioQ patients.

6. Routine use of the CardioQ during surgery is now a core part of the Freeman hospital's "enhanced recovery" or "fast-track" programme for major bowel surgery. This programme delivers amongst the lowest mortality rates, the lowest readmission rates and the shortest lengths of stay not just in the UK but in the whole of the developed world.

DELTEX MEDICAL'S EXPERIENCE OF NICE

7. Deltex Medical wrote to the Chief Executive of NICE on 25 November 2004 seeking advice as to whether it should actively seek a NICE appraisal in the context of "NICE blight". As a small company that has been loss-making for sixteen years we had concerns about losing our momentum on waiting up to two years for a NICE recommendation. We asked whether the clinical and economic benefits our technology is proven to deliver (ie 25% to 40% reductions in length of stay) even fall within the NICE remit to review marginal cases.

8. At a subsequent meeting with NICE representatives in January 2005, Deltex Medical was advised that NICE believed the CardioQ did fall within NICE's remit, but that even if it were selected for a NICE assessment, it was unlikely any such assessment would be completed before 2010.

9. Deltex Medical has attended a number of presentations by NICE staff over the last two years which have stressed that NICE's focus for technology appraisals is on technologies which improve care but at a higher cost to the NHS; the purpose being to enable NICE to issue guidance to the NHS on difficult decisions as to whether the additional benefits of a new treatment merit the additional costs. These presentations made it clear that NICE does not look at technologies such as the CardioQ which improve the quality of care but at *reduced* cost to the NHS; such technologies are labelled "no-brainers" by NICE and are outside the scope of its technology appraisal system.

10. At a time of scarce resources across the NHS, this creates the absurd situation whereby NHS managers divert money which might have funded the introduction of "no-brainer" technologies such as the CardioQ in order to fund technologies or drugs recommended by NICE, even though these may well not have the clinical benefit of the CardioQ. By contrast, accelerated implementation of no-brainer technologies might allow earlier adoption of more of the effective but expensive technologies that are the subject of NICE appraisals.

11. Following enquiries it made to the Department of Health, Deltex Medical was informed in December 2006 that "NICE only has the capacity to look at the most significant new and existing technologies and with a NICE appraisal costing over £200,000 it is a tool we need to use selectively." Furthermore the Department noted "the paucity of trial evidence on new non-drug technologies".

12. The Department further informed Deltex Medical that the Centre for Evidence-based Purchasing (CEP) had accepted a proposal to include the CardioQ in its work programme.

13. We welcomes the involvement of CEP, however it is unclear what form any CEP conclusions might take and whether CEP recommendations have the necessary authority, if indeed they will have any authority, to accelerate adoption of new medical technologies by the NHS.

14. The NHS procurement process is unnecessarily bureaucratic and hinders the uptake of new technology (as outlined in our submission to the Committee's inquiry into NHS deficits in June 2006). However, unless CEP is shown to be effective, NICE further complicates the process by actually disadvantaging those trying to promote the use of new technology in the NHS. NICE itself claims that it does not have time to look at every new technology, particularly if they already have proven benefits. However the result is that patients are being denied potentially life saving technology, and the NHS is being denied technology which has the potential to save it over £400 million a year because of an inherently flawed assessment process.

15. Deltex Medical is a British company which has brought to market a British technology: the vast majority of the clinical and "real-world" evidence supporting the CardioQ comes from British hospitals. Yet the company has found its dealings with the Department of Health and the NHS consistently frustrating over many years. Our recent experiences with the equivalent bodies in the USA have been in marked contrast. In the USA the decision making process is more transparent, faster and considerably less bureaucratic with clearly defined roles for the various bodies and agencies involved.

16. The Centers for Medicare & Medicaid Services (CMS), the US Federal Government body responsible for determining coverage for the reimbursement of medical technologies in the US, recently (26 February 2007) published a favourable draft decision on ODM following an application originally submitted on 22 August 2006. If a technology is "covered" it is possible for hospitals to receive a payment (reimbursement) that covers the costs associated with the purchase and use of that technology.

17. In reaching its proposed decision, CMS had commissioned a Health Technology Assessment (HTA) on ODM from the US Government Agency for Healthcare Research and Quality (AHRQ). The AHRQ report was delivered to CMS on 16 January 2007 and published on CMS's website on 14 March 2007. It grades evidence whether a technology does or does not work into four categories: "strong", "moderate", "weak" and "inconclusive". Strong evidence is where "it is highly unlikely that new evidence will lead to a

change in this conclusion". The HTA concluded that in "patients undergoing surgical procedures with an expected substantial blood loss or fluid compartment shifts requiring fluid replacement" the clinical evidence for ODM was "strong" in respect of the following three statements:

- (a) "Doppler-guided fluid replacement during surgery leads to a clinically significant reduction in major complications";
- (b) "Doppler-guided fluid replacement during surgery leads to a clinically significant reduction in the total number of complications"; and
- (c) "Doppler-monitored fluid replacement leads to a reduction in hospital stay".

RECOMMENDATIONS

18. The NHS needs a transparent, fast-track process for the promotion of uptake of new technologies which are proven to work. The role of NICE in inadvertently hindering this process must be addressed.

19. If CEP is to champion the adoption of 'no-brainer' technologies, its recommendations must, as a minimum, be no less binding on the NHS than those recommendations arising from NICE technology appraisals.

Deltex Medical Group plc

March 2007

Evidence submitted by Diabetes UK (NICE 78)

Diabetes UK is one of Europe's largest patient organisations. Our mission is to improve the lives of people with diabetes and to work towards a future without diabetes through care, research and campaigning. With a membership of over 175,000, including over 6,000 health care professionals, Diabetes UK is an active and representative voice of people living with diabetes in the UK.

EXECUTIVE SUMMARY

- The decisions of NICE may increasingly be challenged as a result of perceptions that their primary objective is measuring cost effectiveness.
- In addition there is concern that the views and experiences of patients and the public are marginalised in the consideration of evidence and the decision making process.
- These in turn will have an effect on public confidence, as will the increased media attention over cases such as Herceptin.
- Deviations from NICE recommendations may be a legitimate decision by a practitioner based on the best interests of an individual patient.
- Increasing transparency of its decision making processes and why it has reached its decisions should assist in maintaining its credibility as an institute, particularly when decisions are altered.
- The willingness to alter decisions is a positive provided the process behind this is fair and transparent.
- Whilst NICE has taken steps to increase patient and public involvement, concerns still exist that patient experiences are not given enough consideration in the evaluation process.
- Implementation of NICE recommendations whether guidelines or technology appraisals, are affected by the funding available locally. If funding is not made available and the recommendations not implemented as a result, this again will impact negatively on public confidence.
- NICE guidance can be misinterpreted resulting in an unfair restriction in access to services required, for example in the case of access to insulin pump therapy.

1. *Why NICE's decisions are increasingly being challenged*

1.1 The concerns highlighted to Diabetes UK overwhelmingly concern two key issues; the role of NICE in measuring cost effectiveness and the extent to which patient experience and wishes are adhered. These issues have increasingly affected the credibility of the Institute in the eyes of some healthcare professionals and patients alike and has encouraged people to challenge the decisions of the Institute. The concerns are that there is an increasing bias towards considerations of cost effectiveness when decisions are made regarding technologies/treatments in particular. For example, as an organisation we have been involved in the consultation regarding inhaled insulin. The initial recommendations were clearly restricting access to people with diabetes based on considerations of cost despite the benefits in quality of life that could be attained for some people with diabetes. There is recognition that the remit of NICE which straddles both

clinical and cost effectiveness can create this conflict of interest creating tensions in their role. In addition, opinion suggests that the decisions reached are based predominantly on the outcomes of Randomised Control Trials and a hierarchy of the evidence base where patient experience and other qualitative evidence is marginalised. This was again reflected in the initial decision made by NICE regarding inhaled insulin.

1.2 Challenging decision is a healthy part of ensuring transparency and that checks and balances are in place. The fact that NICE has altered previous decisions, as with inhaled insulin, not only shows that they are willing to reconsider decisions but that people are able to challenge NICE. However NICE must ensure that their decision making process is clear and transparent and that this is communicated effectively, otherwise, paradoxically, any changes to earlier decisions could be viewed as evidence of a weak organisation that is vulnerable to ill considered decision making.

2. *Whether public confidence in the Institute is waning, and if so why*

2.1 The media have an interest in sensationalising stories and media distortions of some NICE decisions will have an affect on the general public's perception of NICE. Undoubtedly, the increased awareness of NICE and its role through recent media coverage has encouraged scrutiny. This, in turn, can be a positive force for engaging more members of the public in the work of NICE.

2.2 Decrease in public confidence may also be the result of misdirected frustration. NICE make decisions in terms of cost effectiveness as well as examining the evidence working within the financial parameters of a tax based NHS. Funding is central to the question of confidence in NICE. This relates to the implementation of best practice with regards to clinical guidelines and access to new medicines and technologies that improve patients' health and quality of life. NICE guidance is not always implemented at a local level, particularly where there are increased costs involved or savings to be made. We are concerned, for example that NICE recommendations regarding blood glucose monitoring testing strips is being misinterpreted by PCTs in a manner that has restricted or prevented the supply of these testing strips to people with Type 2 diabetes, as evidenced by the level of anecdotal feedback we are receiving about this issue as an organisation. In addition, despite the existence of guidance, local areas are also not providing pump services in a consistent manner.⁷³ Public confidence then may be waning as they find NICE guidance is not being implemented locally by their PCTs.

2.3 Some people have expressed concern regarding the lack of transparency regarding NICE and its decision making process in relation to how it communicates this with the wider general public. By ensuring they communicate clearly and behave transparently regarding their decisions and why they have reached particular conclusions, NICE may improve public confidence and recover potentially lost credibility.

2.4 Clinicians will make decisions based on the best interests of their individual patients and may not always follow NICE guidance as a result. This may have the effect of reducing confidence in NICE from patients who disagree.

3. *NICE's evaluation process, and whether any particular groups are disadvantaged by the process*

3.1 We are aware NICE has made progress in its attempts to better engage with the public and patients, and is also looking at how their guidance can also be better tailored to incorporate matters affecting people from groups traditionally labelled as "hard to reach". However we are also aware that in practice, as mentioned in paragraph 1 the views of patients and the public may not always be given as much weighting as the more traditional sources of evidence.

4. *The speed of publishing guidance*

4.1 There is recognition that although the speed of publishing guidance is slow, this is due in part to the complexity and depth of the task at hand. The length of time can be explained as it enables wider stakeholder consultation and an understanding that patient organisations for example will have their own consultation process with their membership and stakeholders in order to provide a representative response to consultations. However this must be tempered with the need to ensure that guidance is published fast enough to enable patients to take advantage of innovations and receive best care as soon as possible. It is also important so that guidance maintains relevance and that evidence used in the review is not quickly superseded with new evidence making the NICE guideline out of date.

4.2 This is also important in relation to the length of time before guidance is next reviewed. The gap between reviews can be too long. For example confusion has been caused regarding cholesterol levels as a result of the length of time between review of guidelines. The National Prescribing Centre has had to clarify that despite the new evidence identified in the JBS2 guidelines that existing guidance must be followed until NICE have the opportunity to review this new evidence.⁷⁴ Out of date information in a NICE guideline can create a conflict between PCTs and practitioners, and there is the potential for the guidelines to be ignored as a means of restricting access to technologies or medications on the basis of outdated guidelines. It would be helpful if parts of guidelines are reviewed in light of new evidence.

⁷³ Diabetes UK (2006) Policy Research Report: Pump Therapy Restrictions.

⁷⁴ National Prescribing Centre; Boyle, R (2006) Copy of DH statement following National Cardiac Networks Meeting National Policy on Statin Prescribing.

5. *The appeal system*

5.1 The appeal process can be an unfair one and there is concern that decision making is swayed in relation to who is able to create the most vocal demonstration.

6. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)*

6.1 It is difficult to draw comparisons between NICE and SIGN as people tend to have experience of one body or the other.

7. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)*

7.1 The difficulties of implementation in relation to cost have been mentioned in paragraph 4. However there are a number of connected issues relating to costs that affect the ability of NICE guidance to be implemented. Funding is required not only for the material resources such as treatments or technologies but also implementing clinical guidelines through the staff, facilities and training required to implement recommendations effectively. For example insulin pump therapy requires specialist input from competent staff who themselves require training who in turn need the protected time to adequately educate the person receiving the pump and then be available to provide support to the person as they begin to use it.⁸ Our recent survey in relation to cuts in specialist services has highlighted that in many cases all manner of specialist diabetes services are being cut in various guises such as the cutting and freezing of specialist posts and the redeployment of staff on to general wards. In addition we are aware that time allowed and funding for continuing professional development is also being slashed.⁷⁵ In this environment of deficits it is important that the quality and availability of excellent care is not compromised. Having NICE recommendations that cannot be implemented undermines the existence of NICE as a body representing health and clinical excellence.

7.2 The recent commissioning toolkits developed by NICE may help the implementation of NICE guidance. However Diabetes UK is concerned with the lack of engagement with patients and patient organisations in relation to their development. For example Diabetes UK would have welcomed the opportunity to have been involved with the “Foot care service for people with diabetes” commissioning guide. We hope that when this is reviewed we will be able to offer our assistance. We believe that all appraisals and guidance should be accompanied by clear implementation and commissioning guidance. We welcome NICE’s plans to do this and look forward to being involved in this in the future.

7.3 NICE lacks the power to ensure implementation of its guidance and causes problems for patients when they are unable to access the services and treatments to which they are entitled. The technology appraisal over structured education is a case in point. Despite the ministerial funding direction regarding NICE guidance in January 2006⁷⁶ which places a responsibility on PCTs to show that they at least have a plan in place for the delivery of structured education that meets the agreed criteria with clear timescales in place, we are aware that some PCTs will not be able to meet this target and as there is not a strong enough impetus to do so prioritisation of this direction is unlikely. This is compounded by the issues mentioned in paragraph 12 regarding costs for training, development and delivery of such programmes whilst ensuring they are sustainable and that funding is not later withdrawn.

7.4 We are aware that NICE recommendations can also be misinterpreted to restrict the level of provision of certain technologies. This can mean arbitrary decisions are made regarding for example the number of insulin pumps bought in any one year by a PCT. The decisions are made based on the NICE estimations despite the local level of need.⁷⁷ There are inherent difficulties with the position of NICE as their recommendations are neither mandatory but neither are they insignificant in their weight. Therefore there will always be the opportunity for recommendations to be used both positively to seek best care for patients but also negatively to restrict without good reason access to best care and this can hinder the recognition by healthcare professionals of more recent clinical evidence that may contradict NICE guidance. However there would be no merit in arguing that NICE recommendations become entirely mandatory or lose their weighting as this is likely to hinder the delivery of best care to some patients.

Stella Valerkou
Diabetes UK

March 2007

⁷⁵ Diabetes UK and National Diabetes Support Team (2007) Insulin Pump Services Department of Health http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_072777

⁷⁶ Diabetes UK (2007) Cuts in Diabetes Specialist Services—A Report http://www.diabetes.org.uk/Professionals/Information_resources/Reports/Cuts-in-Diabetes-Specialist-Services/

⁷⁷ Information on the funding direction for structured education programmes for people with diabetes http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4138033

Evidence submitted by the Joint Epilepsy Council of the UK and Ireland (NICE 40)

1. INTRODUCTION

1.1 The Joint Epilepsy Council of the UK and Ireland (JEC) represents 22 epilepsy organisations operating in England, Wales, Scotland, Northern Ireland and the Republic of Ireland. Our mission is to promote improved standards of and access to integrated services in health, education and social care for people with epilepsy and their carers and to increase epilepsy awareness amongst politicians, civil servants, service providers and the general public. The JEC includes representation from patient organisations and the International League against Epilepsy (ILAE) representing clinical specialists with an interest in epilepsy.

1.2 Over 456,000⁷⁸ people have epilepsy in the UK. It is the most common serious neurological condition and is a major long-term disability with similar numbers of people affected as insulin dependent diabetes.

1.3 The JEC welcomes this opportunity to submit evidence to the Health Committee relevant to the inquiry into aspects of the work of the National Institute for Health and Clinical Excellence. Areas of particular interest include:

- Why NICE's decisions are increasingly been challenged.
- NICE's evaluation process, and whether any particular groups are disadvantaged by the process.
- Whether public confidence in the Institute is waning, and if so why and how.
- The speed of publishing guidance.
- Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN).
- The appeal system.
- The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this).

2. SUMMARY

2.1 The JEC fully supports the work of NICE in respect of people with epilepsy, their families and people bereaved through epilepsy. Our experience of working with NICE on the National Audit of Epilepsy Deaths 2002 and the NICE Guidelines on the Epilepsies 2004 was particularly positive. These initiatives from NICE represented the first serious attempt by policy makers to address the historically low standards of care for people with epilepsy and to respond to the significant loss of life from three seizure deaths a day. The speed of publication of guidelines has been appropriate to the work necessary to produce important work of this kind. Irrespective of the problems of implementation of guidance highlighted below, the work by NICE has been invaluable to the epilepsy community. For the first time people with epilepsy and people bereaved by SUDEP (Sudden Unexpected Death in Epilepsy) have a benchmark of care which they can campaign for and can use in complaints when services have failed. This is real progress, but not progress likely to be disseminated by the mainstream media.

2.2 The key issue in this area as far as the JEC is concerned is the evidence of non-implementation of NICE Guidelines.

2.3 The main reason for non-implementation of NICE Guidelines has been the absence of any plan (national, regional or local) to address poor levels of knowledge in clinicians managing the medical care and communication needs of many people with epilepsy. There is a critical shortfall in clinicians and nurses specialising in epilepsy and this treatment gap has not been addressed by the development of formal clinical networks that can make the best use of the expertise available in a local area.

2.4 There is evidence that the current shortfall is critically affecting the level of care provided to people with epilepsy, including increased levels of epilepsy related deaths. A consensus group of experts and the voluntary sector recommended in 2004 that the workforce requirements to implement the NICE Guidelines on epilepsy would require in the short term an increase in the number of epilepsy specialist nurses from 140–600. The consensus group also recommends that in the medium term the Government should increase the number of adult neurologists from 352–1,400, paediatric neurologists from 75–150, learning disability specialists from 340–500 and an increase in neuroradiologists from 110–160. Clearly NICE Guidelines in this area may be perceived as failing because of current workforce capacity and current resources for training.

2.5 The NICE Guidelines on epilepsy provide an excellent basis for GPs and specialists to provide high standards of treatment and care for people with epilepsy. In addition, the existence of evidence-based standards of good practice provides people with epilepsy and bereaved relatives with an opportunity to fight to prevent medical accidents in the future.

⁷⁸ *Epilepsy prevalence, incidence and other statistics*. Joint Epilepsy Council: Leeds. 2005.

3. WHETHER PUBLIC CONFIDENCE IN NICE IS WANING

3.1 The JEC's view is that the epilepsy community as a section of the public remains fully confident in the work that NICE has done to date in the field of epilepsy. If public confidence is waning this may be due to concerns about the non-implementation of NICE guidelines at a local level and due to media stories which have not tended to focus on the positive work that the institute does.

3.2 Public confidence may also be waning due to decisions to refuse the funding of certain treatments. Epilepsy medications are very low cost relative to many other new drugs and cost effective given that medication can achieve seizure freedom in seven out of 10 patients. The epilepsy community is very positive about the NICE guidelines on diagnosis and treatment and the technology appraisals, but very concerned that in spite of the cost effective nature of this guidance there are serious problems of implementation.

3.3 The Chief Medical Officer has confirmed that epilepsy has suffered historical neglect and lack of investment compared with other long-term conditions.⁷⁹ As a result there is a serious treatment gap identified since 1950 in six national reports. Seven out of 10 people with epilepsy should be seizure-free on appropriate first-line medication but currently only five out of 10 people are estimated as achieving this. This means two out of every five people experiencing seizures could be seizure free, but are not. In total over 80,000 people with epilepsy are having seizures that could be prevented if they had access to good epilepsy services.⁸⁰

3.4 In 2000 NICE commissioned Epilepsy Bereaved to project manage a UK-wide National Clinical Audit on Epilepsy Deaths 2002.⁸¹ This Audit involving the medical Royal Colleges found that up to 400 of 1,000 epilepsy deaths each year are potentially avoidable through improved management of seizures. The Findlay Fatal Accident Inquiry 2002 also highlighted the need for implementation of national guidelines on epilepsy as a key preventative strategy in respect of SUDEP. SUDEP mainly affects young people and can affect anyone with epilepsy who is not seizure-free.

3.5 It was acknowledged by the Chief Medical Officer in his 2001 report that previous guidelines related to epilepsy had been ignored and the hope was that the NICE Guidelines on epilepsy would address the deficiencies in the previous guidelines. The evidence below suggests that there have been deficiencies in the implementation of NICE Guidelines.

3.6 Prior to the NICE Guidelines a Family Health Services Authority tribunal ruled that a GP could not be in breach of standards because there were no recognised standards of care for people with epilepsy. Focus groups of families bereaved by epilepsy meeting on 18 February 2007 reported positively how they were using the NICE Guidelines to highlight lessons that can be learnt from SUDEP deaths through educational events with clinicians and also through the NHS complaints system. These levers for achieving change are particularly important in a policy context where national waiting list targets do not reflect clinical priorities for people at risk from SUDEP.

4. THE SPEED OF PUBLICATION OF NICE GUIDELINES

4.1 The JEC considers that the speed of publication of the NICE Guidelines in the field of epilepsy was appropriate to the amount of work involved in the production of the Guidelines.

5. THE EVALUATION PROCESS

5.1 JEC is positive about the evaluation process and considers that no group was disadvantaged. There were four patient representatives who were members of the Guideline Development Group and they reported very positively on their experience on the Group.

6. IMPLEMENTATION OF NICE GUIDELINES

6.1 Experts and members of the epilepsy voluntary sector met in November 2004 to review various survey findings characterising the current state of epilepsy care and to compare against standards outlined in the (then) recently published NICE epilepsy guideline.⁸²

6.2 The expert consensus was that services fell well short of the standards set out by NICE in terms of waiting times for specialists and diagnostic tests, and research findings indicated that little was likely to change in the next four years. The main barriers reported by PCTs to implementation of NICE Guidelines were financial and other national priorities. The expert group was aware that the shortage of neurologists and other epilepsy specialists was not going to improve overnight and called for a number of short-term solutions.

⁷⁹ The Annual Report of the Chief Medical Officer of the Department of Health 2001, DH, 2001.

⁸⁰ *Epilepsy prevalence, incidence and other statistics*. Joint Epilepsy Council: Leeds. 2005.

⁸¹ Hanna NJ et al, *The National Sentinel Audit of Epilepsy-related Death*, London; The Stationery Office, 2002.

⁸² <http://www.epilepsy.org.uk/campaigns/lobbying/consensus/index.html>

6.3 In the medium-term the group believed that addressing this shortage is the principal change needed to ensure epilepsy services improve sufficiently to achieve the standards set by NICE. The group called for a national plan to increase the number of epilepsy specialist nurses from 140–600 across all epilepsy disciplines (adult, paediatric, and learning difficulties) within two years. Nurses play a critical role in treatment monitoring, offering advice and support to patients and families, and education for patients and GPs, therefore providing much needed support to people with epilepsy, the primary care team and to neurologists. In the medium term (next five to 10 years) the group called for the Government to immediately put in place a programme to increase the number of adult neurologists from 352 to 1,400; paediatric neurologists from 75–150; learning disability specialists from 340–500; and neuroradiologists from 110–160, all within five to 10 years. This statement was supported by over 100 epilepsy clinicians, seven voluntary sector groups and 115 MPs (EDM 685, 2005).

6.4 Table 2 below sets out JEC estimates of the existing resource and demand and the estimated cost per annum of meeting demand.⁸³

	<i>Existing Resource</i>	<i>Demand</i>	<i>Cost Per Annum</i>
Access to a GP with basic knowledge of epilepsy	Poor knowledge base	Epilepsy Training— One course per year in each PCT	£700,000
A seamless patient journey between GP and hospital	Some informal clinical networks	An epilepsy “Tsar” or lead in each region	£750,000
Access to a specialist nurse	150	600	£12,600,000
Access to a paediatric neurologist with an interest in epilepsy	70	150	£8,000,000
Access to a consultant neurologist	352	1,400	£104,800,000
Access to a clinical neurophysiologist	75	248	£4,325,000
Total			£131,175,000

Footnote: recommended numbers of neurologists, paediatric neurologists and neurophysiologists are taken from the Association of British Neurologists, British Paediatric Neurologists Association and Association of British Clinical Neurophysiologists.

6.5 Focus groups held on 17 March 2007 with families bereaved through SUDEP included reports from recently bereaved families of non-compliance with NICE guidelines. These reports included withdrawal of funding for A&E emergency medications; problems of access to specialists with an interest in epilepsy; deaths of young people whilst waiting for investigations and treatment or access to specialist nurses. Families also reported that clinicians were not informing patients about SUDEP and that deaths had occurred in people who had not started or who had stopped their medication. These deaths included women who had experienced side-effects of medication on pregnancies but had no preconception counselling or information about SUDEP and the importance of medication for controlling seizures.

6.6 A recent Epilepsy Action survey in 2007 revealed that a number of NICE recommendations are not being implemented. A total of 185 responses were received and the results were interpreted. The NICE guidelines recommend that people with suspected epilepsy should be referred to a specialist within four weeks; however, only 27.4% of respondents to the survey said that they had been seen within four weeks.

6.7 NICE recommends that all individuals with epilepsy should have a comprehensive care plan that is agreed between the individuals, their family and/or carers as appropriate, and primary and secondary care providers. The survey by Epilepsy Action revealed that 75% of respondents did not have a care plan.

6.8 The NICE guidelines on epilepsy recommend that “women with epilepsy and their partners, as appropriate, must be given accurate information and counselling about contraception, conception, pregnancy, caring for children, breastfeeding and menopause.” Epilepsy Action carried out an ‘Ideal World’ survey in 2002, which sampled girls and women with epilepsy to gather their opinions and experiences of their information needs in relation to their epilepsy treatment. The survey results show that women are not receiving important information about their condition and the possible effects of anti-epileptic medication. Only 28% of women aged between 19–34 have received information about oral contraception and epilepsy medication and only 46% of women with epilepsy who have had children had been told that their medication might affect their unborn child, which implies that 54% of women who had been through a pregnancy had not been given such information.

⁸³ Epilepsy, the case for, the Joint Epilepsy Council, 2004.

6.9 A paper, by I Minshall and D Smith,⁸⁴ published in 2006 revealed that out of 610 people with epilepsy surveyed; only 41% had been seen by a GP in the previous year.

6.10 Since 2004 there is evidence that although there are a few PCT areas where progress has been made towards implementation of the NICE guidelines on epilepsy, in many areas of the country, services for people with epilepsy have remained or have become more precarious.

Sharon Harvey

General Secretary

Joint Epilepsy Council of the UK and Ireland

March 2007

Submitted on behalf of: Brainwave—The Irish Epilepsy Association, David Lewis Centre for Epilepsy, Enlighten—Tackling Epilepsy, Epilepsy Action, Epilepsy Bereaved, Epilepsy Connections, Epilepsy Research Foundation, Epilepsy Scotland, Epilepsy Specialist Nurses Association, Epilepsy Wales, Epilepsy West Lothian, Fund for Epilepsy, Gravesend Epilepsy Network, Gwent Epilepsy Association, International League against Epilepsy (British Branch), The Meath Epilepsy Trust, Mersey Region Epilepsy Association, National Centre for Young People with Epilepsy, National Society for Epilepsy, Organisation for Anti-Convulsant Syndrome, Quarriers, St. Elizabeth's Centre.

Evidence submitted by the Ethical Medicines Industry Group (NICE 79)

1. INTRODUCTION

1.1 As Chairman of the Ethical Medicines Industry Group (EMIG), I am writing in response to the Health Select Committee's inquiry into the National Institute for Health and Clinical Excellence (NICE). EMIG welcomes the inquiry and is pleased to have this opportunity to provide comments on behalf of small and medium-sized pharmaceutical companies in the UK. While the Association of the British Pharmaceutical Industry (ABPI) will provide a more detailed response, which we support, I thought it would be worthwhile to provide EMIG's perspective on NICE, particularly in terms of the regulatory impact on small and medium-sized pharmaceutical companies.

1.2 By way of background, EMIG was established in 1985 as a forum for small to medium-sized pharmaceutical companies operating in the UK. We are proud to have over 40 member companies and our aim is to represent their views on industry issues that directly affect them.

1.3 To give you some context, data provided by IMS, an independent provider of pharmaceutical data, shows that in 2005:

- 88% of UK pharmaceutical companies achieved annual gross sales of less than £50 million (the majority of our members have sales of under £50 million).
- These companies provided 39% of products, yet only account for 8% of the NHS drugs bill.

1.4 This clearly shows that, while small companies are contributing considerably less to the overall NHS drugs bill, they are contributing essential products to the NHS, many of which the larger pharmaceutical companies do not produce due to their concentration on the development of new therapies.

2. EXECUTIVE SUMMARY

2.1 EMIG regards NICE as an organisation that plays an important role in evaluating the contribution of medicines. In general, we find that NICE accomplishes its work well. However, EMIG believes it would be more appropriate for NICE to focus on the quality of the healthcare outcome rather than its cost or cost effectiveness.

2.2 The regulatory burden imposed by a NICE assessment is much greater on the smaller company, such as those represented by EMIG, compared to larger companies, with greater resources.

2.3 As you will be aware, the recent report by the Office of Fair Trading (OFT) into the PPRS recommended a new system of value-based pricing. Under such a system, we believe it will be difficult to define "value" but also more difficult for smaller companies to illustrate that new products are valuable and to what extent.

2.4 The implementation of NICE guidelines, or sometimes the lack of implementation, can appear very inconsistent across the country. One good example of this is the "postcode lottery" around IVF treatment, which we evaluate in a case study.

⁸⁴ Minshall I, Smith D. The development of a city-wide epilepsy register. *Seizure* (2006) 15, 93–97.

3. NICE'S EVALUATION PROCESS

3.1 The NICE appraisal process has improved, in that it is quicker than it used to be, recognising the need for a pragmatic and flexible approach to the assessment of a wide range of health interventions and the need for stakeholder consultation.

3.2 EMIG members regard NICE as an organisation that plays an important role in evaluating the contribution of medicines. In general, we find that NICE accomplishes its work well. However, EMIG believes it would be more appropriate for NICE to focus on the quality of the healthcare outcome rather than its cost or cost effectiveness. While cost is obviously an important issue for the NHS and Department of Health, NICE should evaluate medicines firstly in terms of efficacy, and then in terms of cost.

3.3 EMIG members generally produce low to medium-priced products and introduce new chemical entities only once a year at most. It is therefore particularly problematic for EMIG members that NICE concentrates most on evaluating new high-priced molecules, rather than low to medium-priced products. New, more expensive molecules may grab headlines but they are a small proportion of the pharmaceuticals available and effective analysis should be undertaken of all products.

3.4 NICE states that it bases its recommendations on both clinical evidence and economic evidence. EMIG believes that the NICE thresholds for "cost-effectiveness" are arbitrary and, where there is uncertainty in the process, patients are often denied the benefit of doubt.

4. REGULATORY BURDEN

4.1 The regulatory burden imposed by a NICE assessment is also much greater on a small pharmaceutical company than on larger companies, who have in-house teams of health economists that can devote time to illustrating the efficacy of products. Other companies (like EMIG members) simply do not have that kind of resource.

4.2 As you will be aware, the recent report by the Office of Fair Trading (OFT) into the PPRS recommended a new system of value-based pricing. It will be difficult to define "value", but also more difficult for smaller companies to illustrate that new products are valuable and to what extent.

4.3 Furthermore, most products launched by small and medium-sized companies are based on incremental changes, such as modifications in delivery mechanisms, which are very important to patients but NICE seldom recognises.

5. IMPLEMENTATION OF NICE GUIDANCE

5.1 In spite of considerable efforts by NICE to dedicate resource to working with the NHS and other stakeholders to improve implementation of its guidance, implementation remains slow and patchy, denying patients access to medicines that have been found to be clinically and cost effective.

5.2 However, there is a long way to go before NICE guidance is firmly embedded into care for patients. Implementation is complex and multi-factorial, involving different organisations and individuals within them.

5.3 The implementation of NICE Guidelines, or sometimes the lack of implementation, can appear very inconsistent across the country. One good example of this is that in early March, there were numerous reports on the "postcode lottery" of IVF treatment, two years after NICE guidelines recommended three cycles of IVF should be funded on the NHS for eligible couples. This is an example of NICE activity with no delivery, indeed the situation for infertile couples is arguably worse now than it was two years ago. A case study based on this example is attached. We would be happy to provide more information on this report and other data.

5.4 Inequality in access to medicines is a result, not of NICE systems, but of its interactions. NICE was set up to try to tackle and resolve the issue of inequality in the use of medicines and inequality in the use of clinical procedures and patient pathways and operations. However, it has failed to achieve these objectives, not because of its own internal processes, but because of the way it interacts with the health system.

5.5 EMIG believes there should be greater funding for all aspects of NICE guidance to ensure guidance is fully implemented, with the appeals process allowing some flexibility for decisions to be changed over time, as appropriate.

6. CONCLUSION

6.1 EMIG supports the ABPI's position on the role of NICE. However, thank you again for this opportunity to put across the views of EMIG members on the role NICE has the potential to play and how its work could be improved, particularly in terms of the impact on smaller pharmaceutical companies. If you have any queries about the issues outlined above, please do not hesitate to contact me.

Leslie Galloway
Chairman, EMIG

March 2007

Evidence submitted by the European Medicines Group (NICE 84)

I am writing on behalf of the 21 members of the European Medicines Group (EMG) to provide some brief input to your Inquiry into the National Institute for Health and Clinical Excellence.

The European Medicines Group is the UK voice of research-driven pharmaceutical companies headquartered in Continental Europe who develop and supply prescription medicines to the NHS. We were founded over five years ago and our members have a wide range in terms of their research interests and the size of their organisations. Most of our members have been involved with the work of NICE over the last few years and many decisions made by NICE have had a huge impact on our members. I enclose a short leaflet which will give you details of our members and a little more background to the EMG.

We work alongside the ABPI, although not all of our members are ABPI members. We fully endorse the points made by the ABPI in their submission to this Inquiry. NICE has achieved a great deal over the past eight years in producing a broad range of evidence-based guidance, and has developed areas of good practice in its processes, such as stakeholder engagement, which should not be under-valued.

However, we believe that the perception of NICE amongst stakeholders (and the broader public) is that it is increasingly becoming a force for cost containment rather than clinical excellence. The increasing focus on cost per QALY value as the over-riding decision-making criterion to determine whether patients in England and Wales have access to NHS-funded treatment supports this view, and has led to some recent contentious decisions, for example in Alzheimer's disease, osteoporosis and brain cancer, that make little sense to either professionals or patients and which put patients in England and Wales at a disadvantage compared with their European neighbours. The uncertainty in cost per QALY methodology means that these calculations should be treated with caution and balanced against other important factors, such as clinical need, availability of alternative therapies, and benefits beyond the health service.

We believe NICE should adopt a broader perspective when assessing value, encompassing carer benefits and costs, social service and other costs to the taxpayer, and overall impact on society. We have recently published two case studies, in Hepatitis C and Diabetes, which demonstrate that the true value of medicines cannot be assessed by simply looking at the costs of the medicine or the total cost of treating all patients. Assessments of value must systematically take into account cost effectiveness, including health gain and wider societal measures such as lost productivity. Whilst we recognise that this is no easy challenge, we would call on NICE to work with industry address this challenge. Copies of our case studies are attached and we will continue to add to this portfolio across a broad range of conditions.

We also believe that a more constructive dialogue between industry, NICE and academic centres would help to address some concerns on all sides about the quality of assessment and the adversarial approach adopted during appraisal that does little to serve the interests of patients. An opportunity should be taken to air and address views, and to change NICE processes, so that dialogue on methods, assumptions, data, etc, can take place from the beginning of appraisal. This should lead to better decision-making and a reduction in the number of appeals. This approach works well in Scotland.

One of the areas of good practice adopted by NICE is the opportunity offered to consultees to appeal its decisions. However, like the ABPI, we would call for a root-and-branch review of the process, which lacks independence and is based on grounds that do not enable valid challenge to poor decision-making. The legalistic nature of the process also acts as a deterrent to consultees with limited resources, such as patient and professional groups, and is inherently inequitable.

NICE has worked very hard to help NHS organisations implement its guidance and has produced an impressive array of tools, learnings and examples of good practice over the past four years. Yet implementation remains slow and patchy, and we share the frustrations felt by NICE. NICE and the industry are working with an NHS whose culture is at best cautious and at worst resistant to innovation and advances in treatment. "NICE blight" is a real phenomenon, where NHS organisations refuse funding until NICE guidance has been issued. Implementation systems vary widely from passive communication of guidance and availability of funding to active financial and project planning to ensure adoption and improvements in patient care. Financial planning is often deficient and leads to a perception of lack of

affordability. We agree with the ABPI that Healthcare Commission assessment and inspection are drivers for improved implementation, and would call on the Commission to work with industry and other stakeholders to improve methods of measuring implementation.

One objective of NICE is to promote adoption of cost-effective innovation in the NHS, an objective supported by our membership, whose purpose is to research, develop and supply medicines that cost-effectively meet clinical need. Our fear is that the evolution of NICE into an economic fourth hurdle, together with an NHS whose culture often sees innovation as a problem rather than a solution, will lead to patients in England and Wales being unable to receive treatments routinely provided in other countries. This will also damage our members' ability to invest and do business in the UK.

Peter Martin

Chair, European Medicines Group

March 2007

Evidence submitted by FEmISA (NICE 49)

FEmISA—Fibroid Embolisation: Information, Support & Advice, an independent voluntary patient group to ensure women are informed about and have access to embolisation to treat symptomatic fibroids.

BACKGROUND

As the co-ordinator for FEmISA I have taken a very active part in 2 NICE reviews—the interventional procedures review for fibroid embolisation [UAE—uterine artery embolisation] and the more recently Clinical Guideline Development on Heavy Menstrual Bleeding, originally Hysterectomy and Alternatives. I have also served as a member of patient fora for both the Oxford City PCT and Ambulance Trust. Originally a scientist [Applied Biology, specialising in Biochemistry] in medical R&D I have experience of clinical trials as a scientist, manager and more recently a patient. I am also a medical marketing professional and senior manager in the healthcare industry and Chairman of the Chartered Institute of Marketing Medical Marketing Group, which spans all sectors of healthcare from NHS to pharmaceuticals. I have a special interest in NICE and experience of the health service in other EU countries and the statistics on health outcomes.

1. *Why NICE's decisions are increasingly being challenged?*

1.1 The UK is the fourth largest economy in the world. However, despite extra spending health outcomes are much worse than our EU neighbours. We have been promised that NHS treatment is “free at the point of need”, but thanks to NICE [and local PCT cost saving] it is not. Patients rightly expect that treatments available in other developed countries—EU and USA should also be available here and yet NICE often denies these life saving treatments on the NHS, especially new cancer drugs. People die from cancer much earlier in UK than the rest of Europe and this has been exacerbated by NICE not allowing many of the new cancer drugs to be used in the NHS. Some of NICE's decisions make us sound like a third world country—NICE ruling on wet macular degeneration—the drug can only be given to patients who are already blind in one eye!

1.2 NICE needs to put more emphasis on clinical excellence and clinical outcomes, benchmarking against other developed countries ie major EU countries, USA, Australia, New Zealand and Canada. Their decisions are based on “cheap to the NHS” rather than clinical excellence and good health outcomes.

1.3 NICE considers only the short-term cost to the NHS. This does not give a true reflection of cost effectiveness, which should include short and longer-term economic and social costs to patients and carers, social services, employers and the economy.

1.4 If a new treatment is rejected by NICE due to cost effectiveness it is killed stone dead and will not be available to anyone on the NHS. Even if a NICE outcome supports a new relatively expensive treatment it does not necessarily become available as PCTs say they cannot afford to fund it. eg IVF.

2. *Whether public confidence in the Institute is waning, and if so why?*

2.1 It is very questionable whether NICE is as independent as they seem. The Health Ministers decide all the topics for review. Some of NICE's decisions are politically very convenient ie with the lack of NHS dentists it was very convenient that NICE decided we only needed dental check ups every 2 years instead of every 6 months.

2.2 NICE is being used as a scapegoat by the Government to stop the NHS providing new expensive treatments, even though they may be cost effective, cure disease and prolong life.

2.3 NICE only counts the costs to the NHS in the short term, pays no regard to long term costs and more significantly to costs to patients—direct, social and economic and to the economy as a whole NICE puts NHS expenditure far above other considerations and there are grave doubts about their economic and financial analyses eg Alzheimer’s disease

2.4 NICE has no teeth. PCTs and clinicians can reject their recommendations on the grounds of local cost pressures.

2.5 Extravagance and Cost of NICE’s Offices—Anyone visiting NICE’s plush offices in Holborn would ask why they need such expensive premises. This is not value for money.

3. *NICE’s evaluation process, and whether any particular groups are disadvantaged by the process?*

3.1 Clinical Evidence

3.1.1 NICE started work with pharmaceutical products and does not really understand medical devices, clinical procedures or interventional procedures. It needs to recruit some people who do. It insists that randomised controlled trials [RCTs] are the highest level of evidence available. This is true for pharmaceuticals, however, when comparing completely different treatments, by different specialities there are too many variables. Other types of trials should be given a higher weight. This was particularly noticeable in the recent clinical guidelines for heavy menstrual bleeding, where some small obscure RCT clinical studies were given high status and the VALUE studies, DoH funded retrospective studies of 37,298 patients showing short and long-term morbidity and mortality of hysterectomy were not included. Thus the longer term costs to patients and the NHS were not included or considered. When patients are making decisions about treatments they want to know how effective the treatment is, how long it will take them to get better, possible side effects and complications, how long it will be before they return to work and feel completely better. NICE does not address these important issues.

3.1.2 In the clinical guidance on heavy menstrual bleeding all stakeholders were asked at the initial meeting to submit any non-published data, such as patient surveys etc. However, the documents asking for evidence specifically stated that non-published data would not be considered and the clinical papers we submitted—the VALUE studies and others, were also not included.

3.2 Side Effects of Recommended Drugs and Alternative Treatments—In the Clinical Guidelines for Colon Cancer a drug 5FU—Folonic Acid is recommended as first line treatment for all. It is cheap, old, and reasonably effective. However, it is stated in the 5FU summary of product characteristics [SPC] that it can cause angina [due to coronary artery spasm] in some patients and the drug cannot be continued. NICE does not recommend an alternative drug. My mother recently had an angina attack due to 5FU. We had a huge battle to get her any alternative chemotherapy at all, as NICE had not made provision for patients suffering serious side effects from 5FU. This was extremely distressing to us all and the next patient in the same position would probably not have the knowledge to get an alternative drug. There should be greater flexibility in NICE clinical guidelines and provision for alternative therapies should the first line not be suitable.

3.3 The Interventional Procedures Review, is very sloppy and does not do a review of the most recent clinical papers or those not written in English, which is essential for new technologies. In the review on uterine artery embolisation NICE initially cited only 9 papers for the advisory committee to review. FEmISA, in a 10 minute search on the internet, found 120 papers, many significant, that NICE had overlooked. One of the advisory committee members, a leading clinician, now conducts an independent search before reviewing NICE’s evidence. The committee cannot be expected to come to a sensible decision if they do not have the clinical evidence. There is a large question mark over the competence of NICE staff.

3.4 Technology Appraisals—Clinical Evidence—NICE deliberately does not invite leading clinicians in the field under review if they have taken part in a clinical trial on the new drug. This deprives the committee of expert evidence.

3.5 Cost effectiveness—NICE’s economic evaluations are very questionable. NICE values human life by QALYs and restricts treatments to a cost of approx £20k, This amount is far too low. Many people pay more than this in tax each year and have certainly contributed more than this in tax. Only the short-term costs to the NHS are considered not the costs to patients and their families, whose taxes pay for the NHS, nor long-term costs to the NHS, nor social services, nor employers or the economy. A true economic evaluation would take all these into account. This leads to very distorted outcomes particularly exemplified by the ruling on drugs for Alzheimer’s disease

3.6 Patient Involvement—NICE invites patients to take part during the working day. They are unpaid and must take holiday from work to attend. NICE will not contemplate evening sessions more convenient to patients and members of the public.

3.6.1 Although registered as a patient group with NICE for uterine artery embolisation FEmISA was not invited to take part. It was only through my personal interest in NICE that I discovered this interventional procedures review was planned and insisted on taking part. I did complain to NICE about this. If registered patient groups are not informed about NICE reviews affecting them, it is unlikely that other small patients groups will be able to take part.

3.6.2 Many patient groups submitted evidence to the clinical guidelines development on heavy menstrual bleeding. These were protesting against the reduction in scope and suggesting other clinical evidence should be considered. I have little confidence that any of the patient submissions were read. The points raised were completely ignored and not addressed at all.

3.7 Lack of Transparency of Decisions—In the clinical guideline development for heavy menstrual bleeding this was originally entitled hysterectomy and alternatives and had a much broader scope. The title and scope were reduced against patient wishes and without explanation or appeal. This change only benefited the Royal College of Obstetrics and Gynaecology and seems to be the result of secret lobbying.

3.7.1 Many patient groups volunteered to take part. One of the two patient representatives did not come from the registered stakeholders and many were upset by the appointment, as there was no explanation. The reasons were not transparent. However, I was impressed with her, her input and outcome, but there should have been a proper explanation.

3.8 Inaccessibility of Evidence, Guidance and NICE Documents—The systematic review in the interventional procedures review of uterine artery embolisation was 110 pages. While it is important that the review is detailed and comprehensive there should be a shorter summary version for patients and busy clinicians to review more quickly.

3.8.1 In the clinical guidelines development for heavy menstrual bleeding a short summary was written, but this bore little resemblance to the full version of 400 pages. It was necessary to read the 400 page document to make sensible comments.

3.9 Guidance for Patients—The patient booklet NICE produced for uterine artery embolisation did not give a clear explanation of what was involved. It did not compare this procedure to the safety and effectiveness of other treatments for fibroids, usually hysterectomy and it did not require gynaecologists to inform women needing treatment of this option. FEmISA brought these issues to NICE's attention at the time and offered to help rewrite it, but was rejected. Subsequently a number of women have contacted FEmISA saying they had been pressured into having an unwanted hysterectomy and were not informed about alternatives.

3.10 Danger of New Treatments not Being Made Available to Patient in UK—The pharmaceutical industry has described NICE as the fourth hurdle to getting a new pharmaceutical product launched in UK. NICE has made it much for expensive to launch new pharmaceutical products in the UK as companies need to commission a lot of extra economic studies just for the UK. Medical device companies are in an even more difficult position as they have much lower profit margins and cannot really afford to fund extra economic studies for NICE. There is a great danger that, due to the cost of NICE, new life saving treatments may not be available to UK patients, when they are available in other EU and US countries. The UK lags greatly behind other countries in making new less invasive and less expensive treatments available, to the detriment of patients and the NHS alike. NICE tends to play a negative rather than positive role in this by making adoption of new less invasive, less expensive treatments much longer.

4. *The speed of publishing guidance?*

The past delays of 3 years or more in reviewing and publishing guidance, particularly on new chemotherapy drugs has had a serious negative impact on the health and outcomes of English patients. PCTs have used future NICE assessments as a reason for not allowing the use of new drugs and technologies. The speed of publishing is about 6 months, which is rather lengthy.

The speed of reviewing a new expensive medical intervention is excessive

5. *The appeal system?*

I have not taken part in an appeal, but have searched the NICE web site and can find no details on how to do so.

6. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)?*

6.1 Why are drugs available in Scotland but not England? Why are the same drugs available in other EU countries but not England? This is not in the interests of NHS patients. We get worse treatments and health outcomes as a result of NICE.

6.2 NICE should be pulling NHS treatment up to a higher level of clinical excellence, instead it is doing the opposite.

7. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)?*

7.1 NICE should be concentrating on clinical excellence and comparing UK/English health outcomes and survival rates

7.2 If a new drug/technology review is negative from NICE it is killed stone dead for use in NHS. Patients can only obtain the benefits by paying for it themselves. If positive then PCTs and Acute Trusts can and do ignore it if it doesn't suit them, citing cost constraints.

7.3 Whatever one thinks of the outcomes of NICE guidance it is a complete waste of time developing them if PCTs and Hospital Trusts can then ignore them. NICE guidance implementation should be mandatory as the lowest level of treatment available to patients. It should be acceptable for the local NHS to offer better treatments if they see fit.

7.4 A recent patient report on the radio on wet macular degeneration showed a patient having to pay £500 per injection for Avastin to stop him going blind, as NICE has recommended that it should not be available on the NHS. The patient said this was ridiculous as blindness costs the NHS, social services and the economy a huge amount of money.

Ginette Camps-Walsh
FEmISA

March 2007

Evidence submitted by GlaxoSmithKline (NICE 86)

OVERVIEW

GlaxoSmithKline (GSK) welcomes the opportunity to contribute to the Health Select Committee inquiry into NICE. GSK is one of the world's leading research-based pharmaceutical and health care companies, developing and supplying medicines to improve patients' quality of life. We make prescription medicines, vaccines, over-the-counter medicines and oral care and nutritional healthcare products. We are proud of our strong, open relationship with the NHS and our British heritage. We employ more than 20,000 people across the United Kingdom and spent £1.3 billion on Research and Development (R&D) in the UK in 2006. This equates to over 40% of our global R&D spend.

1. EXECUTIVE SUMMARY

1.1 Historically, the environment for medicines in the UK has struck a good balance between delivering value for the NHS and stimulating innovation to deliver the medicines for the future. Mechanisms such as PICTF, the Ministerial-Industry Strategy Group (MISG), the MISG Long-Term Leadership Strategy (LTLS) and the UK Clinical Research Collaboration have allowed the perspectives of all stakeholders to be considered.

1.2 As a result of sustained dialogue between industry, government and other stakeholders, the government has been able to develop and implement policies that have delivered a stable environment that is broadly supportive of innovation. NICE is a contributor to an environment which is recognised across the world, aiming to ensure that patients have timely access to new medicines as they become available.

1.3 NICE has developed a positive international reputation, with its processes and methods evolving over an eight year period. These include efforts to consult with stakeholders, particularly patient groups, and inclusion of expertise from a wide range of professional groups.

1.4 The recent reports by Sir David Cooksey on Research Funding and the Office of Fair Trading (OFT) study into the Pharmaceutical Price Regulation Scheme (PPRS) envisage a broader role for NICE. GSK is open to an increased role for NICE, but urges caution against implementing radical changes to the system which may lead to unintended consequences. It is essential that any such changes are pragmatic in nature and continue to ensure that patients gain access to new medicines, the NHS continues to get value for money and the UK-based pharmaceutical industry receives appropriate reward for innovation.

1.5 The UK environment is attractive for a number of reasons, not least its stability and predictability. It will be important to retain, or replicate these attributes to continue to give industry the confidence to invest here and not unduly harm the competitiveness of the UK. Therefore, we believe that there are a number of aspects of how NICE operates today that would need to be reviewed before any broadening of its remit takes place:

- A broader definition of value should be developed. The cost per Quality Adjusted Life Year (QALY) should not be used as the only criteria for decision-making. A broad range of clinical outcomes and societal factors that have a real impact on patients and carers should also be part of the formal assessment.

- In addition, the current cost-effectiveness threshold (£20,000 to £30,000) should be reviewed. Consideration should be given either to increasing it, or assessing how it is applied, perhaps considering other aspects such as areas of significant unmet medical needs, UK health priorities, or a convergence with other government targets such as increasing the number of patients being treated in Primary Care as opposed to in hospital.
- The decision-making process should acknowledge inevitable uncertainty in the evidence base at the time of launch. The benefit of the doubt should favour the patient who should not be unreasonably denied access to the medicine under review when there is uncertainty.
- The opportunity for levels of consultation and dialogue during the current evaluation process should be increased. This could include improved dialogue between manufacturers and academics performing the reviews, and the possibility for manufacturers to present and answer questions at the Appraisal Committee meetings.
- An independent review of the appeals process should be carried out to ensure that it inspires confidence that the decisions reached are fair and based on the evidence available.
- Further measures should be introduced to increase implementation of NICE guidance.
- NICE should work with industry to develop a capacity for early dialogue to inform medicine development.

2. WHAT WORKS WELL WITHIN THE CURRENT SYSTEM

The remit of NICE

2.1 Since the inception of NICE, GSK has endorsed its objective to promote faster and more equitable access to modern treatments, as well as recognising the right of government to use a mechanism to inform rational decisions about the use of medicines and other health technologies. We believe we enjoy relatively good levels of engagement in the process, in terms of participation as a stakeholder, providing expert membership of its key committees, and constructive contribution to consultations and dialogue to help develop its processes and ways of operating. However, as we outline later in this submission, there is room for improvement in some areas.

2.2 GSK believes that NICE should be supported in its efforts to ensure fairness across the country's health system. We endorse its remit to produce robust, workable evidence-based guidance which is free from political interference. We also support its core principles, which represent an attempt to place measured consideration of both clinical effectiveness and value for money at the centre of NHS decision-making.

Ways of working

2.3 GSK recognises that there is much within NICE's approach that is praise-worthy. In 2005, the European trade body EFPIA produced a set of principles (see appendix 1) on the criteria for an effective Health Technology Appraisal (HTA) system and the NICE process fulfils many of these. In particular, we welcome its active involvement of key stakeholder groups including patients and professionals.

2.4 GSK welcomes NICE's decision to base one of its reviews, the Single Technology Appraisal (STA) on a submission from manufacturers. This often takes place in parallel with licensing, a stage where the vast majority of the evidence reviewed will in any case be held by the manufacturer. GSK also welcomes the small but important steps NICE has taken to improve dialogue through the STA process to help ensure that the manufacturer's submission will meet the needs of the appraisal process.

NICE prioritisation

2.5 GSK supports the current approach of NICE which focuses on areas of greatest importance to the NHS. Hence NICE balances its resources to continue to develop clinical guidelines that may arguably have the greatest impact on patient care. It would seem impractical for NICE to review all medicines currently available, or indeed all new indications of those medicines, as this would inject considerable bureaucracy into the system and would not be a good use of either taxpayer's money or industry resources and expertise.

2.6 A further challenge is the need to balance the desire to put into the public domain all evidence that informed the decision-making process, and the desire of companies and researchers to retain the opportunity to initially communicate new evidence via the recognised mechanism of presentation at medical congresses and peer-review publication. GSK took a key role within the Association of the British Pharmaceutical Industry (ABPI) in developing an approach with NICE to address this issue, and now fully subscribes to an agreed policy that minimises the extent and the time that evidence can be maintained as confidential.

3 WHAT COULD BE IMPROVED

Broadening the definition of value

3.1 GSK recognises the desire of governments to develop mechanisms to assess the cost-effectiveness of medicines. There are examples of evaluation leading to increased uptake and patient choice in areas such as cancer and cardiovascular disease. However, in a cost-driven climate, there is a risk that evaluation mechanisms will run counter to what should be their key objective: identifying medicines that bring the greatest benefit to patients, ensuring early access to these medicines, allowing choice among medicines of value and ensuring efficient healthcare through objective, high-quality assessments.

3.2 GSK believes that there is a case for broadening the definition of value. In assessing value, NICE relies on the cost per QALY as its tool. This has some merits but is not an exact science and can be a crude measure of value, in that it imposes an arbitrary, population-based barrier to access for individual patients with varying needs.

3.3 The QALY also finds it difficult to fully capture all the benefits likely to be important to patients, such as an improved safety profile or providing therapy in an oral rather than intravenous form, which may allow a cancer patient to be treated at home. Similarly, the value of a new medicine may lie in improved tolerability, reduced potency or improvements that increase patient compliance that may not be fully reflected in the QALY. This is demonstrated by the EQ5D questionnaire which is the preferred approach for generating QALY's (see appendix 2.) The questionnaire is relatively insensitive to incremental changes in quality of life and may not fully reflect the range of benefits that are important to patients. An example is the reduced impact on cognitive function of newer epilepsy treatments compared to older ones. Any subsequent improvement in educational performance would not register on the EQ5D. Likewise, no validated instruments exist for young children, and for some mental health conditions such as psychosis or depression, measurement is difficult or impossible.

3.4 The benefits and costs of a medicine beyond that of the NHS and Personal Social Services are not currently taken into account in the QALY. For example, the potential to alleviate the stress, anxiety and burden of care imposed on relatives and carers in Alzheimer's disease is a significant benefit not routinely included in decision making. Similarly, the potential to enable people to return to work and therefore contribute to society.

3.5 GSK has particular concerns around oncology medicines, where increasingly the QALY threshold (£20,000 to £30,000) does not appear to take into account the unique challenges of developing medicines in this area. This appears to result in a number of situations where new oncology medicines, with demonstrable benefit in terms of improved survival, are not being made available in the UK due to a delayed or negative NICE appraisal, whereas they have become standard of care in mainland Europe and the United States. An example is Avastin for Colorectal Cancer (made by Roche) which is now used widely in the European Union but not in the United Kingdom. It has been rejected by NICE on the grounds that it does not represent a good use of scarce NHS resources. This decision appears to unfairly disadvantage UK patients and is contrary to the principles of providing a world-class national health service. It also has the potential to develop an inequitable system where a patient's access to medicines is dependent on their ability to pay. This is in contrast to the French philosophy for example, which recognises the value of improvements in survival even in the late-stages of cancer, to both patients and their relatives. Medicines such as Avastin have received high ratings for additional medical benefit (ASMR) leading to rapid uptake in patients in France.

3.6 In addition, it should be considered whether the cost-effectiveness threshold should be increased or applied flexibly within the current system. One example is for "orphan medicines" to allow for the higher cost per patient. Orphan medicines are defined as those to treat diseases which are serious, life-threatening or seriously debilitating and with a prevalence of less than 5 per 10,000 population. These treatments are often the only medicines available for these rare diseases and it is therefore important to ensure that the system does not preclude impacted patients.

3.7 GSK recognises that the QALY provides a common currency for measuring the extent of health gains that result from an intervention, and therefore can be used to assess their relative worth from an economic perspective. However this common currency is by nature inflexible, which means that it is difficult to give greater weighting to defined therapeutic areas even if they have been identified by government as a public health priority. Therefore, GSK believes that if the QALY is to be retained, consideration should be given to introducing a flexible system, where certain agreed disease areas fall into different bands with varying thresholds. Areas of greater need could attract a higher threshold, thereby further aligning the concept of rewarding innovation with meeting the objectives of public health policy.

Developing greater dialogue between NICE and industry in the development phase

3.8 The development of a medicine takes between 10 to 12 years, but there is little dialogue between government, NICE and industry until the medicine has been granted a licence. Increasing dialogue early in the process of a new medicine would be of benefit to all parties if it could be achieved without adding to development times.

3.9 GSK supports Sir David Cooksey's recommendations on the subject of improved dialogue, which have been accepted by the Government. What is needed by pharmaceutical companies is advice and guidance about the sort of dataset that would be required for a positive NICE review at launch, in order that this can be built into clinical development plans. We do not want NICE to propose trial designs or to be overly prescriptive about what trials need to be done, to avoid data needing to be generated for the UK market alone.

3.10 Even with earlier NICE dialogue in place, there will be some medicines where value cannot be demonstrated at launch but for which collection of additional data through usage in clinical practice is likely to prove value. In these circumstances, greater flexibility is needed by both industry and NICE to agree a temporary solution that facilitates patient access to the medicine.

The Evaluation Process

3.11 The process of appraising health technologies remains embryonic and its quality is variable. It is often based on a number of assumptions, particularly in the assessment of new medicines, when all of the data is unlikely to be available. NICE relies upon a number of Assessment Groups (AGs) and Evidence Review Groups (ERGs) to produce independent assessment reports in the case of Multiple Technology Appraisals, or critiques of the manufacturer's assessments in the case of Single Technology Appraisals. The groups are at liberty to take different approaches to their assessment of the evidence and to the production of their reports, often applying varying academic methodologies. This has led to inconsistency and corrections in a number of cases.

3.12 To increase confidence in the decision-making process, GSK advocates a more collaborative approach between industry and the Assessment Groups. This should allow more discussion and potential resolution of any technical or factual issues prior to the Appraisal Committee. In addition, stakeholders should have the opportunity to fully critique the analysis on which the report is based. This would include complete access to working copies of the economic models used by Assessment Groups and the opportunity to provide feedback on the ERG critique prior to the Appraisal Committee within the STA process.

3.13 Currently, clinicians and representatives of patient groups are invited to attend Appraisal Committee meetings to share expertise and respond to questions. This invitation is not extended to manufacturers, who have spent on average a decade amassing the evidence upon which NICE guidance is based. We believe the process would benefit from constructive engagement throughout appraisal, including attendance at the Appraisal Meetings to ensure a fair and balanced hearing.

3.14 NICE has recognised a need to issue guidance on some new medicines more quickly than the original process allowed. GSK broadly welcomed the launch of a "fast-track" process known as Single Technology Appraisal (STA) that allows the NHS to issue guidance nearer to the time that a medicine launches. However, as raised with NICE during the consultation on these proposals, there is again a need for the committees to recognise what evidence can practically be expected at the time of launch. They should not therefore unreasonably deny access to medicines which may in fact be cost-effective, based on a full dataset that can only be generated post-launch. Although we recognise this process is at its early stages, GSK is concerned that this is not being taken into account and therefore some new medicines are being turned down.

The Appeals Process

3.15 GSK recognises that NICE invests considerable resources into its appeals process. However, we would raise questions about its effectiveness. In the 12 appeals undertaken since the process has been made public, no substantive changes have yet been made to the guidance in any particular case. This is despite the fact that 4 cases had points upheld. This discrepancy appears to be a result of the permitted grounds for appeal which are highly restrictive and do not allow a substantive review of the evidence on which the decisions were made. We would recommend a review of the process and consideration be given as to whether the grounds could be broadened. A more robust appeals procedure would ultimately increase confidence that decisions are reached fairly and are based on the presented evidence.

Implementation

3.16 Demonstration of cost-effectiveness will increasingly be required to allow widespread use of new medicines in patients. If a medicine does demonstrate value at launch, the system should facilitate wide and rapid uptake to all appropriate patients, at a price that rewards the value delivered.

3.17 Failure to implement NICE guidance remains a key issue. Since 2001, clinicians have been officially required to implement NICE guidance, but take-up is inconsistent which disadvantages patients. This is largely due to poor horizon-scanning combined with capped budgets within Primary Care Trusts and a sense that some clinicians are cautious to introduce new and innovative medicines. This has led to the perception that whilst all negative NICE decisions are routinely picked up by Primary Care Trusts, some positive ones are blocked. The UK remains one of the slowest adopters of new medicines in Europe which means that patients continue to be denied new medicines which could enhance the quality of their lives.

3.18 Access to, or denial of, a new medicine frequently depends on where a patient lives. The principal barrier to more uniform implementation appears to relate to poor financial planning within NHS Trusts, rather than financial shortages per se. GSK believes that this poor implementation of NICE guidance is the most important issue for the government to address in this area, particularly if the new fast-track process is to have any impact.

3.19 Given the impact of poor financial planning on the implementation of guidance, it is critical to retain the statutory requirement for the funding of NICE approved medicines (including when it is incorporated into NICE guidelines following a review) and to ensure a clear and rapid mechanism for the incorporation of the costs of these medicines into the tariffs operated as part of Payment by Results (PbR.)

3.20 Further implementation of NICE guidance could be driven through the Healthcare Commission reviews, which currently focus on process, but could be extended to monitor and track levels of implementation within Primary Care Trusts. Existing mechanisms such as the Quality Outcomes Framework (QOF) could also be used to drive uptake of guidance. This was introduced as part of the new General Medical Services (GMS) contract in April 2004 and has been instrumental in changing prescribing behaviour. GSK believes that the implementation of NICE guidance could be incorporated into the QOF, which would then reward doctors for implementing good practice in their surgeries. As the criteria are designed around best practice and have a number of additional points for achievement, it follows that this mechanism would drive doctor's behaviour to ensure they implement NICE guidance, as essentially they would be incentivised to do so. This in turn would benefit patients, who would be granted better access to appropriate innovative medicines.

3.21 The government has introduced policy measures which could further help to address issues of implementation. The recent White Paper "Our Health, Our Care, Our Say" (2006) directs more resources towards the Primary Care sector and empowers local healthcare providers by giving them greater control of resources. This could help to overcome poor NICE implementation by providing incentives to adopt NICE guidance quickly and completely. Transparency of process will therefore be critical, as will much improved dialogue and trust.

4. CONCLUSION

NICE plays an important and integral role in the UK healthcare system, which seeks to balance the need to provide patients with access to affordable new medicines while encouraging high-risk innovative research by UK-based pharmaceutical companies. As with all systems which seek to measure value, there are strengths and there are areas for improvement. GSK believes there is a need to review the work of NICE, as outlined above, in advance of NICE taking on an important role in providing guidance to industry early in medicine development. Any reform should be gradual and practical and it should be guided by a range of stakeholders. Due to the UK's leadership in this area, decisions reached in the UK will have ramifications at a European and global level. The challenge is significant, but we are confident that over time it will be possible to come to a system that provides proper alignment between ensuring timely access to medicines for patients, value for money for governments and appropriate reward for companies that discover and develop innovative medicines. GSK looks forward to playing its part.

GlaxoSmithKline

March 2007

Evidence submitted by Help the Aged (NICE 11)

EXECUTIVE SUMMARY

1. Help the Aged recognises the important role that NICE has to play in ensuring the clinical effectiveness of drugs and providing evidence based best practice, clinical guidelines to improve the quality of clinical practice. However, the credibility of NICE is at stake unless action is taken to:

- (a) Establish NICE as a valid assessor of evidence of clinical effectiveness by separating this from the role of "rationing" what is funded.
- (b) Improve communication with stakeholders.
- (c) Redress the balance between implementation of clinical effectiveness of drugs and clinical guidelines.

2. There is a conflict between the roles of making an objective assessment of clinical effectiveness and making a judgement about funding based on economics and cost. These roles should be separated so that NICE is seen as a valid assessor of evidence. Central Government should be responsible for making a decision about funding based on the evidence supplied by NICE.

3. The reports published by NICE on the assessment of the clinical effectiveness of drugs and the decisions for funding are inaccessible to the public as the language is overly technical and there is no attempt to address some of the concerns that will be raised by the public about quality of life and people's experience of using the drugs.

4. The system of stakeholder engagement is too complex and time consuming and therefore excludes many smaller organisations from fully participating.

5. There is an imbalance in the media attention given to decisions on the funding of drugs and the publication of clinical guidelines and the impact of their implementation on the quality of clinical care. This means that the public perception of NICE is as a rationing body for the NHS.

6. Implementation of guidelines for drugs are also implemented and monitored with more vigour than the clinical guidelines which are poorly implemented with no real monitoring or performance by SHAs or the Healthcare Commission.

INTRODUCTION

7. Help the Aged has welcomed clinical guidelines aimed at improving outcomes for older people for example, dementia, falls and continence. We have however been disappointed in the poor implementation of this guidance and the relatively low priority that it is given by the NHS.

8. Help the Aged have been contacted by members of the public who have been unhappy with some of the decisions made about specific drugs, for example those drugs for people with Alzheimer's disease. We have found the information provided to the public on the NICE website to be poorly communicated and inaccessible. We have also been disappointed with the limited focus of NICE in assessing clinical effectiveness against the cost benefit, as it has not taken account of people's experience and the personal cost.

Why NICE's decisions are increasingly being challenged

9. NICE produces clinical guidelines based on best practice and technical analysis of the benefits and costs of drugs, leading to a decision on whether the drugs assessed should be provided by the NHS. It is the latter that receives the most challenge from the public and other stakeholders.

10. The public see the role of NICE as rationing which drugs can and cannot be provided, with the key factor being cost versus clinical effectiveness. The analysis which determines whether a drug is funded or not does not include the evidence of people's experience or the quality of their life. This means that some decisions inevitably provoke a response questioning the decision and requiring the reasoning be explained.

11. Although NICE make the reports available on how they assessed each drug and reached a decision, these are not presented in a way that is accessible to the public. They are very technical reports that could only be easily understood by other medics. The information is not presented in a way that is open to challenge as the language is inaccessible.

12. The decision making process for which drugs can be used by the NHS is therefore exclusive. This means that stakeholders such as charities and the public find other ways of making their views heard, for example lobbying and approaching the media.

13. The disadvantage of this is that some unpopular decisions get better coverage than others, if they are more attractive to the media. This potentially creates an unfair system if increased media coverage and the resulting public pressure leads to a reversal of decisions.

14. NICE have an important role to play in reviewing the clinical effectiveness of different drugs. However, they need to consider benefits within a wider context, including the user's experience and quality of life.

15. Decisions should be communicated in a clear and transparent way with collaborative dialogue that can respond to challenge in a constructive way. NICE should be proactive in explaining why decisions have been made that seem counter intuitive.

Whether public confidence in the institute is waning and if so why?

16. Help the Aged believe that public confidence in NICE is waning and this concerns us, as we recognise the importance of having an independent organisation that ensures the clinical effectiveness of drugs and provides best practice clinical guidance.

17. There is an inherent conflict between making objective clinical and technical assessments and those based on economics and cost. We recommend the separation of these two functions so that NICE is seen as a valid assessor of evidence and not a "rationer" of drugs.

18. The system of stakeholder participation is too complex and time consuming. Smaller organisations do not have the resources to engage or participate fully, thereby excluding important voices.

19. The NICE system excludes “softer” measures of efficacy and focuses on scientific evidence only which excludes important information.

20. There is an imbalance in the implementation of clinical guidelines and those for drugs, with the latter having more rigorous implementation. NICE needs to have adequate funding to promote the implementation of clinical guidelines.

21. NICE needs to develop effective public relations to promote the impact that the best practice guidance is having on the quality of clinical practice. This can only happen if local systems are put in place to audit the effectiveness of implementation and measure the outcomes.

22. Public confidence may well increase if the impact of NICE was more balanced with the outcomes of implementation of clinical guidelines promoted.

Whether any particular groups are disadvantaged by NICE’s evaluation process?

23. The process is not inclusive as it is not communicated effectively to stakeholders. The reports are overly technical and are written in a way that is only accessible to professionals with a medical or scientific background. Neither is there an opportunity for clear and open dialogue, this results in lobbying organisations and individuals finding alternative routes. For example, using the media to help campaign for the use of Herceptin. This drug received a lot of media attention and public support as the cancer lobby is powerful, with a great deal of public support and many campaigners to mobilise. It is unlikely that there would be the same level of interest and support in, continence, for example, which is a far more taboo subject with weaker and less co-ordinated lobbying groups. This is why it is important to get the process right and to ensure that it is inclusive and open to challenge in a fair and constructive way.

The Implementation of NICE Guidance

24. As already stated there is an imbalance of implementation on the guidelines for drugs and clinical practice. Clinical guidelines are not implemented with any vigour. There are not effective local monitoring systems in place or systematic regulation.

25. The Healthcare Commission assesses NHS trusts against the core standard to implement national service framework standards and NICE guidance. However, the arms-length approach of regulation means that performance against specific guidance and NSF standards is not assessed unless part of a one-off improvement review or audit. There is not a recurring and systematic assessment of implementation for specific clinical practice guidance.

26. NHS trusts should carry out internal audits on the implementation of NICE guidance.

27. Strategic Health Authorities need to have robust systems in place to monitor the implementation of clinical guidelines

RECOMMENDATIONS FOR ACTION

28. NICE should provide clear, plain English reports on the clinical effectiveness of drugs in a way that is accessible to all stakeholders.

29. NICE should consider the quality of life to individuals as well as the cost benefit to the state in considering the clinical effectiveness of drugs.

30. The Government should take responsibility for funding decisions based on the independent report of clinical effectiveness provided by NICE. The current arrangement means that NICE has two conflicting roles, assessing clinical effectiveness and making a decision on funding. The funding decision is a political one. The Government is responsible for managing the public purse, and as such should take responsibility and be accountable for the tough decisions as to what the NHS can and cannot afford, based on independent evidence.

31. The implementation of clinical guidelines should be improved by:

- NICE strengthening this role within its own organisation;
- SHAs monitoring the performance of trusts against NICE guidance and NSF standards; and
- NHS trusts carrying out regular audits on implementation of NICE guidance and NSFs.

Help the Aged

March 2007

Evidence submitted by the Hepatitis C Trust (NICE 29)

INTRODUCTION

The Hepatitis C Trust is the only UK national charity for hepatitis C (HCV). It provides information, support and representation for all those affected by the disease. The charity was started, and is fully staffed, by patients.⁸⁵

EXECUTIVE SUMMARY

1. Guidance is being challenged and the public are losing confidence in NICE because of a lack of understanding about the Institute's role and remit. An increased emphasis on 'patient choice' is at odds with NICE's perceived role as gatekeeper to some NHS treatments. NICE have a very difficult job in counteracting these claims and communicating with the public, despite having a good track record at consulting with a wide range of patients. Many PCTs are failing to implement NICE guidance because they lack resources or have miscalculated the need for treatment in their area. This is particularly short-sighted because failure to treat an infectious disease such as HCV will increase future costs and burden of the disease.

Why is NICE Guidance Increasingly Being Challenged and Why is Public Confidence in the Institute Waning

2. The various challenges to guidance could be perceived as due to a lack of confidence in the institute. The two are intrinsically linked.

3. Public confidence is waning and guidance is being challenged because patients misunderstand the role and remit of NICE. In our experience patients often do not realise that NICE is an independent body and see it as an extension of the NHS designed as a gatekeeper to clinical resources, and with an agenda to save money. Therefore when a decision is made not to recommend certain clinical treatment, patients assume this decision is based solely on financial arguments. This idea has been perpetuated by certain sections of the media while NICE's ability to rebut these arguments does not seem particularly strong or effective.

4. The concept of patient "choice" in healthcare may also have had an impact, in that patients could feel they are entitled to treatment that may not necessarily be suitable to their condition. When denied this treatment this is interpreted as being denied to the right to choose. This again could be improved by providing the public with better information about what treatment is appropriate.

NICE's Evaluation Process and Whether Particular Groups are Disadvantaged by the Process, and the Speed of Publishing Guidance

5. In our experience NICE's evaluation process is very thorough. The speed at which guidance is published can be slow at times but we accept this is often a consequence of the rigorous evaluation process.

6. A large proportion of patients with HCV have previously been, or still are, intravenous drug users (IDUs). This is a group that could easily be marginalised and disadvantaged by the evaluation process. In reality we have found that NICE has listened carefully to representations from The Hepatitis C Trust on behalf of such patients and have changed their technology appraisals as a consequence. For example in 2003/4 NICE considered the use of pegylated interferon and ribavirin for moderate to severe chronic HCV but stated that current IDUs "have high rates of discontinuation in trials and relatively high rates of psychiatric comorbidities, and thus do not achieve high success rates with interferon therapy." The Trust objected strongly to this both on the grounds of its accuracy and because we were concerned that the NHS would use this to deny treatment to current IDUs. Our objections were noted and the NICE committee amended the wording accordingly to 'Current injecting drug users can have high rates of discontinuation in trials, and thus do not achieve success rates in trials with interferon alfa therapy as high as those obtained by other participants. However, there is evidence that where adherence is achieved, success rates are not significantly different'. They added: 'the evidence provided by the experts persuaded the Committee that current information indicated that HCV re-infection rates for people on interferon or peginterferon therapy were low in those who continue to inject illicit drugs. Thus, although rates of discontinuation of injecting drug users in trials have been high, the Committee was prepared to accept that in naturalistic settings, the rate of discontinuation would not be so great as to prevent the treatment being cost effective.' We are very happy with this outcome and feel it demonstrates NICE's willingness to engage with patients.

⁸⁵ In regards to this inquiry we would like to notify the committee that we receive approximately 20% of annual funding from the pharmaceutical industry in the form of unrestricted educational grants, but equally receive a similar level of funding from the Department of Health. We are aware of several high profile cases where charities have been accused of pursuing activities which would be of benefit to their pharmaceutical industry backers. Therefore The Hepatitis C Trust would like to put on record our belief that, in line with NICE guidance, clinical treatment for HCV should be available to all who want it but that the decision to take it is a matter for the individual and should be decided on clinical need and personal circumstance.

The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines

7. NICE has issued guidance on the use of combination anti-viral medicine for mild, moderate, and severe, chronic HCV. The decision on whether to treat a patient with mild HCV or whether to wait until the disease has reached a moderate stage is a decision the patient is asked to make. Put simply, if you have the disease and want treatment for it, NICE recommends you have it.

8. It is clear from the audit we carried out on behalf of the All-Party Parliamentary Hepatology Group ('A Matter of Chance') and from demands on our advocacy service that implementation of NICE guidance is patchy across the country, another so-called 'post-code lottery.' Outright refusals to offer treatment are rare but instead patients are made to wait unacceptably long times. As a result waiting times to start treatment vary from a matter of just days to almost 2 years. There appear to be 4 main reasons for this—ignorance of obligations under NICE, budgetary constraints, insufficient staffing levels and problems in the commissioning process between Primary Care Trusts (PCTs) and NHS Hospital Trusts.

9. In particular, some PCTs do not seem to accept that guidance set out in NICE Technology Appraisals is mandatory or they feel it is 'less mandatory' than other priorities such as balancing their budgets or they think that there is no time limit to implementation so that, provided they make NICE treatment available to a patient at some point (say, next financial year or even the one after), they are operating within NICE guidance.

10. In one case we came across a hospital (Addenbrookes in Cambridge) that changed the protocol for HCV treatment from that set out in NICE guidance in order to ration treatment by discontinuing it in certain cases after 3 months where it should have been continued for a full 48 weeks. This allowed them to treat more patients but to the disadvantage of others. The need for rationing appears to have been dictated by the failure of local PCTs to commission services adequately.

The Hepatitis C Trust

March 2007

Evidence submitted by the Improving Surgical Outcomes Group (ISOG) (NICE 75)

1. INTRODUCTION

1.1 The ISOG is an independent medical group comprising surgeons, anaesthetists, critical care consultants and others involved in operative management and care. The group is concerned with improving patient outcomes and modernising care for patients undergoing major surgery.⁸⁶

2. EXECUTIVE SUMMARY

2.1 Overwhelming scientific evidence shows that haemodynamic optimisation (maximising the flow of blood from the heart) of patients undergoing moderate and major risk surgery reduces the number and severity of post-operative complications. As a consequence, as patients feel better and need less post-operative care, they can be discharged sooner.

2.2 The clinical benefit therefore translates into economic benefit as the cost of the patient's hospital stay is reduced. In 2004 it was shown that the benefits shown in the clinical studies, of better patient outcomes at less cost, could be delivered in the NHS at Trust level.

2.3 In February 2005, NICE decided that they did not believe that this procedure falls within its remit and stated that this was because oesophageal Doppler monitoring is considered standard clinical practice with risks and benefits that are sufficiently well-known.

2.4 Despite the fact that NICE decided that oesophageal Doppler monitoring was considered to be "standard clinical practice" the reality is that two years later, up to 90% of all NHS patients are still being denied the monitoring system.

2.5 Despite the fact that NICE made this decision two years ago, there has been no widespread implementation of haemodynamic optimisation in the NHS and as a consequence, ISOG has had to produce an implementation document to drive this treatment forward. The reasons why the NHS has been slow to implement the treatment is multi-factoral but the main reason has clearly been lack of funding.

2.6 This submission will examine only the term of reference concerning the consequences of the NICE decision that oesophageal Doppler monitoring constitutes "standard clinical practice".

⁸⁶ The members of the group responsible for this submission are as follows: Professor Monty Mythen; Portex Professor of Anaesthesia and Critical Care, University College London; Head of The Portex Anaesthesia, Intensive Care and Respiratory Unit, Institute of Child Health, UCL; and Council Member of the Intensive Care Society of Great Britain & Ireland; Professor David Bennett; Professor of Intensive Care Medicine, St George's Hospital, London; Mr Eddie Chaloner; Consultant Vascular Surgeon: University Hospital, Lewisham.

3. TERM OF REFERENCE: THE IMPLEMENTATION OF NICE GUIDANCE

3.1 ISOG welcomes the confirmation by NICE that improving patients' post-operative prospects with haemodynamic monitoring during surgery should indeed be standard practice for patients undergoing surgery but we bitterly regret that this just isn't being implemented in many UK hospitals at the moment. NICE may think this is a standard practice but the figures show that this is in actual fact far from the case.

3.2 Over 90% of patients undergoing surgery are not benefiting from a technology that is totally in line with Department of Health policy to implement the modernisation of care and improve surgical outcomes for patients. The NHS Confederation has also been urging Trusts to make the new NHS a reality by using new practices and technologies that can save lives, time and money.

3.3 Oesophageal Doppler monitoring involves the measurement of blood flow velocity in the descending thoracic aorta using a flexible ultrasound probe.

3.4 The economic benefits of the introduction and use of haemodynamic optimisation are enormous and arise because the technique not only saves lives but also saves money. Government initiatives like "spend to save" however, need to be more proactive to allow the faster introduction of procedures, approved by NICE, that are proven to benefit patients and save money for the NHS.

3.5 The clinical studies suggest typical reductions in length of stay for haemodynamically optimised moderate and major risk surgical patients of around four days and audits of the real world impact have reported reductions of up to three days per patient. Even if these reductions were only in the lowest cost wards in UK hospitals at around £200 per day, this saving still equates to £600 to £800 per patient. It costs £50 to £60 to optimise each patient.

3.6 Based on the body of clinical evidence which has accumulated, mostly from UK hospitals, over the last 10 years, there are about 1,000,000 NHS patients a year who would derive a clear clinical benefit from haemodynamic optimisation. If lengths of hospital stay for these patients were only reduced by two days each, the UK NHS would free up nearly 5,500 beds—the equivalent of 11 hospitals of 500 beds each. The saving would be, at the lowest estimate, £350 million a year rising to over £1 billion. This would represent a magnitude of cost-saving that could allow huge reductions in the deficit of an average NHS Trust

3.7 The resources freed up by haemodynamic optimisation would be redeployed to enable the other two step ISOG recommendations at minimal additional cost.

3.8 The benefits of haemodynamic optimisation are now well accepted by the majority of UK anaesthetists and those involved in intensive care. However, we estimate that no more than 40,000 NHS patients were monitored with appropriate equipment to allow doctors to haemodynamically optimise them in 2004.

3.9 At the rates of technology adoption typical in the NHS it will be many years until the remaining 960,000 patients receive the treatment evidence based medicine and basic economic sense demand they receive today. As a result, thousands of patients will continue to die unnecessarily each year, many more will carry on suffering the pain and misery of avoidable post-surgical complications and NHS hospitals will continue to spend hundreds of millions of pounds treating compromised patients who need not have been so ill in the first place.

3.10 Examples demonstrating better use of surgical/anaesthetic resources include improving surgical outcomes by intra-operative haemodynamic optimisation and other techniques.

3.11 These interventions reduce both the number and severity of post-operative complications.

3.12 A study conducted at York District Hospital on the use of improved intraoperative care involving haemodynamic optimisation and other interventions, combined with the planned transfer of patients to ICU, resulted in a reduction of the mortality rate to 3% compared with 18% in the control group.

3.13 The study also demonstrated a reduction in the patients' length of hospital stay—in terms of total bed days as well as ICU bed days—without increasing costs.

3.14 A Department of Health funded study at Worthing Hospital assessing "goal directed" fluid administration during bowel surgery (using oesophageal Doppler probes) showed a significant reduction in post-operative morbidity, faster return of gut motility and shorter length of stay.

3.15 Recent work from St Georges Hospital using goal directed fluid therapy in high risk surgical patients in intensive care after surgery reduced post-operative infections by 50% and cut length of stay by almost 40%.

3.16 Improvements in pre-operative assessment and preparation, peri-operative care and post-operative support have provided an important reduction in the mortality rate as well as decreasing the number and severity of complications suffered by patients following surgery, which has in turn provided savings in terms of ICU/HDU bed days per patient.

3.17 In addition to reducing the mortality rate, the study conducted at York demonstrated that haemodynamic optimisation reduced the number of ICU or HDU bed days used by 40% compared with routine care (median 3.3 days vs 5.5 days), and total bed days per patient were reduced by 41% (median 13 days vs 22 days).

3.18 The capital and running costs for providing improved pre-operative, peri-operative and post-operative support are marginal in comparison with the potential savings.

3.19 Pre-operative surgical risk assessment of patients undergoing major surgery can be measured by use of Cardio-pulmonary exercise testing (CPX), which is cheaper and more effective at predicting individualised pre-operative risk than many of the tests that are currently conducted to assess surgical risk (such as resting echocardiography) which are poor at predicting actual risk.

3.20 Consistent implementation across the NHS of existing treatments known to be effective at preventing post-operative complications (such as measures to prevent the formation of deep vein thrombosis) would also reduce unnecessary post-operative morbidity. Evidence on this particular issue has recently been given to the Health Select Committee.

3.21 For haemodynamic optimisation, the potential savings in terms of reduced hospital stays have been estimated for an average NHS trust to be in the order of over £2 million, based on reduction in stays of 22–31% and taking into account capital outlay of £60,000 and running costs of £150,000.

3.22 Overall, the package of improvements described would be cost effective. In addition, the introduction and use of haemodynamic optimisation into the NHS could realise savings for the NHS in the region of £1 billion which would have an enormous impact on the current and potential deficits in the NHS.

3.23. Due to the delay in implementing haemodynamic optimisation within the NHS, ISOG had now produced a second document intended to assist Trusts with its introduction. Lack of funding is clearly a major issue for some Trusts and this is severely hampering a technology that will substantially help patients and ultimately save Trusts money.

3.24 NICE has an important role to play in the introduction of such technologies and it is regrettable that despite a positive outcome from NICE, no real advance has been made in the last two years to introduce this technology into the NHS, despite enormous support from the medical profession. Simple, straightforward steps can be taken to allow this to happen which will benefit patients, Trusts and the NHS.

3.25 The ISOG would be prepared to offer oral evidence if requested to do so by the Committee.

4. RECOMMENDATION

4.1 Government initiatives like “spend to save” need to be more proactive to allow the faster introduction of procedures that are proven to save money for the NHS.

4.2 A better system of disseminating information to Trusts is essential to make sure that all stakeholders are aware of NICE Guidance.

4.3 A streamlined system is needed to help facilitate the introduction of NICE appraised devices into the NHS.

4.4 The Government should consider mechanisms whereby the Interventional Procedures arm of NICE can attract compulsory funding in the same way as drugs positively appraised under NICE’s Technology Appraisals arm.

Improving Social Outcomes Group

March 2007

Evidence submitted by the Institute for Innovation & Valuation in Health Care (NICE 18)

1. THE INSTITUTE FOR INNOVATION & VALUATION IN HEALTH CARE (INNOVAL-HC)

1.1 The Institute for Innovation & Valuation in Health Care (InnoVal-HC) welcomes the opportunity to submit a response to the Health Committee’s inquiry into aspects of the work of the National Institute for Health and Clinical Excellence (NICE).

1.2 InnoVal-HC (“the Institute”; www.innoval-hc.com) is an independent not-for-profit scientific organisation dedicated to research into the principles of economic evaluation of health care technologies and their application. The Institute was founded in June 2005 and has since been formally associated with the University of Applied Economic Sciences Ludwigsafen, Germany.

1.3 The Institute’s remit includes to conduct analyses and research into the methods and ethical foundations of health economic evaluations, the mechanisms of delivery of and financing health care, the valuation of innovative technologies, procedures, and products, and the acceptability of technologies based on their cost-benefit and cost-effectiveness ratios.

1.4 The Institute does not operate as a contract research organisation. As a matter of principle, the Institute accepts support exclusively under a policy of unrestricted educational grants. To date, the Institute has received support from policy makers’, payers’, providers’, physicians’, patients’, and pharmacists’ organisations, as well as from the pharmaceutical industry.

2. OVERVIEW

We would particularly like to draw the attention of the Committee to the following points:

- NICE’s international standing
- The logic of cost-effectiveness
- NICE accountability for reasonableness
- Concluding remarks and recommendations

3. INTERNATIONAL PERSPECTIVE

3.1 Internationally, NICE’s technology appraisal programme is broadly considered a role model for health technology assessments including economic evaluation. Following the House of Commons Health Select Committee report of June 2002, NICE commissioned the WHO Regional Office for Europe to carry out a review of its Technology Appraisal Programme. The WHO review team described key principles of the NICE approach as “the use of best available evidence in decision-making, transparency, consultation, inclusion of all key stakeholders, and responsiveness to change.” They concluded that, “in all of these areas, it is clear that NICE is setting a new, international benchmark, for which it can and should be congratulated” (Hill *et al.*, 2003).

3.2 Further to this, NICE has assumed a leading role internationally by fostering methodological advances such as the use of probabilistic sensitivity analyses (intended to capture decision uncertainty) and mixed treatment comparison techniques (in order to enable indirect comparisons of technologies in the absence of head-to-head studies).

3.3 Against this background, guidance issued by NICE, as well as the underlying technology assessments and appraisals, have attracted much attention internationally. For example, the US National Guideline Clearinghouse routinely lists recommendations by NICE on its website (www.guideline.gov). In addition, policy makers in jurisdictions other than the UK (such as the US and Germany) have engaged in debate about the adoption of NICE-like processes in the context of National Health Technology Assessment (HTA) programmes.

3.4 In the context of this international debate, we conducted a qualitative study of the robustness of the NICE approach (Schlander, 2007a). Here we report on some of our key observations.

4. THE LOGIC OF COST-EFFECTIVENESS

4.1 The logic of cost-effectiveness as adopted by NICE—in contrast to traditional cost-benefit analysis—does not represent an application of standard economic theory (eg, Birch and Donaldson, 2003; Birch and Gafni, 2006). The approach was rather developed by decision analysts with an operations research background, striving to transfer methods to optimise the efficiency of manufacturing processes to the production of health (cf. Torrance, 2006). Specifically, NICE has chosen to use cost-utility analysis—a variant of cost-effectiveness analysis—as its reference case, with Quality-Adjusted Life Years (QALYs) as a universal and comprehensive measure of health-related outcomes (NICE, 2004).

4.2 It is a fundamental and well established principle of decision analysis that “the identification and structuring of objectives essentially frames the decision being addressed. It sets the stage for all that follows” (Keeney and Raiffa, 1993). To be relevant, analytic decision support relies on prior clarification of values and objectives to be pursued (Keeney, 1992). Then, to a great deal, applying the logic of cost-effectiveness to inform health care resource allocation decisions hinges on the assumption that “the principal objective of the National Health Service (NHS) ought to be to maximise the aggregate improvement in the health status of the whole community” (Culyer, 1997; earlier for instance: Weinstein and Stason, 1977). While it appears trivial that health care services (should) produce health, it is by no means self-evident to make a quick leap from here to an assumed “principal objective” of collectively financed health care to simply maximise some construct (QALYs or else) of health-related consequences.

4.3 In fact, there is little if any evidence that the maximisation view (sometimes justified with an asserted “consensus in the literature” without specifying sources; see Torrance, 2006) is shared by the general population (Coast, 2004). On the contrary, there has been a rapidly growing body of studies, which collectively show that this assumption is “empirically flawed” (Dolan *et al.*, 2005; and others). Controversial issues revolve around (but are not limited to) a higher social priority for interventions when the severity of the patient’s condition increases, with life-saving interventions most highly valued (this is sometimes referred to as “the rule of rescue”, cf. Jonsen, 1986; Hadorn, 1991; Nord, 1999; Ubel, 2000; McKie and Richardson, 2003), and for people in so called double jeopardy (ie, with more than one condition causing impairment) who have less QALYs to gain from successful interventions compared to otherwise healthy individuals (cf. Singer *et al.*, 1995; Harris, 1995; McKie *et al.*, 1996). As a consequence, there has been a call for more research into “empirical ethics” by leading health economists (eg, Richardson and McKie, 2005).

4.4 The maximisation assumption has also been critiqued from a *normative* perspective. Concerns prominently include the implied valuation of human life as a function of health status, as opposed to viewing the value of life as a dimension distinct from health (Harris, 1987; Arnesen and Nord, 1999; and many others).

4.5 In the absence of a gold standard against which to judge criterion validity of the logic of cost-effectiveness, it has been proposed to use the so-called reflective equilibrium approach to examine the social acceptability of the resulting rankings of health care programmes (Daniels, 2001; Nord, 1992). Thus the problems involved in the application of standard decision rules derived from the logic of cost-effectiveness are perhaps best illustrated using an example: Assuming the (incremental) cost per QALY gained was, for example, approximately £3,600 for sildenafil in erectile dysfunction (Stolk *et al.*, 2000), approximately £7,000 for pharmacotherapy of children with attention deficit hyperactivity disorder (NICE, 2006), and > 120,000 for beta-interferons and glatiramer in multiple sclerosis (NICE, 2002), would this ranking reflect the comparative social desirability of these interventions (cf. McGregor, 2003)?

4.6 Far from representing a phenomenon encountered in England and Wales only, the issue of counterintuitive rankings had been a major obstacle already faced by the protagonists of cost-effectiveness analysis for resource allocation in the Oregon Health Plan (cf. Hadorn, 1991). It is a conspicuous observation that reviews of the usefulness of such rankings (“QALY league tables”) by many health economists have addressed a variety of technical issues in detail but did not pay attention to the issue of the validity of such rankings. (eg, Drummond *et al.*, 1993; Mauskopf *et al.*, 2003).

4.7 Importantly, the issue of counterintuitive rankings should not be confused with the problem of distorted human judgments due to “heuristics and biases” (Gilovich *et al.*, 2002), as moral intuitions in the sense of reflected values and beliefs cannot be invalidated simply on grounds of their incompatibility with competing normative claims. Of note, it has even been argued by philosophers that there may exist an irreducible pluralism at the foundations of normative ethics (cf. Nagel, 1979).

5. NICE ACCOUNTABILITY FOR REASONABLENESS

5.1 Recognizing both the difficulty of democratic societies to achieve consensus on distributive principles for health care and the need for legitimacy of allocation decisions, Norman Daniels and James Sabin (2002) proposed a framework for institutional decision-making, which they call “accountability for reasonableness” (A4R). In order to narrow the scope of controversy, A4R relies on “fair deliberative procedures that yield a range of acceptable answers” and consists of four conditions.

5.1.1 *Publicity*, ie, resource allocation decisions must be public, including the grounds for making them. Transparency should open decisions and their rationales for scrutiny by all affected, not just the members of the decision-making group.

5.1.2 *Relevance*, ie, “the grounds for decisions must be ones that fair-minded people can agree are relevant to meeting health care needs fairly under reasonable resource constraints.” Arguments should rest on scientific evidence, though not necessarily a specific kind of, and appeal to the notion of “fair equality of opportunity.” Although Daniels and Sabin acknowledge that *stakeholder participation* may improve deliberation about complicated matters, they believe it is neither a necessary nor a sufficient condition of A4R.

5.1.3 *Revisions and appeal*, ie, there must be an institutional mechanism to engage a broader segment of society in the process, providing those affected by a decision to reopen deliberation, and to offer decision-makers an option to revise funding decisions in light of further arguments.

5.1.4 *Enforcement* entails some form of regulation to make sure that the first three conditions are met.

5.2 Seeking to combine legitimacy and pragmatism, and realizing that utilitarianism “has next to nothing to offer in eradicating health inequalities” (Rawlins and Dillon, 2005), NICE put aside questions whether matters of content can “be resolved solely with a reference to ‘due process’” (Hasman and Holm, 2005) and has explicitly subscribed to the principles of accountability for reasonableness (Rawlins and Dillon, 2005). At the same time, NICE reaffirmed its preference for cost-utility analysis with QALYs “as its principal (though not only) measure of health gain.”

5.3 A preliminary case study of a recent NICE Technology Appraisal (No. 98; see www.nice.org.uk) focused on the processes adopted by NICE. It confirmed the high (albeit not perfect) level of transparency, predictability, and the participatory nature of the NICE approach (Schlander, 2007b). While largely in agreement with the positive WHO review (Hill *et al.*, 2003), the analysis also indicated a need for further in-depth inquiry.

5.4 A subsequent more comprehensive in-depth review focusing on the technology assessment report informing NICE Technology Appraisal No. 98 did not confirm the expected robustness of the NICE evaluation process, revealing a striking number of limitations and anomalies (Schlander, 2007c). Collectively these left the assessment open to critique regarding all essential components of a technology review question, namely the population studied, the choice of interventions, the clinical and economic criteria used, as well as the study designs and selection criteria (cf. CRD, 2001). Furthermore, the structure of the economic model itself was prone to distortion and bias in various ways, and an unsettling number of

consistency problems were identified within the assessment report. As a consequence, the assessment did not fully consider the best available evidence and was unable to identify any differences in clinical effectiveness between the treatment options evaluated.

5.5 A number of underlying problems were suggested to explain the observed limitations, notably including an insufficient integration of clinical and economic perspectives, a high level of standardisation demanding to make the problem fit a preconceived solution approach (including [but not limited to] the use of QALYs as effectiveness measure), and issues related to the technical quality of the assessment itself (Schlander, 2007a).

5.6 Process-related observations may be compared to the conditions of accountability for reasonableness:

5.6.1 *Publicity.* The overall process was well structured and followed well-defined timelines with predictable opportunities for (some) stakeholders to provide input; key documents were continuously published at the NICE website. Major limitations of transparency were related to the use of commercial-in-confidence information (a situation on which NICE has taken action meanwhile), the economic model developed by the assessment group, and decision-making criteria beyond cost-effectiveness used by the appraisal committee. Designating economic models as “proprietary” insulates a major component of technology assessments from public scrutiny and does not meet established standards of good economic modelling practice (eg, Philips *et al.*, 2004; Brennan and Akehurst, 2000). It might be added that this practice prevents academic debate as well and, therefore, is not conducive to the further development of health economic evaluation methods. As admitted by NICE (cf. above, 5.2), quasi-utilitarian maximisation of QALY gains irrespective of their distribution does not provide for a sufficient basis for health care resource allocation in tune with social preferences. Thus, it is a critical transparency issue that decision criteria other than cost-effectiveness have not (yet) been codified by NICE.

5.6.2 *Relevance.* In the absence of codified criteria for fairness and with its heavy (albeit not exclusive) reliance on cost-effectiveness benchmarks, the specific NICE approach may be characterised as an “efficiency-first” strategy (cf. Richardson and McKie, 2006). It has been argued by observers that this approach in practice will result in the marginalization of other factors “as outside of NICE’s terms of reference” (Redwood, 2006). It seems unlikely that the current approach will enable to adequately capture social preferences for health care provision. A current example nicely illustrating these issues is the debate about the cost-effectiveness of expensive drugs to treat patients with rare disorders (“orphan drugs”). Given the high fixed (ie, volume-independent) and low variable cost structure of the pharmaceutical industry, applying the logic of cost-effectiveness would inevitably deprive these patients of any chance to receive effective treatment (cf. McCabe *et al.*, 2005, 2006; Hughes, 2005, 2006). While not meant to dismiss *any* need to make thorny trade-off decisions, this example may serve to illustrate the role of budgetary impact for reimbursement decision-making—which NICE has repeatedly denied to take into consideration (Rawlins and Culyer, 2004; Pearson and Rawlins, 2005), despite at least some indications to the contrary (Dakin *et al.*, 2006). While this position taken by NICE appears questionable on both theoretical and pragmatic grounds, it is evident that recognition of the relevance of budgetary impact would have fatal implications for any attempt to interpret the logic of cost-effectiveness in a normative way (Donaldson *et al.*, 2002; Schlander, 2003, 2005).

5.6.3 *Revisions and appeal.* NICE provisions for appeal are more restrictive than those provided for by A4R. Appeals are limited to specific grounds and do not allow to reopen debate. It seems unlikely that these limitations are compensated for by opportunities for (invited) consultees and commentators to provide inputs during the process, owing to the relatively short windows of opportunity compared to the massive amount of data to be reviewed and due to their limited transparency (cf. above, 5.6.1).

5.6.4 *Enforcement.* There is no indication that NICE has implemented an effective quality assurance system for technology assessments. Design of effective provisions would have to take into account that conventional peer-review processes are unlikely to be up to the task to assess the quality of economic evaluation models (Brennan and Akehurst, 2000; Hill *et al.*, 2000).

5.6.5 *Implementation.* Following Hasman and Holm (2005), proper enforcement of decisions should ensure that reasoning is “decisive in priority setting and not merely a theoretical exercise”. Although NICE and the NHS have made substantial efforts to improve actual implementation of guidance, there remain issues in this area as well (cf. Sheldon *et al.*, 2004; Freemantle, 2004). It has been suggested that guidance may be “more likely to be adopted when there is strong professional support, a stable and convincing evidence base” and that “guidance needs to be clear and reflect the clinical context” (Sheldon *et al.*, 2004)—conditions that were arguably not fulfilled in the case of Technology Appraisal No. 98 (Schlander, 2007a,c).

5.7 NICE has established a “Citizens Council” to provide input “on the topics it wants the council to discuss” and to ensure that its “value judgments resonate broadly with the public” (Rawlins and Culyer, 2004), while maintaining that its guidance “is based on clinical and cost-effectiveness evidence” (NICE, 2007). The Citizens Council has shown some concern for considerations of social justice but endorsed NICE’s approach, concluding that “cost-utility analysis is necessary but should not be the sole basis for decisions on cost-effectiveness” (NICE, 2005a,b). It might be worthwhile to explore in more depth whether the Citizens Council was confronted with the issue of cost-per-QALY rankings such as those cited above (see

4.5), ie, with the logic that providing 10 people with a utility gain of 0.1 for the rest of their life (equivalent to sildenafil treatment for men with erectile dysfunction) is indeed considered equivalent to saving the life of a single (otherwise healthy) person.

5.8 Summing up, there are good reasons to be suitably impressed by the attempts by NICE to ensure rigorous systematic reviews, objective economic evaluation, stakeholder participation, and transparency of process as well as value judgments. This notwithstanding, NICE is still in its infancy (cf. Williams, 2004), and—in our conclusion—there remains a long way to go before conditions of accountability for reasonableness will have been met.

6. CONCLUDING REMARKS AND RECOMMENDATIONS

6.1 At this point in time, our observations do *not* confirm “NICE’s use of cost effectiveness as an exemplar of a deliberative process”, as one of its founding fathers recently claimed (Culyer, 2006). In our conclusion, a more balanced perspective would seem commendable, as there is reason for concern as to the robustness of NICE health technology assessment processes as well as their specific focus on “efficiency” in terms of aggregated QALY maximisation.

6.2 In particular, in our view it would seem justified to (re)consider (a) more flexible approaches in terms of process as well as analytic procedures (enabling to adapt the problem-solving strategy to the clinical decision problem at hand), (b) the extent of reliance on QALYs as (exclusive?) clinical effectiveness measure, (c) the level of integration of clinical and economic perspectives, (d) the implementation of an effective quality assurance system for technology assessments. From an international perspective, we further note that the value judgments of NICE are not universally shared.

Professor Michael Schlander
InnoVal^{HC}, Eschborn, Germany

16 March 2007

Evidence submitted by Johnson & Johnson (NICE 74)

1. EXECUTIVE SUMMARY

1.1 Johnson & Johnson is the world’s most broadly based manufacturer in health care. With significant presence in the pharmaceutical, medical devices and diagnostics markets, Johnson & Johnson has potentially the most diversified experience of NICE. With an interest in $\geq 19\%$ of published Technology Appraisals, five more in progress, our interest includes appraisals of pharmaceuticals, medical devices and surgical procedures. We also have an interest in a similar proportion of Clinical Guidelines, including the management of urinary incontinence, surgical site infections, diabetes, bipolar disorder and smoking cessation.

1.2 Summary of Issues: We recognise that NICE has made moves to reduce the time it takes to produce and release its guidance to the NHS.

- We are concerned however that in reducing the development time of its guidance, stakeholder involvement and consultation has been eroded, resulting in inconsistencies and inaccuracies in guidance, (Terms of Reference (ToR) 1, 3, 4)
- This has resulted in guidance being more frequently challenged, through an appeals system considered weighted heavily against the appellants (ToR 5)
- We believe that Technology Appraisals are being rolled in to Clinical and Public Health Guidelines too quickly, without due consideration given to the potential implications of the context or wording of the new recommendations or the associated changes in funding status (ToR 3,7)
- The Office of Fair Trading (OFT) report on the Pharmaceutical Price Regulation Scheme (PPRS) advocates that, for prescription medicines, NICE should adopt new powers in that they will have responsibility for price setting of products as an integral part of the health technology assessments that they conduct today. This document lays out some fundamental flaws in the activities of NICE in the way it operates today. We believe that it would be wholly inappropriate for NICE to adopt such new powers in the light of the evidence and observations outlined below.

1.3 Recommendations to the HSC Review

- All stakeholders to be given the opportunity to comment on the Evidence Review Group (ERG) report prior to the first Appraisal Committee meeting for an STA review
- Manufacturers to be given the opportunity to address the Appraisal Committee in order to answer questions relating to the evidence submission

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- The mandatory funding direction of Technology Appraisals to be retained when they are incorporated in to Clinical and Public Health Guidelines, or they should remain “stand-alone” guidance
 - Re-introduction of an open call for evidence during the development of Clinical Guidelines.
 - Two stakeholder consultation periods to be reinstated in to the development of clinical guidelines
 - A review of the NICE Technology Appraisal appeals process and the introduction of a fair and truly independent appeals system.
 - NICE decision-making to be inclusive beyond cost/QALY, with transparency in explaining which factors drive the decision

2. STAKEHOLDER INVOLVEMENT IN DEVELOPING NICE GUIDANCE

2.1 *Reduction in stakeholder consultation during process.*

2.2 The drive to speed up the publication of NICE guidance through the STA process has introduced inequities into the NICE technology appraisal process. First, the opportunity for stakeholders to comment on the output of the independent academic group has been removed. Under the Multiple Technology Appraisal (MTA) process, all stakeholders had the opportunity to comment on the Assessment Group’s interpretation of the evidence prior to the 1st Appraisal Committee meeting. In the new STA process, that opportunity has been removed in an effort to shorten development times. This has removed a critical opportunity for stakeholders to comment on one of the key pieces of evidence the Committee considers in their deliberations. The absence of this critical step undermines many stakeholders’ perceptions in the inclusive and consultative nature of the STA process for developing guidance.(ToR 3; Recommendation 1)

2.3 *Inequity of voice at the Committee meeting.*

2.4 A continuing failing of the NICE technology appraisal process is the lack of representation of the manufacturer at the Appraisal Committee meeting to answer questions or address issues that are identified during review, and this is more acute in the new STA process. Other key stakeholder groups are represented, but the one group, who are certain to hold the majority to the evidence base for technologies reviewed under the STA process, the manufacturers, continue to be excluded.

2.5 It seems perverse that at a time when NICE is seeking to streamline its processes, that issues arising through the ERG or from the Committee on the day of the meeting cannot be clarified in real time by the presence of the manufacturer to address specific issues. The attendance of manufacturer representatives could be a significant positive step forward to reducing the development time for NICE guidance, for example, by reducing the number of occasions on which the Committee fails to reach a preliminary decision at its first meeting.(ToR 3; Rec. 2)

2.6 *Reduction in consultation in Clinical Guidelines Process*

2.7 In April 2006, following consultation under the banner of “improving the development process”, NICE announced changes to the Clinical Guideline (CG) programme. Previously, NICE asked stakeholders to provide any evidence considered to be relevant to the development of the Clinical Guideline. Following the April 2006 amendments, NICE now asks the relevant National Collaborating Centre (NCC) to carry out the initial search for evidence and follow up with a “focused call” on a series of specific clinical questions. This raises the possibility of important information being missed during guideline development and we recommend that the original open call for evidence at the start of guideline development be reinstated.

2.8 Second, and possibly the most significant change to the development process was the reduction from 2 four-week consultation phases to 1 eight-week consultation period. This has a significant impact on how stakeholders can comment. It removes the iterative nature of the process, leaving stakeholders only one opportunity to provide feedback. There is therefore no opportunity to clarify misunderstandings of feedback, or opportunity to challenge changes to recommendations which, as a stakeholder, you may have approved in the original draft. There is also no right of appeal.

2.9 This reduction in consultation has negatively impacted our ability to enter into meaningful dialogue with NICE during the development of two recent guidelines; Urinary Incontinence (CG40) and Heavy Menstrual Bleeding (CG44), discussed below as they involve the incorporation of Technology Appraisals (TA) into Clinical Guidelines.

2.10 Furthermore, the decision by NICE to halt the development of the Clinical Guideline on the management of Surgical Site Infections in 2006 on the grounds that it may not have had appropriate stakeholder input also suggests that the Clinical Guideline Programme is attempting too much, too fast, without appropriate consultation or validation.(ToR 3, 7; Rec. 4, 5)

3. INCORPORATION OF TECHNOLOGY APPRAISALS INTO CLINICAL AND PUBLIC HEALTH GUIDELINES

3.1 The process of incorporating Technology Appraisals into Clinical or Public Health Guidelines appears to be ill thought-out, and raises a number of issues. We have experience of five such appraisals, which have either been included in guidelines, or are about to be, and each raises concerns. These can be categorised as 1) mandatory funding issues, and 2) impact on future technology development through the inconsistent application of evidence needs.

3.2 *Mandatory Funding of Technology Appraisals*

3.3 This has been identified as an issue for:

- TA46: Surgery for Morbid Obesity into CG43: Obesity Guideline.
- TA43: Atypical antipsychotics for schizophrenia into the update of CG1: Schizophrenia guideline (in progress).
- TA39: NRT & bupropion for Smoking cessation into Public Health guideline on Smoking cessation (in progress).

3.4 In each of these cases, the movement of the TA guidance already has or will impact patient access to the specific technology. This is perverse, as access to the original technology was clearly considered of high enough priority by the Department of Health to justify the original Technology Appraisal. Specific details with examples of each issue are presented in Annex 1

3.5 The funding uncertainties for obesity surgery, atypical antipsychotics, and NRT for smoking cessation are clearly perverse, especially when each is addressing a high priority health issue for the NHS. These uncertainties therefore only serve to undermine confidence in the processes operating within NICE, and the ability of it to develop joined up guidance for the NHS. (ToR 3, 7; Rec. 3)

3.6 *Inconsistent Evidence Requirements*

3.7 This has been identified as an issue for:

- TA78: Second Generation Ablation Techniques combined into CG44: Heavy Menstrual Bleeding guideline.
- TA56: Tension free vaginal tape for stress urinary incontinence combined into CG40: Urinary Incontinence guideline.

3.8 The publication of Clinical Guideline CG44—Heavy Menstrual Bleeding (HMB) has raised concerns within our organisation regarding the guideline development process and some of the objectives driving it. This is reinforced by previous recommendations in CG40—Urinary Incontinence.

3.9 Our concerns are that the evidence based recommendations in the Technology Appraisals have been reduced to procurement recommendations, explicitly and implicitly, which are not evidence based. They have “genericised” the interventions without referral to appropriate evidence. We have examples of NHS Trusts interpreting the recommendations in this manner. Specific details are presented in Annex 2.

3.10 These clinical guidelines serve to question the need to invest in evidence generation and justification in these areas. Whilst the Technology Appraisal recognises that each intervention has to prove its way before gaining a positive recommendation, the clinical guideline process appears to assume that all technologies are the same, and implies that evidence for one is evidence for all. Internally, questions are being asked as to the value of our randomised controlled clinical trials, as the cheaper, fast follower competitor offerings that are winning NHS tenders have no substantive evidence to support their devices.

3.11 Both of these guidelines were published under the new process, with only one stakeholder consultation period. The recommendations of concern were not included as explicitly in the consultation drafts. Apart from in their own right being of concern regarding “dumbing down” appraisal recommendations and the potential impact of future research, they also serve as an example that further stakeholder consultation (such as a second consultation period under the old process), may have mitigated some of these issues. (ToR 3; Rec. 4, 5).

4. RELIANCE ON “COST PER QALY” THRESHOLD IN TECHNOLOGY APPRAISALS

4.1 NICE decisions give undue weight to cost per QALY estimates derived through computer simulation modelling. We acknowledge that cost-effectiveness is an important consideration in a NICE appraisal. However, it is not an appropriate basis on which to solely make a decision, which is increasingly the case in NICE decisions.

4.2 An over-reliance on cost per QALY based decision-making is flawed for several reasons:

4.3 *Economic modelling provides an indicative direction of travel rather than a definitive answer.*

4.4 Cost-effectiveness ratios derived through computer simulation modelling are almost always estimates of what the future cost-effectiveness of the technology might be, rather than robust primary evidence. Despite the uncertainty inherent in simulation models, the answers they produce dominate the decision at the expense of other important factors such as the innovative nature of the technology, the level of unmet need and the disease under consideration.

4.5 The burden of proof also appears to have shifted in the move from MTA to STA, where the onus is now on the manufacturer to prove cost-effectiveness before a product is considered for use. However, as appraisals are being undertaken earlier, there is less real-life experience to underpin regulatory trials, and the uncertainty in the cost-effectiveness evaluation is therefore greater, leading to the Appraisal Committee apparently being more cautious. As NICE moves to undertake reviews at an earlier stage, it also needs to recognise that less data will be available, and be more pragmatic in its decision making process, possibly with re-reviews scheduled on the delivery of new evidence.

4.6 *QALYs fail to consider the full range of factors which are of importance to patients and prescribers.*

4.7 Whilst NICE states that it considers a range of factors in the decision-making process, the weight given to these other factors is unclear and they are rarely if ever explained in the Final Appraisal Determination (FAD). Examples of issues which the QALY cannot readily capture, but which are critically important from a societal perspective, include the degree of unmet need, the innovative nature of the technology, and the severity of the underlying condition. A classical example of this is the Velcade (bortezomib) appraisal for multiple myeloma.

4.8 QALY analyses provide a disincentive for companies to invest in areas with the highest levels of unmet need

4.9 In conditions where few new treatments have been launched, new entrants into a class must compare against generic treatments which have been on the market for many years, rather than against other branded products. These are often the areas where innovation is most valued, but where achieving acceptable cost per QALYs can be most challenging. As an example, in the recent appraisal of VELCADE the main comparator (and only licensed alternative) was the generic drug dexamethasone. This situation arose because there are very few options for this patient group due to historic low levels of research and innovation. Dexamethasone costs around £80 per year making it almost impossible to achieve an acceptable cost per QALY, despite highly significant and impressive survival advantages with VELCADE being demonstrated in clinical trials. The £80 cost of dexamethasone is the cost of manufacture and distribution without any R&D element factored into the cost, as the patent has expired. Such comparisons present an impossibly unfair hurdle for comparative cost effectiveness assessments.

4.10 *The scope of £/QALY evaluations excludes societal costs*

4.11 The scope of costs considered in determining the cost per QALY for technologies is restricted to those incurred by the NHS & PSS. This excludes significant costs that can be incurred by patients and carers. An example of this is the review of Alzheimer's disease, where full-time institutional care costs funded by the patient were excluded from the calculation, resulting in an evaluation that inflated the cost per QALY for Alzheimer's drugs. The recommendation that resulted was based on this inflated QALY result, meaning that it was more cost effective to the NHS to let patients progress and be admitted in to institutional care earlier (as a proportion fund themselves), rather than use acetyl-cholinesterase inhibitors and delay the progression to full-time care. The transcript from the appraisal appeal hearing (13 July 2006, p221–229) elaborates this point. See OFT report on the PPRS, p81, Section 5.67.

4.12 This over-reliance on cost per QALY thresholds may in part explain why English cancer patients are denied access to many important and life extending cancer treatments such as VELCADE, which are becoming standard of care across Europe. We believe that if NICE's decisions are to become more acceptable to the general public, it is imperative that the obsession with predictive computer modelling of potential future benefits be balanced with a more considered view on the wider societal and clinical benefits of the treatment. (ToR 3, Rec. 7)

5. NICE APPEALS PROCESS

5.1 Johnson & Johnson welcomes the fact that NICE's Technology Appraisal process includes an appeals procedure which allows stakeholders an opportunity to challenge the decisions made by the Appraisal Committee. However, we have fundamental concerns with the manner in which the current appeals process is administered.

5.2 Most importantly, we believe that an appeals process should be truly independent. The current appeal process is administered by NICE itself and it has a vested interest in upholding the decisions that are made by its own appraisal committee. Specifically:

- The appeal panel is always chaired by one of NICE's directors, often the Chairman of the Institute itself.
- Of the five places on the appeal panel, at least two are always directors of NICE.
- NICE controls membership of the appeals panel.
- NICE has drawn up the grounds for appeal and makes a decision on the admissibility of appeal points before the hearing.
- NICE administers the process and issues the appeal determination.

5.3 In the two years since appeals have been held in public, it is striking that none has resulted in a change to section 1 of the guidance documents. The lack of balance in the appeals process was demonstrated in the Appeal lodged by Janssen-Cilag Ltd against the FAD for Attention Deficit Hyperactivity Disorder (ADHD). In this appraisal, the academic assessment group had failed to include the only high quality, randomised controlled trial comparing Concerta XL with atomoxetine in their evidence appraisal. Despite this omission, the appeal was rejected on the basis that the omission of this evidence did not change the overall decision. Given that the foundation of NICE decision-making should be based on high quality clinical evidence, this decision is nonsensical. Johnson & Johnson would strongly support a review of and the establishment of a fair and truly independent appeals system. (ToR 5; Rec. 6)

6. CONFLICTS OF INTEREST

6.1. We recognise that NICE has published a new code of practice for declaring and dealing with conflicts of interests (November 2006). This document covers all stakeholders in the NICE process, from employees, manufacturers, advisory committees, and academics involved in NICE projects. We are particularly pleased to see the specific statement 3.5; “A personal non-pecuniary interest in a topic under consideration might include, but is not limited to: i) a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review”.

6.2 We continue to be concerned over the involvement of the Liverpool Assessment Group in the ongoing review of coronary Stents, given the position communicated in their research paper published in Heart, 2005, before the current appraisal had started. They continue to be involved, developing new analyses for NICE at this time. Their latest analysis is due early April '07. Our initial letter of concern to NICE, dated January 2006 is attached as Annex 3.⁸⁷

6.3 The continued involvement of this review group in the appraisal continues to undermine our and other stakeholders' confidence in the Institutes processes (ToR 2)6.4. 6.5. 6.6.

Johnson & Johnson

March 2007

Annex 1

1. EXAMPLES OF ISSUES ENCOUNTERED WITH MANDATORY FUNDING OF TECHNOLOGY APPRAISALS WHEN MOVING TO CLINICAL AND PUBLIC HEALTH GUIDELINES

1.1 *Surgery for morbid obesity*

1.2 The original guidance was issued in 2002. However it was exempt from the 3 month funding directive, as it required a degree of service re-configuration to implement the guidance. This however has been interpreted by the majority of the NHS (purchasers and providers) as an exemption to “ever implement”. Uptake is currently well below that predicted by NICE. If the guidance had remained as a Technology Appraisal, when reviewed as part of a Core Standard there would at least be a drive to change current clinical practice. However, under the clinical guideline, the immediate need to develop a strategy for implementation is again deferred, and any negative impact on a Trust/PCT's assessment is removed, as in effect it has been shifted from a core standard to a developmental standard. An independent review carried out for NICE reported that 90% of all obesity surgery is focused in just 12 Trusts. Furthermore, the self-pay market in the UK significantly out-strips NHS activity, demonstrating that the clinical need is present, and it is patients who are losing out through NHS inactivity, supported by the change in NICE guidance.

1.3 *Atypical Antipsychotics*

1.4 NICE has decided to subsume the Technology Appraisal guidance for atypical antipsychotics (TA43) into the update on the guideline for Schizophrenia (CG1, in development). In communicating this decision, NICE made the following policy statement “At the time that the guideline updating the appraisal is issued, the existing appraisal guidance will be withdrawn, and from this point, the statutory obligation to provide funding for the technology will no longer apply. The NHS should have had ample time to fund the original guidance, and the case for a formal directive is substantially reduced.” This statement is still to be found on the NICE website at: <http://guidance.nice.org.uk/page.aspx?o=267029>

1.5 This decision means that patients' access to cost-effective medicines in this vulnerable patient group could be put at risk due to an unfortunate change in funding status of the guidance.

1.6 *Smoking Cessation*

1.7 Our confidence in the ability of NICE to run joined-up processes is further undermined when we consider what will happen to the existing Technology Appraisal on smoking cessation therapies (TA39). The guidance has been widely implemented, but has a resource impact on the NHS, not just in terms of

⁸⁷ Not printed here

prescribing, but also in additional support services. Much of the uptake has been underpinned by the mandatory nature of the guidance, in that PCTs have been bound to provide funding where physicians deem the intervention to be clinically appropriate for their patients, in line with funding directions issued by the DH to the NHS. We now have evidence of a PCT withdrawing these services for a period of time in an effort to help balance the end of year finances.

1.8. This may well be an isolated case, however we have been informed by NICE that the mandatory funding nature of the guidance will be lost once the new Public Health Guidelines on smoking cessation are published, as the recommendations contained within TA39 will be incorporated into and updated with the new guidance. PCTs will therefore have an effective “loop-hole” within which they will be able to legitimately withdraw such services without scrutiny from the HealthCare Commission or any other body, and, again, only patients will suffer. This could undermine the significant efforts to increase access to NRT made by the Government over recent years.

1.9. Furthermore, the Technology Appraisal programme is in the process of developing guidance on the use of varenicline which if approved, would attract mandatory funding. We could therefore be in a position where local funding is withdrawn from the proven technology NRT, and diverted to varenicline, if budgets are stretched. This may sound far-fetched, however this concern appears to also be held by both people within NICE and specialists within the smoking cessation field, giving some credence to the fears.

Annex 2

2. EXAMPLES OF INCONSISTENT EVIDENCE REQUIREMENTS BETWEEN TECHNOLOGY APPRAISALS AND CLINICAL GUIDELINES

2.1 In CG44 we are concerned by the recommendation:

1.5.7 Second-generation ablation techniques should be used where no structural or histological abnormality is present. The second-generation techniques recommended for consideration are as follows. Providers should ensure that when purchasing any of these that they buy the least expensive available option.

2.2 The inclusion of what amounts to purchasing or procurement advice in the guideline is surprising, especially given that it reads as if it applies only to the acquisition cost of the device, and not to the total cost of delivery of the surgical pathway for the patient. Furthermore, by not discussing outcomes, it assumes that the patient outcomes are at best equivalent and at worst irrelevant: it fails to recognise that the patient’s desired outcome should be a key consideration, such as either reduced menstrual bleeding or complete cessation of menstrual bleeding, as recognised in the original Technology Appraisal (TA78). It is also surprising that a focus on cost has been allowed in the final recommendations, whilst recommendations regarding patient safety and alternative operative options in surgical delivery have been omitted. For example, the comment recognising some options can be delivered via local anaesthetic rather than exposing patients to a potentially more risky general anaesthetic, present (and supported by us) in the draft, was removed from the final recommendations. Finally, there is also no recognition of the body of evidence (or lack of) that supports each technology now covered by the recommendation. Some of the cheaper devices available (and clearly more likely to be purchased under the above recommendation), have no RCT evidence to support their safety or efficacy, a hurdle that was required by the first three devices to market to achieve a positive outcome in TA78. This is therefore a perverse incentive to future research efforts, as the Clinical Guideline is, in effect, rewarding follow-on technologies on the basis of cheapness, and not on the basis of demonstrable patient safety or effectiveness.

2.3 Similarly, with the guideline on urinary incontinence, CG40, a recommendation is that sub-urethral slings should be used, without recognising that different slings have different properties, and very different evidence bases to support their usage. An Interventional Procedures guidance was previously retracted on the evidence that one particular device had a very high failure rate. The recommendations now in the clinical guideline however imply that long term follow up evidence is available for all retropubic mid-urethral tape procedures using a “bottom-up” approach, a generalisation that is simply not true. Indeed, there is more evidence for some transobturator foramen approach devices than some retropubic mid-urethral tapes.

2.4 We recognise that the Institute may be seeking to increase competition in the market through these guidelines, and that is an understandable objective where it is appropriate to do so. However, the manner and context within which this appears to have been undertaken in CG44 & CG40 will serve only to further reduce the incentive for evidence generation. The procurement recommendation may well have been well intentioned, but it has directly resulted in NHS Trusts now using it specifically to assist negotiating acquisition prices.

Evidence submitted by KCI Medical UK (NICE 14)

EXECUTIVE SUMMARY

Introduction

Founded by an emergency room physician in 1976, Kinetic Concepts Incorporated (KCI) is a global corporation providing leading edge innovation in wound care, pulmonary care, bariatric care, and circulatory improvement in all care settings. KCI manufactures, delivers and services one of the largest offerings of speciality beds and related medical devices. The company is dedicated to taking an active role in the healing process, helping to save patients lives, improve the quality of patients' lives, and reducing the overall cost of healthcare.

KCI Therapies have clinical evidence and/or are financially justified in more than 350 publications, including approximately 280 peer-reviewed clinical articles. Through research-based protocols and a clinically trained support team, KCI helps ensure that the right patient receives the right therapy for the right length of time.

KCI welcomes the Health Select Committee's inquiry into the work of the National Institute for Health and Clinical Excellence (NICE).

Overview

KCI recognises that NICE and its guidance to the NHS is seen as the gold-standard at an international level. Guidance, particularly clinical guidelines, which to date have been of most relevance to KCI, can have beneficial effects in changing NHS practice and in developing the most effective way of managing conditions. For this reason, it is essential that guidance is developed through consultation with the most appropriate clinical experts. It is also vital that the timescales associated with the development of guidance do not result in the publication of advice that is considerably lagging behind medical technology innovation and clinical practice.

Recommendations

- Research is carried out in the initial phases of the development of clinical guidelines to identify the most relevant clinical experts for that area, who are then invited to be involved in the scoping exercise.
- There is an assessment of the speed of publication of clinical guidelines and other NICE guidance, including guidance reviews, to ensure that there is a process for timely update to reflect advances in technology and clinical practice.
- A formal process to monitor how NICE guidance is used in the clinical setting is both developed and implemented.
- A formal process is developed for the dissemination of clinical guidelines to relevant healthcare professionals.

KCI'S VIEWS ON THE COMMITTEE'S TERMS OF REFERENCE

1. Why NICE's decisions are increasingly being challenged

1.1 NICE is recognised across the world for the guidance it provides to the NHS. One of the roles of the Institute is ensuring that the NHS receives the best value from limited resources by assessing clinical and cost effectiveness through technology appraisals. It also provides advice to the NHS on the best ways to manage treatment pathways for certain conditions, through clinical guidelines. Guidance from NICE, especially given the statutory implementation element of technology appraisal guidance, is considered to be the marker by which many NHS organisations make their funding decisions. This is especially true for treatments that are innovative and/or perceived to be "high cost". Often in these instances, funding will not be made available for a treatment unless it is subject to positive guidance from NICE. Therefore, should a treatment either not be subject to NICE guidance or receive guidance that does not recommend its use on the NHS, this can be the end of access to an innovative treatment and acts as a significant barrier to clinical decision-making.

2. NICE's evaluation process, and whether any particular groups are disadvantaged by the process

2.1 The most important element of the development of effective and useful clinical guidelines is the scoping phase. It is the opportunity for all the relevant stakeholders to ensure that the remit of the guideline fits with clinical practice and will provide a useful and necessary addition to NHS care. Currently however, it is at this stage that the most appropriate clinical experts are not always consulted. Details of the proposed

scope are published by NICE, but it is often not until the guideline is in development, or until it is published that the most relevant clinical experts are aware of the guideline. As the scoping phase is the most important, it is vital for clinical experts to be involved in this process.

2.2 In order to further ensure that clinical guidelines are the most relevant, it is also vital to ensure that the appropriate clinical experts are included on the guideline development groups. While there is clinical representation on these groups, it is essential that these clinicians and healthcare professionals appropriately reflect the necessary clinical expertise to understand the impact and practical application of a guideline.

3. *The speed of publishing guidance*

3.1 Currently, from the initial scoping and referral phase for a clinical guideline, it takes at least two years for the guidance to be published by NICE. In practice, it is often longer than this time frame, due to adjustments to the guideline as it develops and for logistical reasons. It is then, as standard, at least three years before the guideline is reviewed. The innovative nature of medical technology means there is a relatively rapid pace of development. Clinical practice also alters to reflect this technological change. It is therefore possible for a clinical guideline to be behind both technology and clinical practice by the time it is published by NICE, and significantly behind by the time it is assessed in relation to carrying out a review.

3.2 This not only means that the NHS is charged with implementing guidance that may no longer be the most appropriate, but that with a potential seven year time frame between the initiation of a guideline and assessment of the need for review, the impetus to develop high standard evidence on a technology is reduced.

4. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)*

4.1 Guidance provided by the Scottish Intercollegiate Guidelines Network (SIGN) for NHS Scotland and by NICE for NHS England and Wales, can be beneficial for the development of services and the care of patients. However, in relation to the timing of guidance, the timescales for the review of guidance from SIGN can be greater than those for NICE guidance. As outlined in relation to NICE guidance in the section above, timescales like this can result in significantly out of date guidance.

5. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this.)*

5.1 KCI's experiences indicate there is a lack of universal implementation within the NHS for NICE clinical guidelines. Without the statutory implementation in terms of funding and timeframe that is associated with technology appraisal guidance, there is a significant diversity in approach to clinical guidelines. NHS organisations charged with implementing guidelines have different levels of awareness of guidance—especially at the appropriate levels to ensure best implementation—and different processes for the dissemination of guidance to relevant front-line healthcare professionals. In order to ensure a more universal implementation of guidance, there needs to be a specific process for the dissemination within the NHS and a formal process for monitoring this by an appropriate independent body.

Claire Weston
KCI Medical

March 2007

Evidence submitted by Kidney Cancer UK (NICE 90)

INTRODUCTION

1. Kidney Cancer UK (KCUK) is a registered charity that was founded in 2000. Its objectives are to provide patients and their carers with improved access to reliable information about kidney cancer and its treatment, and to establish a network of individuals and groups capable of offering mutual support. It draws its membership from across the whole of the United Kingdom.

2. KCUK welcomes the opportunity to submit evidence relating to the work of the National Institute for Health and Clinical Excellence (NICE). For this is something about which KCUK is much exercised at the present time. Two of the Select Committee's terms of reference are especially germane to KCUK's concerns, namely the question of whether any particular groups are disadvantaged by NICE's evaluation process, and the issue regarding the speed at which NICE publishes its guidance. KCUK's particular concerns focus on the lack, so far, of any guidance on a new class of drugs used in targeted therapies for metastatic kidney cancer.

KIDNEY CANCER

3. There are approaching 6,700 new cases of kidney cancer in the UK each year. All but about 100 of these are of the renal cell carcinoma (RCC) type, the type that the new class of drugs is designed to combat. Some 50% of patients with RCC either present with, or go on to develop, metastatic disease which, without treatment, is usually fatal. In 2004 there were 3,300 kidney cancer deaths in the UK. The median survival once metastatic disease has developed is only 10 months (Motzer, Mazumdar *et al*, 1999).

4. Up to now systemic treatment options for metastatic RCC have been extremely limited. Standard care in the UK has been with single agent interferon-alpha, but the results from this have been very disappointing in the terms of lengthening survival. In the United States high-dose interleukin-2 is licensed by the Food and Drug Administration, but this drug is highly toxic and generates some serious side-effects. There is therefore a pressing need for more active agents; and it is to meet this need that two new drugs have been developed.

NEW DRUGS

5. The drugs in question are Sutent (the brand name for Sunitinib Malate) and Nexavar (the brand name for Sorafenib Tosylate). These drugs work by blocking signals in kidney cancer cells which lead to the tumor growing, spreading and developing a blood supply. Their effects have been studied in a number of large fully randomised clinical trials (Eisen *et al*, 2006; Escudier *et al*, 2005; Motzer, Michaelson *et al*, 2006; Motzer, Rini *et al*, 2006; Motzer, Hutson *et al*, 2006; Ratain, *et al*, 2005; and Motzer, Hutson *et al*, 2007). In summary these studies showed that the new drugs resulted in some tumour shrinkage in about 75% of patients and at the same time doubled, or more than doubled, a patient's progression free survival time. It is true that neither drug can eradicate the cancer, but they have a crucial role to play in stabilising the disease and keeping patients alive possibly long enough to benefit from other innovations in the more distant future (such as stem cell research or vaccines for kidney cancer). The other advantage of the new drugs is that they are more easily tolerated by patients, generating less serious side-effects.

6. Both drugs have received the approval of the US Food and Drug Administration and the European Medicines Agency for the treatment of metastatic RCC. They are both licensed, initially for second line treatment (ie when other treatments have failed) and later for first line treatment (meaning that clinicians can now prescribe them instead of interleukin or interferon). The view of clinicians expert in the treatment of metastatic RCC is that these drugs "should now be made routinely available in the management of this disease in the UK" (NCRI Renal Cancer Clinical Studies Group, 2006). Despite all this, neither drug has so far been reviewed by NICE. Nexavar has made it onto the list of drugs to be reviewed; but Sutent has not been accorded even that.

IMPORTANCE OF NHS FUNDING

7. In the absence of a "cost-effectiveness badge" awarded by NICE (or by the equivalent authorities in Wales and Scotland) primary care trusts are not obliged to fund the new drugs, even when these are recommended by the patient's clinician. In fact, under these circumstances, only a very few PCTs do fund the drugs, and then only on an "exception" basis. When the drugs are not approved for NHS funding, the consequences for individual patients can be very serious.

8. The new drugs work out rather expensive on a per patient basis, at something between £3,000 and £3,500 per patient per month. This is inevitable given the enormous research and development that had to be undertaken to produce them, much of the R & D effort being necessitated by the difficult nature of the disease itself. Most patients in the UK do not carry private medical insurance; and even if they did it is not always certain that the insurer will cover the cost of drugs not approved as cost-effective by NICE. Many patients simply do not have the financial resources to fund treatment for what, it can now fervently be hoped, is a considerably longer period of time. Some who have been refused funding by their PCTs have been considering some desperate measures, like selling (or at least remortgaging) their homes or commuting annual pensions into immediate lump sums. But these courses of action can of course affect other members of the patient's family and consequently cannot be entered into lightly. In some cases a patient's children come to the rescue, but the magnitude of the sums required often militates against this. As things stand, there are many kidney cancer patients who could benefit greatly from the new drugs but who are not currently being treated with them. That compares most unfavourably with the position in many other advanced countries, in which Sutent and Nexavar now constitute a standard of care for RCC patients.

CONCLUSIONS

9. The UK is often one of the last of the advanced countries to agree funding for new drugs (not just in the case of kidney cancer but in the case of other forms of cancer as well). This seems to be partly a result of the well-meaning objective of NICE to attempt to enable equality of healthcare across the country and partly due to the intense financial pressures under which many PCTs currently operate. But whatever the reason, the relatively slow uptake of new drugs could well have something to do with the UK's position somewhat down the international "league table" of cancer survival rates.

10. Maybe not by intent, but most certainly in effect, a lack of NHS funding for Sutent and Nexavar bears spectacularly unfairly upon kidney cancer patients. After all these are patients who may not—for the most regrettable of reasons—constitute much of a charge on NHS funding. Hence, it seems only fair that when new treatments arrive promising to stabilise the disease, a little extra should be spent on them.

11. KCUK is calling upon the Government to make the newly licensed and approved drugs, Sutent and Nexavar, available to kidney cancer patients throughout the country on prescription and fully funded by the NHS. To this end KCUK has drawn up a petition on the No 10 Downing Street website. At the time of writing this petition has been signed by 2,638 people. The question of NHS funding is vital. Without it, more and more treatments for kidney cancer will become the preserve of the wealthy. Also, over the longer term, improvements in treatment could well lead to cancer changing from a killer disease to a chronic condition that is manageable. In other words cancer might join other chronic conditions such as diabetes, heart disease and asthma as illnesses with which people can live but will not inexorably lead to death. If the UK is to avoid establishing a two-tier system—under which the rich (and well informed) can search out and pay for the most effective new treatments, while the poor are forced to make do with second-rate care—then the process of NICE approval for NHS funding has to change.

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Dr Pat Hanlon
 Kidney Cancer UK
 March 2007

Evidence submitted by Leukaemia CARE (NICE 64)

BACKGROUND

Leukaemia CARE is a national charity founded in 1967, which exists to provide vital care and support services to patients, their families and carers during the difficult journey through the diagnosis and treatment of all forms of blood cancer (leukaemia; lymphoma; Hodgkin's lymphoma; non-Hodgkin's Lymphoma; multiple myeloma; myelodysplastic syndrome; myeloproliferative disorders and aplastic anaemia).

EXECUTIVE SUMMARY

1. Leukaemia CARE is grateful for the opportunity to have an input into this inquiry to review all aspects of the workings of the National Institute of Health Clinical Excellence (NICE). Leukaemia CARE believes that the current approach by NICE and the NHS over the access to new and innovative treatments for patients affected by leukaemia, lymphoma and the allied blood disorders is disadvantageous to these patients, and is in need of urgent and fundamental review.

2. This inquiry is very timely with regard to the future development of new treatments for patients suffering from all blood cancers; and the consequent impact that those cancers, and cancer treatments will have on the quality of life (QOL) of patients undergoing treatment. There is an increasing public awareness of these newer treatments and an increasing public pressure for the provision of equal and equitable treatment of all patient groups by NICE such that no patient groups are seen to be disadvantaged by NICE pronouncements:

- There are an increasing number of new blood cancer treatments coming through the research pipeline.
- The development of specific targeted treatments means that a unique but smaller patient group can be selected to benefit from innovative research.

- More sophisticated differential diagnostic techniques are making it possible for physicians to identify in advance which patients will benefit from these newer treatments thus further fragmenting an already small target patient population.
- NICE is out-of-step with Europe and the United States when it comes to the definition and treatment of Orphan drugs (and by default orphan diseases).

3. NICE has a challenging and important role to play in guaranteeing the economic health and future of the NHS, but equally it has a vital role to play in developing an equitable and homogenous health service that is not just fair to all who have a need to use it, but is seen to be fair to all. There are certain aspects of the NICE process that could benefit from change to move closer to this ideal:

- The use of appropriate expertise on the appraisal committees, (there are no consultants with a knowledge of haematological cancers sitting on any of the committees who pass judgement on blood cancer products).
- A more pragmatic approach to the consideration of QOL issues; and a greater degree of involvement of the “patient expert witnesses”. The NICE appeals I have attended where “patient experts” were allowed to give evidence in my judgement were there only as a nod protocol, and not because their evidence was being taken seriously.
- Transparency of cost considerations, ie does the cost of treatment involve just the drug costs, or does it take into account the total cost of treating that patient (all indirect costs should be considered during the appraisal process, even if these considerations ultimately do not impact on the final guidance outcome). Silo budgets are the bane of an efficiently run business, and particularly so the NHS.
- Successful appeals (eg erythropoietin) should not be sent back to the same Evidence Review Group for further consideration, but go to another independent body.
- An earlier involvement in drug development in order to enable faster assessment of new drugs.

4. Because the NHS does not have an unlimited budget, sound health economic strategies will be vital if we want to ensure that the NHS survives in a recognisable form well into the future, and NICE should have a pivotal part to play in formulating those strategies, but not in isolation, the Government, the Pharmaceutical & Biotechnology Industries and the patient and research focused not for profit organisations should all have an input to make certain that we have an equitable and homogenous health service that will deliver that same standard of care to all, not matter what your post-code or socio-economic status.

NICE'S EVALUATION PROCESS, AND WHETHER ANY PARTICULAR GROUPS ARE DISADVANTAGED BY THE PROCESS

5. Leukaemia CARE believes that patients suffering from the rarer diseases (specifically the blood cancers) are being disadvantaged by NICE's evaluation process.

6. Given the pipeline of targeted cancer medicines, many of which may only be appropriate for a small number of patients we believe there are several issues that need to be explored in detail.

7. The costs involved in Research and Development of treatments for the rarer diseases (including all blood cancers) are the same as those for developing treatments for the very common diseases, over £500 million for pharmaceutical products, and over £800 million for biotechnological advances. It was recognised many years ago by the United States of America (USA) that special incentives were required if pharmaceutical manufacturers were to be encouraged to develop and market treatments in this area.

8. In 1983 the USA designated the term “orphan drug” to this group of rare diseases (“orphan diseases”), and granted research based pharmaceutical companies certain specific incentives to develop and market drugs for these diseases including; exclusive marketing rights for a 10 year period; assistance with clinical trial protocols; reduced regulatory fees etc.

9. The USA defined an orphan disease as one with a prevalence of less than 200,000 people; (in the USA that equates to $> 7.5/10,000$).

10. Legislation by the European Parliament and the Council and Commission Regulation on orphan medicines entered into force January 2000 and their definition of an orphan disease was one with a prevalence of $> 5/10,000$.

11. NICE reviewed orphan disease status in 2006 (23 years after the USA, and six years after the rest of the EU), redefined the term, and decided on an incidence of $> 1/50,000$, referring to this group of diseases as “ultra-orphan”, but by their own terms of reference it is an “informal subcategory” and has no legal definition, recognised by no other authoritative body in the USA or throughout Europe.⁸⁸

12. NICE suggest that orphan drugs can be fairly appraised using the normal assessment process⁸⁸ para 17(a), however in para 17(b), go on to state “Many however, have had incremental cost effectiveness ratios (ICERs) at the high end of what NICE and its appraisal committee consider to be cost effective”.

⁸⁸ National Institute for Health and Clinical Excellence, Appraising Orphan Drugs, 2006.

13. Drugs that would normally fall into the generally held view of “orphan status” when considered by NICE have fared particularly badly when reviewed using the standard methodology, eg bortezomib.⁸⁹

14. Leukaemia CARE feels that this single act of NICE (redefining orphan to ultra-orphan) will disadvantage all blood cancer patients, because the prevalence of the different blood cancer types will fall outside the NICE definition of “ultra-orphan” but inside the USA and EU definition of “orphan”.

15. Leukaemia CARE suggests that this “informal sub-category” designated by NICE as “ultra-orphan diseases” should be removed as the facts used to define the need for this sub-category are fundamentally flawed, and are in no way concordant with the rest of Europe, or the USA.

16. Leukaemia CARE further suggests that NICE adopt the definition of orphan disease status as defined by EU regulations, and that the rarer diseases should be appraised through a separate process where additional criteria are considered, including clinical efficacy, unmet need, total “global” costs to the NHS and patient quality of life issues.

WHY NICE’S DECISIONS ARE INCREASINGLY BEING CHALLENGED

17. Leukaemia CARE believes that NICE’s decisions are increasingly being challenged, because:

- They are being seen as not treating all patient groups equally and equitably. Eg the undue haste with which Herceptin was given clearance to specific patient groups even though the evidence base was clearly not there and the perceived lack of consideration to QOL issues to cancer patients suffering from chemotherapy induced anaemia/fatigue by its decision not to issue guidance on erythropoietin, and its decision to withdraw treatments for Alzheimer’s disease.
- There is a lack of use of appropriate expertise on the appraisal committees. Leukaemia CARE has been involved in several NICE guidance reviews, and no haemato-oncologist has ever played a part in the appraisal process.
- There is a lack of consistency in the criteria considered when making an appraisal determination. Eg during the erythropoietin appeal, we were told that QOL issues took a second place to survival data when the FAD was made, but during the bortezomib appeal we were informed that QOL issues superseded survival data in determining the outcome of the FAD (both of which were negative!).

18. Leukaemia CARE would suggest that both survival and QOL issues should carry equal weight when making a Final Appraisal Determination, because to the patient both are of paramount importance. There is no way of knowing in advance which patients want improved QOL, and which patients want extended survival, some may wish to live to reach a special wedding anniversary, or to see one last Christmas with the family, or see a son, daughter or grandchild born or christened; and some just want their last days on Earth to be pain free and joyous, Leukaemia CARE would like this to be a decision between the patient and the doctor, not decided by dictat from NICE.

WHETHER THE PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING

19. If the media is to be believed about recent decisions made by NICE, then the suggestion is that public confidence isn’t high. This may be due in part to a lack of understanding of the role of NICE, and the processes undertaken by NICE when producing guidelines. Leukaemia CARE believes however that certain areas of that process do need attention.

20. The use by NICE of evidence from patient expert witnesses was/is an excellent idea (and much publicity can be made from this), and should only elicit praise from all of the reviewers involved in this enquiry, unfortunately NICE appears only to pay lip-service to their evidence. Having patients experts attend NICE should inform and give an insight into the “human” aspect of the treatments under consideration, but the feedback from those attending was that their presence merely enabled NICE to tick the appropriate box, and to move onto more weighty matters.

21. Leukaemia CARE suggests that if patient experts are to be consulted, (and due notice should be taken of para 19), then NICE must report on the impact that their evidence has had on the final outcome of the appraisal document.

22. Despite being a requirement for all NICE appraisals to take into account the recommendation from other Government bodies, this isn’t always seen to be the case. Eg concerning the appraisal reviewing the use of erythropoietin for the treatment of chemotherapy induced anaemia, NICE ignored the 2002 Health Services Circular that instructed Trusts to take action to avoid unnecessary use of donor blood and to consider effective alternatives.⁹⁰ Also during this particular appraisal (erythropoietin) NICE were seen to be completely out of step with guidelines and recommendations that should have impacted on this appraisal

⁸⁹ National Institute for Health and Clinical Excellence, FAD Bortezomib, October 2006.

⁹⁰ National Institute for Health and Clinical Excellence, FAD Erythropoietin March 2006.

from many other pre-eminent bodies, EORTC (European Organisation for the Research and Treatment of Cancer), WHO, BCSH (British Committee for Standardisation in Haematology, ASH & ASCO (American Society of Haematologist & American Society of Clinical Oncologist).

23. Leukaemia CARE applauds NICE's determination to make completely independent decisions, but in order to engender public confidence in those decisions, NICE should at least explain why it has come to such radically different conclusion to other widely respected advisory organizations on those occasions when it does, because not to exhibits a lack of transparency and displays an air of arrogance.

THE APPEAL SYSTEM

24. Leukaemia CARE feels that the appeal system in the main is fair, and applauds NICE's intent to give all stakeholders sufficient time and scope to appeal both the ACD's and FAD's. There is however one aspect of the appeal system, that until recently was untried, that Leukaemia CARE feels does need to be addressed. The appeal against the FAD of cancer-treatment induced anaemia: Epoetin (alfa & beta) and darbepoetin alfa was up held by the appeals committee, but then it was sent back to the original Evidence Review Group (ERG) for reappraisal. Leukaemia CARE feels that this is unacceptable, as the ERG may come to the re-appraisal process with preconceived ideas of how the outcome should be. Leukaemia CARE feels that under these circumstances if an FAD appeal is upheld, then a different ERG should be commissioned to re-review the evidence presented.

THE SPEED OF PUBLISHING GUIDANCE

25. Leukaemia CARE feels that the time to issue appraisals through NICE has improved but is still not optimal. Leukaemia CARE welcomes the introduction of NICE's Single Technology Appraisal (STA) process, which has been shown to be faster and effective. However it is important that the existence of the STA does not disadvantage drugs being appraised by NICE not selected for this process. Patients with rarer diseases (including blood cancers) are still waiting too long for access to new treatments once they have been shown to be effective in clinical trials/research and/or have received an EMEA marketing authorisation:

- Clearer guidance should be issued by NICE to commissioners in the interim period before final Health Technology Assessment (HTA) appraisals are issued where treatments are already available in the NHS.
- Guidance should also be issued where treatments are available for an unlicensed indication of a medicine on the market that has not yet be appraised. (This may occur in cancer treatments where initial licenses are usually gained in late stage diseases and there is a time delay before marketing authorisation of a new indication can be put before NICE again for guidance.
- For rarer blood cancers guidance is also required for commissioners for treatments that will not be reviewed at all by NICE.
- One of the main issues with NICE that constantly frustrates Leukaemia CARE, is the speed with which NICE picks up and reviews new and innovative treatments. NICE does not begin to assess new agents until they have been through EMEA/UK approval and gained Marketing Authorisation. Leukaemia CARE believes that this disconnect is out of step with the otherwise professional approach that NICE takes in its role in assessing new agents:
 - Leukaemia CARE would like to see NICE involved at a much earlier stage in drug development in order to enable faster assessment of clinical and cost effectiveness.
 - NICE should be involved with new drugs when they are being submitted for approval to the regulator, and could even have input into the approval process, by for example recommending support for a drug being used in a national phase 3 trial.

SUMMARY

26. Leukaemia CARE feels that the role NICE plays in the delivery of a health care system that is fair and equitable to all at the point of delivery is, and will be a fundamental one, but it also needs to be seen to fair and equitable. It has got many things right in the short time it has been in existence, and should reap due praise for that. Now it needs to be made ready to appraise future technology, and make the revolutionary developments, which in the greater part are being made by British scientific research, available to the citizenry of the UK. (This is currently not the case—within Europe the UK is the slowest to adopt innovative new treatments).

27. Leukaemia CARE is in agreement with the finding published in the Cooksey report,⁹¹ Cooksey highlighted three main barriers that hinder the pharmaceutical sector's ability to deliver new medicines, diagnostics and devices "at prices that reward innovation and are affordable to health systems (in the UK

⁹¹ The Cooksey Review of Health Research Funding, Sir David Cooksey, December 2006.

and abroad)". Firstly the NHS culture is cautious with respect to innovation; secondly, regulation has not kept pace with advances in drug development science and technology. Thirdly, the NHS Health Technology Assessment limits uptake of new drugs.

Anthony M Gavin

Chief Executive Officer, Leukaemia CARE

Evidence submitted by Lifeblood: The Thrombosis Charity (NICE 35)

EXECUTIVE SUMMARY

Lifeblood: the thrombosis charity is pleased to respond to the House of Commons Select Committee Inquiry into NICE. As the Medical Director of Lifeblood and a practicing consultant physician, I consult regularly with colleagues from other disciplines and charities on matters of patient care and health policy.

We all agree that there is a definite need for an authority such as the NICE to exist, to produce evidence-based guidelines for healthcare professionals. However, we are well aware of the increasing number of challenges to NICE decisions, not just with regards to technology appraisals, but also with regards to the formulation and implementation of clinical guidelines.

In particular, we have become increasingly concerned by the process used by NICE to draw up clinical recommendations and can point to occasions where these have been fundamentally flawed as a result of a misinterpretation of the evidence-base.

We feel strongly that the processes NICE uses in setting clinical recommendations could be substantially improved, leading to additional benefits for patients and the health service at large.

In addition, as a small charity we find it increasingly difficult to respond on behalf of patients to consultations, assessments and draft guidelines from the three different authorities in England, Scotland and Wales, which all have different protocols and guidelines for identical conditions. This compounds the ability of many stakeholders and medical professionals to effectively feed into guideline development and to then share best practice which would ultimately benefit patients in the long term.

Positive systematic changes need to be addressed by NICE as a matter of urgency to stem the slide in confidence of both the public and the medical professions.

1. INTRODUCTION TO LIFELOOD

1.1 Thrombosis has been—and remains—a major cause of death in the United Kingdom, yet astonishingly this fact is not widely known. Most people have little or no understanding about the causes and effects of thrombosis, and how it can be prevented. Within the medical field, many see thrombosis as a peripheral area.

1.2 Lifeblood: The Thrombosis Charity was founded in February 2002. Although small in size, Lifeblood is the leading thrombosis charity group in the UK, increasing awareness and commissioning research. Our ambition is to improve the understanding of its causes, the impact on sufferers and the treatments available.

2. *Why NICE's Decisions are Increasingly being Challenged*

2.1 As a practicing Consultant Physician and Medical Director of a small charity with a strong interest in thrombosis I converse regularly with colleagues about the work of NICE—since the clinical guidance and recommendations published by the institute have an impact on the work of medical professionals on a daily basis.

2.2 Lifeblood firmly believes that in the absence of any alternative, there is a definite need for an authority such as NICE to exist to produce evidence-based guidelines, enabling healthcare professionals to work within minimal acceptable standards for care across the NHS.

2.3 However, in recent years Lifeblood have become acutely aware of the increasing prevalence of high profile challenges to decisions made by NICE. Most of these concern NICE's technology appraisals and the issues surrounding patient eligibility for cancer and central nervous condition medicines. This does not help instil public and professional confidence in the process.

3. NICE's Evaluation Process

3.1 Whilst any proposal that seeks to strengthen guidelines should be welcomed, recent examples have suggested that the way in which NICE formulates its recommendations can lead to flawed, capricious decisions. These are a result of a misinterpretation of the evidence-base that the expert committee uses to reach its conclusions.

3.2 The focus of this submission outlines our deep concern about the process by which NICE recommendations go against internationally accepted evidence based best practice.

Clinical Guidelines

3.3 An example of our concerns is the recent draft clinical practice guideline on “*The prevention of pulmonary embolism in high risk surgical patients*”.⁹² This is an area where excellent international guidelines already exist, the gold standard being the American College of Chest Physicians (ACCP) guidelines. It is interesting to note that all the international guidelines are written by experts in the field and they all recommend the same practice.

3.4 NICE reviewed the same scientific data as all the other guidelines including ACCP but came up with a very different set of conclusions, resulting in very different recommendations. This has resulted in a huge amount of work by advisory organisation, to comment on the proposals, in the hope of changing the guidelines. Surely it would be better to attain correct guidelines in the first place, so that time could be usefully used elsewhere? We believe the inconsistency between NICE and the ACCP guidelines occurred for several reasons.

3.5 The Independent Guideline Development Group assembled to review the data and provide guidance to the statisticians performing the systematic review consists of non-experts in the area. In addition, the Chairman is not required to be an expert in the field. Although this is laudable—excluding those with a possible conflict of interests—it also may result in a Guideline Development Group that lacks a detailed understanding of the scientific data they are reviewing. The risk is that this “lay” committee is unable to recognise the quality of the studies being reviewed, and therefore does apportion the appropriate weights to superior and inferior studies. Furthermore, experts are consulted to give evidence to the committee, however there are no predefined rules as to what NICE considers constitutes “an expert”. There does not seem to be an independent review mechanism objectively scanning CVs to determine eligibility. Thus many worthy or suitably qualified individuals are not considered.

3.6 In addition, whilst the selection of the NICE Guideline Development Group is undertaken by the National Collaboration Centre in conjunction with NICE, often the selection of group members has a lot to do with the preferences of the Chairman of the Guideline Development Group and the number of nominations received by the sifting group in topic selection, rather than objective criteria for expertise. There is also a tendency to encompass all relevant stakeholders rather than the range of clinical scientific opinions in the field. As a result, relevant dissenting views are not consulted during the guideline development process. This often leads to an unfortunate tendency towards “group think” and subsequent surprise when the final guidelines are not greeted positively:

- We propose that the National Collaboration Centre revises the criteria it uses to recruit for membership of guideline development groups to ensure experts in the clinical area should be included in the Independent Guideline Development Group, on the proviso they declare all their conflicts of interest. Only those with substantial interests (eg 10% of gross salary or grant income £100,000 from interested parties) should not be invited to contribute to the guideline process. We also suggest that NICE uses a simple but formal assessment tool to determine expertise—perhaps evidence of substantial clinical publications in the area being reviewed.

3.7 We also believe there can be divergence due to issues with data gathering. In some instances the overly-prescriptive formulaic approaches to data gathering lead to many worthwhile, though imperfect, large studies being ignored, while very small randomised trials are considered useful—despite the latter having significant limitations in terms of statistical power. There is also a tendency to use mixed meta-analysis—lumping together a large number of studies that experts in the field would argue were completely different. Similar experiences have affected colleagues involved in draft guidelines in the fields of hypertension and hyperlipidaemia, which also needed dramatic revision at a late stage before final publication. Recently, concerns have been raised about the post-myocardial infarction guideline process for similar reasons.

- We propose that NICE should revise the criteria used to gather data and minimise the use of mixed meta-analysis that can on occasion lead to misleading conclusions as a result of a misinterpretation of the evidence-base.

⁹² <http://www.nice.org.uk/page.aspx?o=369379>

4. Comparison with the Work of the Scottish Intercollegiate Guidelines Network (SIGN)

4.1 As NICE decisions only apply to the NHS in England and Wales it can be confusing for a small charity such as ours when having to deal with each of the relevant authorities' different protocols and guidelines for identical conditions. The Cooksey Review and Office of Fair Trading have proposed a UK-wide Health Technology Appraisal organisation:

- Development of a single body to assess technologies and clinical guidelines throughout the UK could also encourage wider sharing of best practice and might ultimately result in better levels of patient care. A single UK body would also reduce workload for small patient groups which have limited resources to make submissions and respond to consultations.

5. Summary of Recommendations

We propose that the National Collaboration Centre revises the criteria it uses to recruit for membership of guideline development groups to ensure experts in the clinical area should be included in the Independent Guideline Development Group, on the proviso they declare all their conflicts of interest. Only those with substantial interests (eg > 10% of gross salary or grant income > £100,000 from interested parties) should not be invited to contribute to the guideline process. We also suggest that NICE uses a simple but formal assessment tool to determine expertise—perhaps evidence of substantial clinical publications in the area being reviewed.

We propose that NICE should revise the criteria used to gather data and minimise the use of mixed meta-analysis that can on occasion lead to misleading conclusions as a result of a misinterpretation of the evidence-base.

Development of a single body to assess technologies and clinical guidelines throughout the UK could also encourage wider sharing of best practice and might ultimately result in better levels of patient care. A single UK body would also reduce workload for small patient groups which have limited resources to make submissions and respond to consultations.

6. CONCLUSION

6.1 NICE is in a unique position to develop a coherent set of guidelines that could potentially save many more thousands of lives each year. We believe that the processes NICE currently use could be substantially improved, leading to significant additional benefits for both patients and the health service and improved confidence in the system.

Dr Beverley Hunt
 Medical Director
 Lifeblood: The Thrombosis Charity
 March 2007

Evidence submitted by Lilly (NICE 94)

SUMMARY AND RECOMMENDATIONS

1. Lilly recognises that NICE offers a valuable service to the NHS in providing it with guidance on which medicines are clinically and cost-effective. We appreciate the aim of the Government is to provide a publicly funded health service with evidence on the value of our medicines and we were supportive of the Institute at its inception.

2. Two recent reports—The Office of Fair Trading report on the Pharmaceutical Pricing Regulation Scheme and the Cooksey Review of Health Research Funding—have both advocated an expanded role for NICE in the future. In light of these recommendations, and the ongoing public debate about the Institute's decisions, we believe this inquiry by the Health Select Committee to be timely and welcome the opportunity to contribute.

3. We urge the Committee to review NICE in the context of the current processes of the Scottish Medicines Consortium (SMC) and the All-Wales Medicines Strategy Group (AWMSG). We believe the Government should conduct an independent review of health technology assessment (HTA) before any considerations for reform of the Pharmaceutical Price Regulation Scheme can be made.

4. Lilly believes that over the eight years that NICE has been operating, a number of serious flaws have emerged in its processes, which are undermining confidence in the Institute's recommendations. NICE is tasked with making very tough decisions and it is therefore essential that all stakeholders in the process can be confident that those decisions are made in a constructive, fair and transparent manner with rigorous consideration of the evidence.

5. In order to build more confidence in the NICE process and improve the transparency and speed of decisions, there are a number of improvements we would recommend:

- The current reliance on the incremental cost per Quality Adjusted Life Year (QALY) as pivotal to the decision of the Appraisal Committee (AC) should end. There are important technical and policy reasons why this is the case. NICE itself has listed a number of other factors that should be considered—these should be given greater weight, and other measures of cost-effectiveness used where the QALY may not be appropriate.
- The advice given to NICE by its external advisers (Technology Assessment Groups and Evidence Review Groups) should be subject to quality review either within or without the Institute, to ensure that all advice is of an equally high standard.
- A mechanism should be found whereby NICE does not completely reject a drug that is being appraised early in its lifecycle on the basis of insufficient evidence of cost-effectiveness. More creative solutions to confirming value after launch could be considered other than “use only within clinical trials”.
- The Institute should follow the example of the SMC in using a flexible, constructive and open process of engagement with stakeholders rather than the generally adversarial system it currently employs. This should include the opportunity for manufacturers to have dialogue with AGs/ERGs and the ACs throughout the process.
- The appeal system should be made independent of NICE and the grounds for appeal widened to allow substantive review of the scientific merits of the AC’s decision.
- A cost benefit analysis of performing an assessment for a given drug should be a consideration in topic selection. This would help to avoid lengthy and time consuming appraisals of medicines that may have minimal budget impact. Together with central funding and commissioning for rare diseases, this may also lead to more pragmatic decision making for expensive but rarely needed treatments.
- All of these are of little merit however, unless the fundamental issue of implementation of NICE guidance is addressed. To hasten access to approved medicines by patients, and to reduce the burden on business in line with the principles of Hampton and Arculus, all medicines approved for use by the NHS should automatically be placed on local formularies without further debate or delay.

6. We have set out below our views on some of the issues that the Committee specifically wants to address.

Why NICE’s Decisions Are Increasingly Being Challenged

7. The simple explanation is that more and more decisions are negative. Prior to 2006, approximately 80% of appraisals recommended use or restricted use of the drug in question by the NHS. In 2006 NICE introduced the Single Technology Appraisal (STA) process, which aimed to issue faster guidance on life-saving drugs closer to launch to avoid the incidence of “NICE blight”.

8. 80% of first draft recommendations (ACDs) for the 16 single technology appraisals currently ongoing have not recommended the drug for use by the NHS. These documents are all in the public domain so it is inevitable that negative decisions are questioned by patients, clinicians, industry and the media both formally and informally.

9. The Institute’s own processes and behaviour contribute to the increasing number of challenges. It is very difficult for industry to have constructive dialogue with the Institute, which compares very unfavourably with the SMC and the AWMSG in this respect. For example, there is no opportunity for manufacturers to meet with ACs to explain their data, clarify areas of confusion or misunderstanding or challenge the analysis provided by NICE’s external advisers. While there may be some commercial justification for this where many medicines are being appraised simultaneously, there is no justification for it in the STA process.

10. In the event of a negative decision, the only option for manufacturers or other stakeholders is a formal appeal. The SMC in contrast gives reasons for why it has not recommended a drug for use in Scotland, and allows companies to resubmit their case—perhaps to present new evidence or make the case for use of the drug in a more rigorously defined sub-group of patients. NICE does not allow resubmission of evidence in this way, which consequently leads to a greater number of formal appeals.

The Evaluation Process

11. We have a number of concerns about the Institute’s evaluation process for Health Technology Appraisals.

Stakeholder engagement with the process

12. It is difficult for many stakeholders to engage effectively with the process. Although NICE encourages and accepts evidence from a range of stakeholders, in reality it is hard for patients and healthcare professionals to play a meaningful role in a lengthy and economically complex evaluation. NICE appoints a “clinical expert” for each appraisal, who in effect should be representing wider medical opinion. It is not unusual for these “experts” to come from an unrelated medical field or to have no actual experience of using the drug in question. Patient groups cannot be expected to provide evidence on cost-effectiveness, but their views on clinical benefit, societal benefit and patient choice are important and should be heard. The increasing reliance of ACs on the incremental cost per QALY calculation (see below) above all other considerations disenfranchises patients and risks their participation becoming a “tick box” exercise.

Technology Assessment Groups/External Review Groups

13. NICE commissions independent academic centres (AGs/ERGs) to review the manufacturer’s submission and the published evidence on a medicine. The group prepares a summary report for the AC either using its own economic models, or making alterations to the manufacturer’s models.

14. The quality of reviews varies considerably between the groups, with reports sometimes lacking fairness and balance. For example, in the ongoing appraisal of Alimta (pemetrexed) for Mesothelioma, the ERG questioned its efficacy, in direct contradiction of the findings of the medicines regulator.

15. The reports produced by external centres show a poor understanding of the pharmaceutical development process. The AGs/ERGs would benefit from training and better ongoing dialogue with the industry. Their reports should be subject to quality review.

Realistic expectations of evidence

16. NICE has increasingly begun to suggest manufacturers should carry out new clinical trials to provide further evidence about a medicine and in some cases it has recommended use “only in the context of research”. Unfortunately, by the time this decision is made it can be too late to design a clinical trial to meet the needs of patients in the UK, which reflects the Institute’s poor understanding of the realities of commercial pressures driven by licensing and patent law. The research suggestions are sometimes unrealistic from an ethical perspective and would not necessarily answer the decision problem under consideration. The Institute’s fixed timelines for re-reviewing guidance do not allow sufficient time for trials to be set up from scratch and data analysed in between reviews.

17. The high number of negative recommendations at the first stage of the STA process shows ACs are clearly uncomfortable making positive recommendations based on the range of data typically available early in the lifecycle of a medicine, a case of “guilty until proven innocent”. Studies prior to launch focus on efficacy and safety to meet the requirements of the licensing regulators, not the different requirements of HTA bodies round the world. In our view, NICE needs to be realistic about what data can be provided at this stage, and to accommodate a degree of uncertainty. A negative decision means patients may be denied a medicine on the basis of uncertain rather than incontrovertible evidence and that “real life” data can then only realistically be collected from general use in patients overseas, which may have limited applicability here.

Measures of cost-effectiveness

18. NICE uses a measure known as cost per Quality Adjusted Life Year (QALY) to determine whether the cost of a medicine can be justified by the impact it has on health. There is a value of £20,000 per incremental QALY below which a medicine would be considered more cost-effective than the comparator treatment. When a medicine exceeds this NICE will only recommend it for use if there are other important factors.

19. No measure of health outcomes is perfect, and while the QALY is a plausible and attractive concept, there are a number of technical limitations in practice:

- The QALY is essentially the arithmetic product of length of life (LY) and health-related quality of life (QA). One of the key assumptions is that these things are independent of each other and the amount of time a person is willing to trade for an improvement in quality of life is independent of how long they have left to live. In terms of health, it is easy to see why this will not hold—patients’ quality of life is likely to be influenced by the amount of time they have left to live, especially if they have a terminal condition. This is the reason why many feel the QALY biases against people with shorter life expectancy eg terminal stage cancer, the elderly.
- The health-related quality adjustment (QA) that is needed to obtain the QALY can be calculated in a number of different ways, each producing a different answer. This introduces a high degree of uncertainty around the cost per QALY estimate.

Cost-effectiveness versus other considerations

20. Of fundamental concern to us is the reliance of NICE on a QALY threshold as pivotal to its decision making. We believe that while it is appropriate to have a threshold as a guide, particularly for comparing one medicine against another, the QALY should be one of the factors considered in reaching a decision, and not effectively the only one.

21. While the academic jury is still out on the QALY, we believe NICE should adopt a more pragmatic approach to the assessment of cost-effectiveness, and should consider taking into account “cost of life year gained” analyses, particularly in the appraisal of end of life therapies. Additionally consideration should be given to the broader impacts of a medicine, as valued by society. These might include innovation, affordability, burden on carers, societal benefit and contribution to the UK economy.

22. When a drug exceeds the QALY threshold, the Institute has listed the other factors it will consider. A number of recent decisions indicate to us that these are in fact given little, if any, weight in comparison with the QALY calculation:

- (a) Alimta (Pemetrexed)—not recommended for use in non small cell lung cancer. There was a considerable degree of uncertainty surrounding the calculation of cost/QALY, which ranged from £9,010 to £1.8 million.
- (b) Alimta (Pemetrexed) for Mesothelioma. Lilly is appealing negative guidance on the use of Alimta for mesothelioma. Mesothelioma is a rare but devastating industrial disease caused by exposure to asbestos. The government has committed to compensating victims, but at the same time, NICE is denying them access to the only licensed medicine for their condition, giving little weight to the particular features of this population.
- (c) Evista (Raloxifene). In the appraisal of Evista for osteoporosis, NICE refused to include in its evaluation of cost-effectiveness full consideration of the wider costs and benefits associated with the demonstrated reduction in breast cancer risk in people taking Evista.

Clinical guidelines development process

23. The Institute has declared its intention in the future to focus more and more on developing clinical guidelines, which incorporate technology appraisals. Since the guidelines do not have the same statutory backing as the technology appraisals, this will result in less dedicated funding, less uniform implementation, and more variability in local practice, contrary to the founding objectives.

The Speed of Publishing Evidence

24. NICE does not evaluate all medicines at the time of launch and has not evaluated many of the medicines currently in use. When there is no guidance from NICE, decisions are made at a local level based on financial budget, clinical benefit, value for money and affordability. NHS trusts and PCTs frequently cite “waiting for NICE” as a reason to prohibit prescribing, which can lead to wide variations in use across the country. The Government and NICE have taken steps to tackle this problem, by issuing advice and introducing the Single Technology Appraisal (STA) process, respectively.

25. While we appreciate the need for NICE to be rigorous in its analysis of each drug, the processes—both STA and MTA (multiple technology appraisal)—for publishing guidance are far too slow and the timelines lack flexibility. Appendix 1 includes a case study which illustrate this.

26. Numerous efforts have been made to address the issue of NICE blight, but it remains a serious problem that causes immense emotional and physical cost to patients and limits the return on investment to pharmaceutical companies during the period of patent protection, which has a knock-on effect on investment in the next cycle of medical discovery. The speed of issuing guidance must be addressed through improvements to the appraisal process and more appropriate resourcing.

27. As the review process for NICE STA is similar to that of the SMC—consideration should be given to adopting SMC advice across England, Wales and Northern Ireland. This would result in NICE avoiding duplication of effort as well as reducing resource costs and more importantly it would enable patients to have quicker access to medicines that are considered to be clinically and cost effective.

The Appeal System

28. We believe there are a number of deficiencies in the current appeal procedure which, if addressed, would improve the fairness of the process and ultimately the credibility of guidance issued by the Institute.

29. NICE’s constitution requires the appeal panel to be chaired by the Chairman or Vice Chairman of NICE, and for at least one other member to be on the NICE Board. While we do not in any way question the integrity of current members of the Board, a conflict of interest nevertheless exists. The appeal panel should be independent of NICE.

30. There is no opportunity to appeal other than on process issues or perversity of recommendation, so no chance to question whether the scientific interpretation of the data is fair. The possible grounds for appeal should be widened, particularly given the absence of dialogue between ACs, their external advisers and the manufacturer and the subsequent potential for misinterpretation of evidence.

31. The practice of disclosing new evidence in the Final Appraisal Determination (FAD) must be discontinued—there should be a requirement that if there is significant change following the ACD, then a second ACD should be issued for consideration, in order to allow for comment and to reduce the likelihood of appeals. The danger is of introducing further delays in the process but this could be avoided by better dialogue with manufacturers throughout the process.

32. When an appeal point is upheld there is no subsequent opportunity to appeal the appraisal committee's reconsideration of that point.

IMPLEMENTATION

33. The NHS has been directed to implement NICE guidance within three months in England and Wales and within 18 months in Northern Ireland. Implementation does not consistently happen within the required timescale, and sometimes not at all.

34. While we recognise that manufacturers have a role in providing evidence on the value of our medicines, we are now forced to do so many times at different levels in the health service. When a national HTA body such as NICE has appraised a drug, there should be no need for local duplication. NICE has long recognised that implementation is an issue and has recently created a department with a £2.5 million budget to address it.

35. Fundamentally, issues around implementation stem from its affordability to the NHS and the priority placed on it by the Health Care Commission. Cost-effectiveness and budget impact are different things and both affect decisions by the local NHS on when, if and how to implement recommendations. For this reason, we believe implementation would only be assured if it were accompanied by ring-fenced funding and assigned a higher priority by the HCC than currently. It is not acceptable that the money which should be allocated to fund medicines recommended by NICE, is being used elsewhere in the health economy to meet budget deficits.

36. There is no obligation on the NHS to implement NICE clinical guidelines (which offer a whole system approach to the treatment of a disease), which are a developmental standard as opposed to a core one. For this, and other reasons, it is unlikely the health service will attach much priority to guidelines—a worrying situation as NICE is increasingly moving the re-reviews of technology guidance into the guideline process, and thereby removing any obligation to implement.

Helen Llewellyn

Lilly UK

March 2007

APPENDIX 1

In this appendix we set out two case studies to illustrate why we feel the processes used by NICE in publishing guidance are too slow and lack flexibility.

1. ALIMTA (PEMETREXED) FOR MESOTHELIOMA

Timescale

November 2004	Alimta receives licence
July 2005	Scottish Medicines Consortium advice published
August 2005	Submission of evidence to NICE
June 2006	Final appraisal determination published
October 2006	Appeal hearing
December 2006	Appeal board asks committee to reconsider several points
March 2007	Original appraisal committee reconvenes
May 2007	Final appraisal committee meeting
August/September 2007	Final Guidance anticipated
February 2009	Scheduled re-review begins
February 2010	Re-review decision

Impact

It will be three years from licence to guidance, during which time NICE blight has widely impacted use of Alimta. Should the appraisal committee reaffirm its negative guidance after considering the appeal points, it could be 2010, if ever, before NHS patients have the opportunity to use this drug, which has been recommended for use in Scotland by the SMC since July 2005. We estimate that approximately 300–350 patients in England and Wales in the last year could have benefited from treatment with Alimta but have effectively been denied it. Those people would, on average, have gained an additional 4.8 months of life. The estimated cost of this medicine to the NHS is £3.2 million this year, rising to £5 million by the end of the decade.

Evidence submitted by the 25% ME Group (NICE 19)

BACKGROUND

This submission is limited to just one aspect of the workings of NICE, namely its production of a Guideline for the management of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). There is no curative treatment for the disorder.

There is significant concern because the draft Guideline that is currently out for consultation is seriously flawed and is potentially life-threatening to patients, especially the severely affected, yet on 22 February 2007 Professor Peter Littlejohns (Clinical Director at NICE) indicated to the All Party Parliamentary Group on ME that, despite the enormous number of representations NICE had received about its draft—said to be the highest ever on any NICE project—it was unlikely there would be a second consultation process. He stated that even if the final Guideline were to be rejected by all the UK ME/CFS charities, the Guideline would still be published.

The management regime favoured by NICE is cognitive behavioural therapy and graded exercise therapy (CBT/GET), which is a psychiatric intervention based on a behavioural modification programme. It is tirelessly promoted throughout Departments of State by a group of (mostly) psychiatrists who do not accept the WHO classification of ME/CFS as a organic neurological disorder (a classification that has existed since 1969); instead, they advise Government bodies that “ME” is nothing but a “belief” which does not exist except in the minds of patients who think they suffer from it, and that “CFS” is a “biopsychosocial” (behavioural) disorder. They have designed a management regime whose aim is to change what these psychiatrists believe is patients’ “aberrant” thinking about the illness in order to convince patients that they do not have a physical illness.

It is vital that NICE is compelled to pay due heed to the biomedical evidence on ME/CFS it has received, because in oral evidence on 10 July 2006 to the Gibson Inquiry on ME/CFS held at the House of Commons, Professor Anthony Pinching (lead adviser to the Department of Health on “CFS/ME” and Principal Medical Adviser to the charity Action for ME) was emphatic that once published, the NICE Guideline would be imposed nationally in 2007.

This submission attempts to demonstrate that NICE and its advisers are failing in their duty to produce a Guideline that is evidence-based and that medical science has been usurped by politics, which in turn have been usurped by vested interests.

EXECUTIVE SUMMARY

In the production of its “CFS/ME” draft Guideline, NICE has demonstrably failed to conform to the AGREE Instrument to which it is party and to whose criteria it is obliged to conform in the production of its Guidelines. Specific examples are provided under the Committee’s Terms of Reference.

THE HEALTH SELECT COMMITTEE’S TERMS OF REFERENCE*1. First Term of Reference: Why NICE’s decisions are increasingly being challenged*

1.1 NICE’s decisions are increasingly being challenged because it can be shown that they are driven by Government policy, not by the evidence that has been submitted to NICE; it is thus a case of NICE creating “policy-based evidence” instead of evidence-based policy, no matter that the “policy-based evidence” is damaging to patients.

1.2 In the production of its Guidelines, NICE is obliged to conform to the criteria set out in the AGREE Instrument (Appraisal of Guidelines Research and Evaluation). The AGREE collaboration started in 1998 and originates from an international collaboration designed to enhance effective healthcare policy by the dissemination of high quality clinical guidelines.

1.3 The following examples of failure to conform to the AGREE Instrument are cogent reasons why NICE’s decisions are being challenged by the ME community.

1.4 All Guideline Development Group members must declare any conflicts of interest: in the “CFS/ME” draft Guideline, no mention was made of the proven vested financial interests of certain Group members, notably the fact that one member is Chief Executive of a medical insurance company in whose interests it is to keep ME/CFS categorised as a “mental” disorder so that claimants are excluded from benefit.

1.5 Patients about whom a Guideline is intended must be specifically described: in the case of ME/CFS, failure in this regard underpins the resultant confusion: “CFS/ME” is not the same as ME/CFS: the former includes anyone with medically unexplained “fatigue” lasting for as little as one month and specifically includes those with psychiatric disorders, whereas the latter is a formally classified neurological disorder, one symptom of which is post-exertional fatigue and malaise, together with multi-system dysfunction—see below.

1.6 Patients’ views and experience should be sought and used; these should have equal status with other evidence such as random controlled trials: the Government’s own guiding principle for the NHS is that it must be patient-led (see “The Expert Patient: A New Approach to Chronic Disease Management for the 21st Century”; Department of Health; September 2001; see also “The Expert Patient” by John Illman published in March 2000 by the Association of the British Pharmaceutical Industry, which notes that the Department of Health is inviting patients to join the information revolution and that patients who do not develop these skills could become the underclass in the health system). In the case of ME/CFS, NICE has completely disregarded this approach. This is the most significant area of concern. Patients with ME/CFS are in general far better informed about the disorder than most physicians and policy-makers.

1.6.1 Overwhelming evidence has been submitted to NICE that CBT/GET is not only of no lasting benefit, but may result in a permanent worsening of the condition for a substantial number of patients. This is because it has been conclusively demonstrated that exercising muscle in ME/CFS patients is a prime contender for free radical generation. An article called ‘A Final Farewell to the Psychiatric Fallacy?’ refers to the work of the Vascular Research Unit at Dundee (see www.meactionuk.org.uk/A_FINAL_FAREWELL_TO_THE2_PSYCHIATRIC_FALLACY.htm) and points out that in ME/CFS, raised levels of isoprostanes (abnormal prostaglandin metabolites which are highly noxious by-products of abnormal cell membrane metabolism) have been demonstrated and that these raised levels of isoprostanes precisely correlate with patients’ symptoms. Such raised levels of isoprostanes have never been documented in any other known disorder.

1.6.2 There are many other documented biomedical abnormalities that NICE has deliberately ignored and denied. These include abnormalities of the central nervous system (there is evidence of a chronic inflammatory process, with oedema or demyelination in 78% of patients tested; neuro-imaging has revealed inflammatory lesions in the brain of approximately 80% of those tested, as well as evidence of a significant and irreversible reduction in grey matter volume); abnormalities of the autonomic and peripheral nervous systems; cardiovascular dysfunction (with evidence of endothelial dysfunction, haemodynamic instability, aberrations of cardiovascular reactivity, and a left ventricle ejection fraction as low as 30%); respiratory system dysfunction (there is evidence of significant reduction in many lung function parameters including a significant decrease in vital capacity); there is a disrupted immune system, with evidence of an unusual and inappropriate immune response, including increased apoptosis (programmed cell death). There are documented virological abnormalities which include evidence of persistent enterovirus RNA in ME/CFS patients, as well as abnormalities in the 2-5 synthetase/RNase L antiviral pathway, with novel evidence of a 37 kDa binding protein not reported in healthy subjects or in other diseases; there is evidence of the presence of HHV-6, HHV-8, EBV, CMV, Mycoplasma species, Chlamydia species and Coxsackie virus in the spinal fluid of some ME/CFS patients. There is indisputable evidence of muscle pathology, including laboratory evidence of delayed muscle recovery from fatiguing exercise and evidence of damage to muscle tissue; there is evidence of impaired oxygen delivery to muscle, with recovery rates for oxygen saturation being 60% lower than in normal controls; there is evidence that creatine (a sensitive marker of muscle inflammation) is excreted in significant amounts in the urine of ME/CFS patients. There are documented neuroendocrine abnormalities, including evidence of HPA axis dysfunction, evidence of a profound loss of growth hormone and even when the patient is euthyroid on basic screening, there may be thyroid antibodies and evidence of failure to convert T4 (thyroxine) to T3 (tri-iodothyronine). There is evidence of defects in gene expression profiling, with an expression profile grouped according to immune, neuronal, mitochondrial and other functions, the neuronal component being associated with CNS hypomyelination. There are documented abnormalities in HLA antigen expression. There are documented disturbances in oxidative stress levels, with mounting evidence that oxidative stress and lipid peroxidation contribute to the disease process in ME/CFS: circulating in the bloodstream are free radicals which if not neutralised can cause damage to the cells of the body (a process called oxidative stress): there is evidence that incremental exercise challenge (as in graded exercise regimes) induces a prolonged and accentuated oxidative stress. There is evidence of gastro-intestinal dysfunction, with objective changes including delays in gastric emptying and abnormalities of gut motility; there is evidence of swallowing difficulties and nocturnal diarrhoea; there is evidence going back to 1977 of hepatomegaly, with fatty infiltrates: on administration of the copper response test, there is evidence of post-viral liver impairment; there is evidence of infiltration of splenic sinuses by atypical lymphoid cells, with reduction in white pulp, suggesting a chronic inflammatory process. There are abnormalities in the reproductive system, with clinical evidence that some female patients have an autoimmune oophoritis; there is evidence of endometriosis; there is evidence of polycystic ovary syndrome;

in men with ME/CFS, prostatitis is not uncommon. There is visual dysfunction, including latency in accommodation, reduced range of accommodation and decreased range of duction (ME patients being down to 60% of the full range of eye mobility).

1.6.3 The above list is by no means comprehensive but merely gives an overview of documented abnormalities seen in ME/CFS that can be accessed in the international medical literature, as well as in the abstracts and reports of Clinical and Research Conferences.

1.6.4 It is beyond reason that so many documented abnormalities in people with ME/CFS should be disregarded by NICE, especially as there is no credible evidence—as distinct from opinion and assertion by a small group of psychiatrists and their adherents who act as Government advisers—of abnormal illness behaviour in patients with authentic ME/CFS.

1.6.5 It is clear from the draft Guideline that not only the voice of the patients has been ignored, but so also have the views of those healthcare professionals who understand this complex illness and who have spent a professional lifetime dealing with it—a state of affairs that is indicative of a dictatorship, not a democracy.

1.7 The benefits, side effects and risks of the recommendations must be considered: NICE acknowledges in its draft Guideline that it is aware of patients being damaged by Graded Exercise Therapy (GET) but then ignores this in its recommendations, stating on page 257 of the draft Guideline that the severely affected should receive the same management regime as that of any person with “CFS/ME”—in other words, NICE is recommending a “one size fits all” policy, even though NICE has been made aware that numerous surveys of over 3,000 patients carried out by patients’ charities, support groups and independent researchers universally concluded that graded exercise makes many patients worse. Notably, exercise regimes have converted patients who were moderately affected into those who are severely and chronically affected, with some patients requiring tube-feeding.

1.7.1 There is incontrovertible evidence that ME/CFS patients’ ability to work is impaired and this can be shown by a serial exercise stress test: patients do not recover in 24 or even 48 hours after exercise. These changes in serial testing point to a significant and confirmable physical abnormality. The test/re-test is 100% objective and can prove that ME/CFS is neither malingering nor faking. In ME/CFS, the measurement declined by about 25%, far more than in other significant diseases such as chronic obstructive pulmonary disease and even heart failure. For NICE to recommend a national policy of forced exercise—and to compel such patients to undergo these exercise regimes on pain of having their benefits withdrawn if they do not comply—amounts to persecution of very sick people that is totally unjustified and unacceptable. Whilst NICE is at pains to emphasise that these regimes are for those who want to recover (which is not only patronising but implies a degree of choice, since NICE emphasises that the cornerstone of any management regime is “patient choice”), the end result is that benefits are contingent upon compliance.

1.8 Cost implications of the recommendations must be considered: given that there is indisputable evidence that CBT/GET is of proven limited and short-lasting benefit and is not curative, there is no factual basis for NICE to recommend such regimes, especially as the cost of providing and delivering such inappropriate interventions throughout the country would be logistically impracticable and financially indefensible. Equally, less expensive programmes that deliver advice about “pacing” and/or counselling are unnecessary: most patients with ME/CFS do not lie in bed all day unless they are too sick to do otherwise, and they use common sense in the daily management of the disorder. They do not need professional therapists to instruct them how to manage their physical limitations—experience has taught them what they can and cannot do. Given that NICE is prohibiting life-prolonging drugs for other diseases on the basis of cost, the money that NICE is channelling into costly but ineffective and potentially harmful psychotherapy for ME/CFS patients would be far better spent on appropriate investigations such as immunological assays and neuro-imaging that address the pathology and so might in time offer hope of curative treatment.

1.9 The recommendations must be supported by evidence: in a House of Lords decision in 1997, Lord Browne-Wilkinson said that medical evidence must be “*capable of withstanding logical analysis*” and if it is not, then “*a judge is entitled to hold that the body of opinion is not reasonable or responsible*”. In the case of its recommendations for the management of ME/CFS, the evidence on which NICE relies is exceedingly weak and is based on a small number of research trials that had a number of serious shortcomings (for example, there were a limited number of outcome measures and no objective measure of activity levels against which the results could be measured; in one such trial, activity levels were decreased). A detailed Report by Professor Malcolm Hooper and Horace Reid which comprehensively exposed the flawed methodology of the York Systematic Review on the claimed efficacy of behavioural modification regimes in “CFS/ME” upon which NICE relies—to the exclusion of other credible evidence—was sent to NICE in January 2006 (“Inadequacy of the York (2005) Systematic Review of the CFS/ME Medical Evidence Base”); Nancy Turnbull, Chief Executive and Project Lead, National Collaborating Centre for Primary Care, acknowledged its receipt and gave written assurance that the Report would be considered by the NICE Guideline Development Group, yet the draft Guideline largely ignored the important evidence contained

in this Report, including evidence of high withdrawal rates and patients' dissatisfaction. The Report showed unequivocally that the York Review was biased in favour of current Government policy and that it knowingly excluded the evidence that CBT/GET has little benefit in ME/CFS.

1.10 The Guideline Development Group must include relevant specialists: in the case of its "CFS/ME" draft Guideline, NICE did not include representatives from the relevant medical and scientific disciplines.

2. *Second Term of Reference: Whether public confidence in NICE is waning*

2.1 Extensive biomedical information about ME/CFS was supplied to the Guideline Development Group but was ignored in favour of the pre-determined "biopsychosocial" model, so it is not surprising that public confidence in NICE is non-existent. There has been much media coverage about the lack of public confidence in NICE's recommendations, not only in ME/CFS but also in areas such as Alzheimer's Disease, breast cancer and osteoporosis. 'Pulse', a medical magazine, reports this week that NICE has drastically revised its proposals for patients with osteoporosis and has effectively done a U-turn after coming under what was described as 'a barrage of criticism' from clinical groups over its original plans to limit treatment for people with osteoporosis. In the case of ME/CFS, patients, as well as clinicians and medical scientists who support them, are aware of the extent of significant evidence that NICE has deliberately disregarded for political reasons, so inevitably there is no confidence in NICE.

2.2 There is a widely-held belief that NICE is simply a mouthpiece for the Department of Health, whose advisers on ME/CFS are known to have vested financial interests in maintaining the status of ME/CFS as a "psychosocial" (ie. mental) disorder. These advisers are psychiatrists who also work for the medical insurance industry which, as long it can get away with claiming that ME/CFS is deemed by its own "experts" and "Government advisers" to be a "mental" disorder, can deny payment of rightful benefit under its terms of exclusion. A recent inquiry by a Committee of Parliamentarians (the Gibson Inquiry) found that this was such a serious matter that the Committee called for an investigation by the Standards body.

2.3 There is also evidence that the pharmaceutical industry controls both medical institutions and medical education in the UK and that its aim is to create "life-style disorders" (ie. "psychosocial disorders") for which doctors are urged—even bribed—to prescribe unnecessary mind-altering drugs for the life of the hapless patient. Many think that this is where ME/CFS currently finds itself. In 2001 a leading Cambridge academic presented evidence that multi-national corporations are taking the place of elected governments and argued that the surrender of Government to big business is the greatest threat facing democracy. The alleviation of suffering used to be paramount in medicine but has now been replaced by the dictates of corporate interests whose life-blood is profit ("Politics Isn't Working: The End of Politics". Noreena Hertz; Channel 4 documentary; 13 May 2001). This disease-mongering for profit was established by the Health Select Committee itself in 2004 when it carried out an investigation into the influence of the pharmaceutical industry and looked specifically at the industry's influence on NICE. Members of the Health Select Committee are on record as being "horrified" by the evidence they heard (see www.meactionuk.org.uk/HoC_Select_Ctte_Inquiry_into_Pharma.htm).

3. *Third Term of Reference: NICE's evaluation process and whether any particular groups are disadvantaged by the process*

3.1 There were many problems for patients with ME/CFS in this respect. The consultation process itself was badly thought-out and insufficient time was allowed for sick people to participate. The documents that were sent out were enormous and were too heavy for many people with ME/CFS to be able to hold or use. The York Review was 488 pages and was so large that when sent out by NICE's preferred option (ie. by email) caused computers to crash, so a printed version had to be sent by Royal Mail. This apart, many people with ME/CFS do not have—or are too sick to use—a computer. The following Questionnaire contained misleading instructions (which meant that replies were likely to have been skewed in favour of NICE's pre-determined recommendations); it was incomplete and it was very badly worded. The draft Guideline itself was also huge (269 pages), with the same difficulties for those with ME/CFS. The short version was 48 pages, but if people relied upon that version, they were likely to have been misled. In particular, many of NICE's self-protecting caveats and reservations set out in the full version have been omitted from the short version.

3.2 Due to NICE's insistence that all replies concerning the consultation process must be by email, an unknown number of patients with ME/CFS were prevented from participating in the consultation process (which is in breach of the AGREE Instrument). There were confusing instructions on NICE's website about the format of the responses that NICE would accept: because so many patients were unable to use NICE's online pro-forma, NICE was contacted and written confirmation was sent by NICE clearly stating that as long as responses were typed, they would be accepted. NICE did also confirm that if people were unable to type, and submitted hand-written responses, these would be transcribed by sub-contracted temporary staff, but any handwritten responses must be sent in well before the deadline. People struggled to send in a response, believing it would be accepted and heeded. However, just a day or so before the deadline, NICE changed its mind and said it would only accept on-line responses. It took a personal letter from Dr Ian

Gibson MP to the Chairman of NICE, Professor Sir Michael Rawlins, before this impasse was sorted out and a written promise was given by Sir Michael that all responses—in whatever format—would be considered with equal weight. Few people have any confidence that this will occur.

4. *Fourth Term of Reference: the speed of publishing guidance*

4.1 It is over five years since the Report of a Working Group to the Chief Medical Officer on “CFS/ME”, at the launch of which (on 11 January 2002) the Chief Medical Officer stated NICE would be asked to draw up guidance for the treatment of the condition; the Medical Research Council’s “CFS/ME” Research Advisory Group’s Report was issued on 1 May 2003; neither of these so-called milestones resulted in any improvement in access to appropriate investigations or in the provision of necessary care and support for those with ME/CFS (as distinct from those with psychiatric “chronic fatigue”). It was not until 23 February 2004 that the Health Minister (Lord Warner) announced that clinical guidelines for the diagnosis and management of “CFS/ME” would be developed by NICE. Three years later, there is still no Guideline.

4.2 In the US, ME/CFS is regarded as a Priority One category. In November 2006, the US Centres for Disease Control initiated an awareness campaign, at the launch of which Dr Nancy Klimas, Professor of Medicine at the University of Miami and President of the International Association for (ME) Chronic Fatigue Syndrome stated: “*There is evidence that the patients with this illness experience a level of disability that is equal to that of patients with late-stage AIDS, patients undergoing chemotherapy and patients with multiple sclerosis*”. That message continues to escape NICE, whose only recommendation is that patients with the disorder must be given psychotherapy to try to brain-wash them into abandoning their conviction that they are physically sick and that they must undergo compulsory “physical rehabilitation” regimes so that they can exercise back to fitness and return to gainful employment. This is a medical scandal in the UK of breathtaking proportions.

We hope that the Health Select Committee on NICE will take on board the submission made by the 25% ME Group.

Simon Lawrence,
Chairman, 25% ME Group

March 2007

Evidence submitted by the ME Association (NICE 28)⁹³

SUMMARY

The terms of reference for your Inquiry with which this submission is concerned are:

- why NICE’s decisions are increasingly being challenged;
- whether public confidence in NICE is waning; and
- NICE’s evaluation process and whether any particular groups are being excluded.

We, the undersigned, are charities and support organisations working in the field of Myalgic Encephalomyelitis and Chronic Fatigue Syndrome (ME/CFS). This neurological illness affects an estimated 250,000 people in the UK and is a multi-system, multi-organ illness. For the 25% of those who are severely affected, the illness is complex with many developing more disabling symptoms and neurological complications and some need to be tube fed. The estimated cost to the UK of this illness is £6. 4.billion per annum (AfME campaign research/Sheffield Hallam University).

NICE has, for the last two years been preparing a new clinical guideline on the clinical assessment, treatment and management of ME/CFS. A draft of the guideline was sent to stakeholders for their comments late last year but our understanding is that it is unlikely that there will be any significant alterations as a result of this extensive consultation process. NICE now intends to publish a final version of the guideline in August 2007, without any further consultation with patients or their representatives. Throughout the development of the guideline we have placed before the guideline development group cogent evidence about the illness. This has been largely ignored.

⁹³ On behalf of:
Action for ME;
The Young ME Sufferers Trust;
Chrome;
The Blue Ribbon for the Awareness of ME;
The National ME Centre;
West Midlands Group Consortium (NICE stakeholder-ME/CFS Guideline, November 2006);
South West Alliance for ME;
Suffolk Youth and Support Group for young people with long term illnesses and their parents;
ME Positive—East Midlands.

1. The Government's own guiding principle for the NHS is that it must be patient-led (*The Expert Patient, DoH 2001*). Patients after all are the only people with direct physical experience of an illness. In an illness such as ME/CFS the input of patients is even more vital. Indeed for the severely affected, because they are too ill to participate in trials, the only management treatment must come from their own experience. There is no known agreed causation, no known cure, there are no universal diagnostic criteria. Diagnosis is therefore a difficult task for any doctor and treating the illness requires a close collaboration between doctor and patient.

2. From the publication of the two versions of the draft of the guideline issued by NICE it was apparent that not only had the voice of the patient been largely ignored but so were the views of those health professionals who understand the complex physical nature of this illness. We are under the impression that the united criticism of the guideline from patients, patients' support groups and their medical advisors is not going to result in any major changes to the overall recommendations. Recently NICE has changed its policy to using "consensus" and only have one consultative process, instead of the two previously held. We believe this is a mistake in the case of this guideline for ME/CFS where there has been much controversy and which has provoked, as NICE admits, one of the biggest feedbacks that it has ever received. We ask that you review this process and allow flexibility for a second consultation with stakeholders in such cases.

3. At the heart of the guideline is NICE's proposal for the treatment of ME/CFS. In using this word "treatment" it must be stressed that there is no known cure for ME/CFS and that in the context of the illness "treatment" refers to the management of some of the symptoms. The proposals on treatment are vital. It is what the GP in his surgery will turn to after he has diagnosed a patient with ME/CFS. The NICE guideline for the treatment of ME/CFS recommends the use of cognitive behaviour therapy (CBT) and graded exercise therapy (GET) as first line options for ME/CFS. This is a gross error by NICE and will be challenged, because:

- (a) It is accepted that people with ME/CFS are a mixed population. They range from the severely affected who are either bed bound or house bound, to the moderately affected who may be housebound, to the mildly affected whose everyday activity is restricted. CBT and GET are only suitable for a part of that population. NICE has failed to offer other treatments for:
 - those patients with severe neurological and immunological problems, especially the severely affected group that comprises some 25% of those with ME/CFS;
 - children with ME/CFS who are a particularly vulnerable group in this respect.

In addition the treatments recommended by NICE pre-suppose the "fitness" of the patient to be able to undertake them thus excluding and gravely disadvantaging the severely affected group.
 - (b) The recommendations by NICE are based on a few research trials which had many shortcomings:
 - A flawed patient selection process.
 - A limited number of outcome measures.
 - No objective measure of activity levels to confirm that the aim of GET was achieved.
 - No evidence to show a significant increase in activity levels in patients. Indeed, in some cases, activity levels actually fell (eg the Friedberg trial).
 - It is also known that the outcomes of CBT and GET are usually transient. These approaches do not resolve the long term problem.
 - (c) NICE failed to consult with experts in the field of ME/CFS who have other views of treatment, which offer evidence based alternatives to GET and CBT, eg pacing. (Jason, Taylor, Goudsmit, Wallman, Ho-Yen).
 - (d) The guideline development group was dominated by supporters of the biopsychosocial model; few had direct clinical experience of the illness they were advising upon and the three patient representatives were outnumbered and their views effectively ignored.
 - (e) All experts in the field of ME/CFS (including those who wrote this guideline) accept that the illness affects different people in different ways. Some can increase activity and some cannot. Management recommendations need to cover a range of patients, not just the small minority of those who may benefit from the CBT and GET model.
 - (f) Biomedical research has shown that inappropriate exercise in people with ME/CFS can prove harmful or dangerous, eg it can cause cardiovascular problems, mitochondrial dysfunction, autonomic disturbance, oxidative stress and muscles responding differently to exercise. (We can provide research papers and data to support this.)
4. Representations were made to NICE querying:
- the findings of those trials upon which the treatments rely;
 - the exclusion of the severely affected from those trials; and
 - the effectiveness of the treatments proposed and the cost implications to the NHS.

These representations were not examined with the scientific rigour that is to be expected from NICE. The process of CBT for each patient is lengthy and costly. It requires a great deal of energy on the part of the patient and energy is one thing that they do not have. CBT focuses on the illness beliefs and emotional aspects of illness and therefore does not address the severe neurological problems that patients have to cope with. CBT is not recommended as a first line treatment for physical illnesses in other NICE guidelines but merely as a coping strategy alongside the management of the underlying illness (eg in MS). (We can provide the Committee with data for controlled trials of CBT, GET and a multidimensional programme emphasising pacing, indicating that taking fatigue as the outcome measure does not support the superiority of CBT/GET.)

5. We do not advocate psychological management as a treatment for this illness. ME/CFS is a neurological illness, classified as such by the World Health Organisation under the category G93.3, and this is accepted by the Department of Health. We do however accept that symptomatic management advice may help some patients cope better with their illness. There is evidence from controlled trials that a simpler, cheaper and equally effective form of symptomatic management than CBT/GET is available (Goudsmit 1996, Ridsdale *et al* 2001, Taylor 2006). These trials involved people with chronic fatigue which, whilst by no means the same illness as ME/CFS, has a few of its symptoms. The trials showed that a programme of pacing and counselling is as effective in addressing some of the symptoms of ME/CFS as the more expensive treatment recommended by NICE. Pacing is a common-sense approach that is automatically adopted by patients with chronic health problems. It does not require expensive medical guidance. Counselling helps patients cope in coming to terms with a chronic physical illness. The cost per patient of providing CBT as recommended by NICE is approximately £1,000 per course. The cost of a treatment programme consisting of counselling is approximately £700 per course. The total cost of assessing and treating the 180,000 people with mild to moderate ME/CFS using CBT and/or GET will be approximately £180 million. The alternative of pacing and counselling will be approximately £126 million. In the Research Paper “Chronic fatigue in general practice: economic evaluation of counselling versus cognitive behaviour therapy” (*British Journal of General Practice*, January 2001) the conclusion reached was that:

“The lower unit cost of counsellor’s time, together with their greater availability and similar effectiveness may represent decisive factors for primary care groups and GPs when faced with the choice of which treatment strategy to pursue.”

Moreover not only is the latter option more cost effective but such counselling and pacing programmes are more acceptable to patients. The use of a programme of counselling and pacing is a “win-win” situation for the NHS in that:

- (a) it will save the NHS (the Taxpayer) millions of pounds;
- (b) it will be available to far more patients in a far shorter time; and
- (c) it is far more acceptable and found to be more helpful to ME/CFS patients.

6. NICE is in effect recommending the most expensive option. Professor Richard Layard, an economist who advises the Government, acknowledged last year that CBT is appropriate for only 40% of the patient population overall. The Department of Health will surely want to know why NICE is recommending a form of treatment which is both more expensive and at the same time less appropriate than other more helpful and cost effective management strategies, ie symptom control, pacing and counselling. NICE proposes training therapists to deliver the treatments but this again will take time and money. CBT services are already in a position where they cannot cope with a rapidly increasing referral rate for common psychiatric conditions such as anxiety and depression—a steadily worsening situation that NICE has been well aware of for some time. In addition, if the expected outcome of the guideline is to help patients recover and get back to work or regain their previous quality of life and, by doing so come off benefits, then the net overall gain must be examined. If only a minority of patients have these outcomes then the reality is that there will be a “double spend”, ie cost of treatment plus cost of benefits.

7. At a time when they are rejecting life saving and life prolonging drugs on the basis of cost, this decision in relation to ME/CFS is hard to understand and justify. Moreover, if the guideline is implemented:

- There will be a huge outcry from the patients and patient organisations. MP’s mail-boxes will be full.
- Research has shown quite clearly that a significant number of patients have abnormal and sometimes harmful responses to minimal exercise, so graded exercise programmes can be completely inappropriate. This is especially so in the case of the severely affected. This has already been pointed out by the British Psychological Society, the organisation that represents most of the therapists who will be involved in providing the behavioural treatment proposed by NICE.
- The potential fallout for NICE in recommending a treatment that then causes damage to patients, when NICE has been warned of this by the relevant professionals, is huge. Who is going to take responsibility for this?
- Public confidence will be lost.

8. It is well known that “the devil is in the detail”. It is most certainly with NICE. The “full guideline” runs to 269 pages. This contains many caveats, concerns and acknowledgements that the treatments recommended have not always been applied appropriately; that GET has not been researched for children

and the severely affected and that patients must be given the opportunity to agree to the proposed treatment. But the medical professionals will not be sent this “full guideline”. Instead they will a shorter version. In this “short version” those caveats, concerns and acknowledgements become much less clear. We say this is wrong and potentially dangerous. The final reading matter that is distributed to GPs must make crystal clear the concerns which are expressed in the “full guideline”.

9. We believe that, because of its cost, limited availability and its potential for harm, the treatment regime recommended by NICE will add to the criticisms levelled against NICE. We are not alone in this and will produce in evidence a copy of the submission to NICE prepared by Dr Charles Shepherd, a world renowned expert on ME/CFS, on the unbalanced account of CBT and GET in the guideline. Dr Shepherd will be available for questioning by the Committee.

10. We believe that NICE has failed the ME/CFS population with this guideline. It has failed to:

- Recognise that ME/CFS is a neurological illness.
- Acknowledge and recommend the use of the Canadian Clinical Guidelines on ME/CFS (2003), which is a clinical guideline produced by international experts who have seen over 20,000 patients. Instead it has been listened to the voice of medical representatives who have little clinical experience of the illness.
- Recommend urgent bio-medical research into the illness.
- Recommend that ring-fenced funding for the 13 regional specialist ME/CFS clinics in England, of which many are under threat of closure, is continued.
- Recommend the opening of new bio-medical clinics for patients with ME/CFS.

11. We believe that the competency of NICE is in question because:

- It has paid lip-service to the principle of a patient-led NHS.
- Patient representatives have sat at the table with NICE and patients and patient organisations have submitted evidence but NICE has sidelined their views.
- It has chosen to ignore research trials and other evidence that do not uphold the basis of their preferred treatments.
- It has chosen to listen to one view of the illness from a small part of the medical establishment instead of following the precedent set by the Chief Medical Officer’s Working Party on ME/CFS which weighted patient evidence in a more balanced way.
- Its own evaluation process has disadvantaged children with the illness and the 60,000 patients of the severely affected group.
- The proposed “short version” guidance to GPs insufficiently covers the widespread concern over CBT and GET.
- The guideline will not help medical professionals effectively diagnose and manage ME/CFS.
- Stakeholder and patient evidence has not been adequately acknowledged in the guideline.

12. Oral evidence supporting our submission will be available should this be desired.

The failings outlined above will all invariably result in further challenges to NICE and public confidence in NICE will wane further. We call upon the Select Committee for Health to investigate these failures.

Neil Riley, Chairman
ME Association

22 March 2007

Evidence submitted by the Medical Technology Group (NICE 52)

1. EXECUTIVE SUMMARY

1.1 The Medical Technology Group (MTG), launched in 2000, is an active coalition of patient groups, medical professionals and industry, committed to promoting patient access to technologies, such as diagnostic equipment and surgically implanted devices, as well as ensuring the introduction of new innovations. Now in our seventh year, we are making a big difference in widening patient access to medical technology, including the latest treatments for heart conditions, diabetes, stroke, orthopaedics and continence. We want to see a modern and effective NHS responsive to the needs of the patient.

1.2 The Medical Technology Group welcomes the opportunity to be able to comment on the work of the National Institute for Health and Clinical Excellence through the Health Select Committee inquiry. Medical technologies are in a unique situation in that they can be subject for inclusion in technology appraisals, clinical guidelines, and the interventional procedures programme. Therefore the Medical Technology Group is extremely well placed to comment on the work of the Institute.

1.3 Recommendations:

- NICE guidance should take in to consideration long-term—across the board—saving gains that can be produced by medical technologies.
- An independent mechanism should be put in place to determine initial topic selection.
- NICE guidance for medical devices should be produced more quickly so as to not stifle innovation and ensure patients can get access to the latest medical technologies.
- Implementation of NICE guidance should be monitored more closely.
- There should be a joined up strategy between NICE and procurement systems to ensure that medical devices which have positive NICE guidance are made available to patients in a timely fashion.

MTG RESPONSE TO THE COMMITTEE'S REMIT

2. WHY NICE'S DECISIONS ARE INCREASINGLY BEING CHALLENGED

2.1 The National Institute for Health and Clinical Excellence is renowned the world over as the gold standard for assessing the clinical and cost effectiveness of treatments, including medical devices, via technology appraisals, clinical guidelines and its interventional procedures programme. As NICE guidance is increasingly becoming *the* determining factor by which Trusts allocate their limited resources, the importance of receiving a positive determination from NICE is more important than ever.

2.2 Therefore industry, patients and clinicians are all more likely to appeal against a negative decision for a treatment that they consider to be clinically important to ensure that it remains available for those who require it. This is particularly the case if the reason for the negative determination has been made primarily on cost effectiveness rather than clinical effectiveness. Long term vision is lacking and long term savings that medical technologies can achieve are ignored in the NICE process, with its narrow focus on institutional budgets.

3. WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING, AND IF SO WHY?

3.1 In September 2006 the Department of Health announced that NICE will play a bigger role the topic selection process. NICE's new extended role means that it will be the principal point of contact for individuals and organisations which want to suggest topics. It is now also responsible for the initial "sifting" of suggestions. This allows the Institute to be open to questions of impartiality—and therefore confidence—as this system may be perceived by the public and the health service as biased. The Medical Technology Group believes that NICE should not have control over initial topic selection. A body independent of NICE should be given a mandate to determine which topics are to be taken forward—and at what time—in the NICE process. Without an independent and transparent topic selection process the Institute could be subject to criticism that high profile treatments and conditions are given precedence over equally essential but less well known treatments and conditions. By ensuring that the topic selection process is entirely independent and transparent, NICE will not be open to criticism in this way.

3.2 Public confidence in the Institute is also waning due to inconsistent implementation of NICE guidance. The MTG view on implementation is included in section six of this document.

4. NICE'S EVALUATION PROCESS, AND WHETHER ANY PARTICULAR GROUPS ARE DISADVANTAGED BY THE PROCESS

4.1 NICE makes recommendations on a case-by-case basis taking into account both clinical and cost effectiveness, and rejects the use of an absolute cost threshold. Many medical technologies have an initial high cost but create long term savings within the National Health Service. The NICE process should take this into account when producing guidance. For example medical technologies—such as a stent or hip replacement, where specialist techniques and instruments are used—facilitate faster recovery times, lower morbidity and reduce beds days. These techniques have the potential to offer significant benefits both to individual patients and the NHS.

4.2 As recovery times are significantly reduced, patients are able to get back to normal life more quickly. Using medical technologies means that patients can be back at work, contributing to the economy much quicker and the length of inpatient stay can be greatly reduced. The Medical Technology Group believes that NICE does not give enough weight to wider societal implications when constructing guidance. At a time when financial resources are becoming scarce, considering the long term cost-saving benefits of medical technologies should be considered in the production of NICE guidance.

5. THE SPEED OF PUBLISHING GUIDANCE

5.1 NICE guidance can be viewed as one of many barriers which is stifling innovation in the UK. The UK market for medical devices is extremely small. If companies are not able to innovate and gain timely NICE guidance for new products then there is the possibility that medical device manufacturers will move overseas to more favourable markets which support innovation. This would be the worst possible outcome for patients in the UK as they will not be able to get access to the latest innovations in the medical technology market through the National Health Service and will either have to pay a premium for these things in private practice, go overseas for the most innovative treatments, or miss out on the best treatments completely.

5.2 Sufferers in some areas have been faced with “treatment blight”—the reluctance of doctors to prescribe devices because no decision has been made by NICE, ie a product either hasn’t been through the NICE process at all, or it is in the process of being appraised prior to a final determination being made.

5.3 The MTG considers that implementation of the Single Technology Appraisal process needs to ensure that manufacturers and patient groups are given a right to reply to the “Evidence Review Group” Report before submission to the Appraisal Committee. This ensures the same degree of consultation is afforded as in the existing Multiple Technology Assessment process.

6. THE IMPLEMENTATION OF NICE GUIDANCE, BOTH TECHNOLOGY APPRAISALS AND CLINICAL GUIDELINES (WHICH GUIDANCE IS ACTED ON, WHICH IS NOT AND THE REASONS FOR THIS)

6.1 NICE guidance has no impact on patient care unless it is implemented. The Medical Technology Group is concerned that there is variation in the uptake of some NICE technology appraisals relating to devices and surgical procedures and recommends that NICE institutes a compliance mechanism which demonstrates mandatory rapid—within three months—adoption of guidance.

6.2 Implementation of national policies and guidance relating to the use of technologies is often lost in a plethora of other priorities. Guidance issued by the technology appraisal advisory committee of NICE supposedly carries a mandate under the Health Services Act, yet its implementation is haphazard. Guidance on Insulin Pumps was issued in 2003, clearly defined a population who might benefit, but patient groups, who support pump wearers and their families, still commit enormous resources to fighting local battles where PCTs will not act on the guidance. NICE itself has an implementation systems directorate which supports, rather than monitors, implementation and the issue does not appear to be a sufficiently high priority for the Healthcare Commission. Given the resources committed to NICE, failure to rigorously enforce its guidance represents a significant loss of opportunity for patients to benefit from clinically and cost effective treatments.

6.3 The financial costs of insulin pump therapy are often mentioned as a barrier to its wider application across the diabetic population. A pump, covered by the manufacturer’s warranty for four years, costs on average £2,400, plus £800 pa for consumables (infusion sets, insulin cartridges, batteries, etc). If a pump is replaced every four years, the average yearly cost of the therapy is £1,400. One overnight stay in hospital following admission to A&E for a diabetic emergency costs £350. One procedure of dialysis treatment for diabetic kidney disease costs £504. One course of laser treatment for diabetic retinopathy costs £847, plus incalculable weeks off of work. In light of these costs for treating poorly controlled diabetes, insulin pump therapy as preventative medicine seems extremely cost effective.

6.4 The Medical Technology Group is concerned that new product procurement processes put in place by NHS Supply Chain will not be rapidly responsive to reflect positive NICE guidance. NHS Supply Chain was created to facilitate centralised procurement for Trusts. Trusts can opt in and out of this process, however the 40% market share NHS Supply Chain has is likely to encourage NHS Trusts to procure through it. This may mean that a device which has received positive NICE guidance will not be used widely by Trusts until it is included on the preferred supplier lists which may be created by NHS Supply Chain and closed for a number of years. The Medical Technology Group would like to see a mechanism put in place which allows devices which have been given positive NICE guidance to gain easy and timely access to patients.

6.5 The Medical Technology Group believes that the implementation of NICE guidance should be actively monitored by the Healthcare Commission. The Healthcare Commission Annual Health Check provides the basis for NICE’s implementation monitoring. However, at present, NICE does not receive specific feedback from the Healthcare Commission about the implementation of individual pieces of guidance, even on a broad scale. The Medical Technology Group believes that it is essential that NICE receives information about the implementation of its guidance and a feedback mechanism is put in place to ensure that Trusts which do not implement guidance within the required timescale are made to do so.

7. RECOMMENDATIONS FOR ACTION

7.1 NICE guidance should take in to consideration long term—across the board—saving gains that can be produced by medical technologies.

7.2 An independent mechanism should be put in place to determine initial topic selection.

7.3 NICE guidance for medical devices should be produced more quickly so as to not stifle innovation and ensure patients can get access to the latest medical technologies.

7.4 Implementation of NICE guidance should be monitored more closely.

7.5 There should be a joined up strategy between NICE and procurement systems to ensure that medical devices which have positive NICE guidance are made available to patients in a timely fashion.

The Medical Technology Group

March 2007

Evidence submitted by Medtronic Ltd (NICE 15)

EXECUTIVE SUMMARY

Issues relating to topic selection and methodology are undermining public confidence in NICE.

Recent changes to the way the Institute operates have not helped in this regard.

Medical device technologies face peculiar and additional barriers to their uptake following guidance compared with pharmaceuticals.

Medtronic welcomes the opportunity to submit evidence to the Health Select Committee, addressing the important issue of the National Institute for Health and Clinical Excellence (NICE). Medtronic provides advanced medical devices for patients in the United Kingdom. Since the inception of NICE in 1999 we have been an active stakeholder in over 50 work programmes of the Institute. As well as working with the Institute during the production of its guidance we are also closely engaged with other organisations who are interested in ensuring that such guidance is acted upon.

We would like to offer the following evidence, appropriate to the Committee's terms of reference. The evidence reflects our experience described above.

Whether Public Confidence in the Institute is Waning, and if so Why

1. We believe that this is the case, and would cite issues around topic selection, conflict of interest within the health technology community and concerns over methodologies employed.

2. The topic selection process to decide which technologies and conditions are looked at by the Institute has recently been overhauled. The new system give the Institute far more say in which topics are considered than was previously the case. We have concerns that this will see the Institute support the selection of technologies that are easy to appraise at the expense of those that might be more problematic, but have wider societal benefit. We believe the topic selection process should be independent of the Institute.

3. We are concerned that conflict of interest is rife amongst the institutions involved in the production of the independent health technology assessments considered by the Institute. As academic institutions they are keen to publish research and lead thought in methodology and policy in the area. They also derive revenue from their work undertaking assessment reports and economic modelling for NICE, and many are also employed by industry to do the same on behalf of manufacturers during a technology appraisal. All of these individual elements are perfectly legitimate in their own right, however there is a problem when institutions attempt to combine all four elements at the same time. For example, during the current review of coronary artery stents, the review group conducting the independent assessment report published an article in a peer reviewed journal concluding that the technology could not be considered cost effective. In such situations it seems to us that stakeholders arrive at the table knowing that other key parties have already made up their mind about the likely outcome. This, we believe, brings the appraisal process into disrepute.

4. NICE's decisions during a technology appraisal are very heavily determined by the estimates of incremental cost effectiveness ratios. We accept that a key role of the Institute is to decide on what represents value for money for the NHS, however are not convinced that the methodologies employed are robust enough to make such decisions consistently and accurately. Quality Adjusted Life Years (QALYs) derived using one methodology in one population, probably measure something fundamentally different from QALYs derived using another methodology in a different population, yet comparisons between the two are regularly made. Health economics does not appear to be a mature enough discipline to answer the questions that are being asked of it, and we believe that the assessment groups and appraisal committee are sometimes

disingenuous about the uncertainty inherent in the economic models they favour. Whilst it is fair to say the models used often represent the best available estimation of cost effectiveness, sometimes those estimates are not robust enough on which to base important decisions for patients and the NHS.

5. We are concerned also that the cost effectiveness thresholds that NICE indicates as acceptable are arbitrary.

The Speed of Publishing Guidance

6. We accept that there is need for the Institute to ensure that its quality standards and consultation processes are robust, and that this means that it will take some time to produce final guidance. We do feel, however, that the current process could be achieved more quickly by a simple reduction in the time allocated to the production of independent assessment reports.

7. We believe that the current attempt to shorten the process by the use of single technology appraisals (STA) is misguided. One of the strengths of NICE's existing process is that the assessment is seen as independent and there is inclusive and meaningful consultation, with the views of stakeholders demonstrably being taken into account. The problem with relying only on a manufacturer's submission, as is the case with STA, is that a consultative process is turned into an adversarial one. We feel that the instinct of the Committee, understandably, will be to be more suspicious of a manufacturer's submission than they would of one produced by an independent assessment group.

The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines (Which Guidance is Acted on, Which is Not and the Reasons for This)

8. Our experience is that the deciding factor on the successful implementation of guidance is the presence of a local champion. Our work with Cardiac Networks Device Survey Group illustrated that for pacemakers and implantable defibrillators, there was no correlation between implant rates and deprivation, number of cardiologists or type of cardiology centre. Rather it was apparent that a single, strong local advocate could have a very significant impact on the provision of local services.

9. Medical devices, such as implantable cardioverter defibrillators (ICDs), have an additional challenge to their uptake because of the way they are commissioned. Pharmaceutical technologies approved by NICE often have no other barrier to their increased utilisation than changing the prescribing behaviour of doctors, whereas many technologies require infrastructure alterations, increased provision of specialised services or bespoke training and education programmes.

10. Furthermore, the cost of decisions relating to such technologies is often more visible at an individual patient level than that of changes in prescribing, even if the overall impact is much less. For example when guidance on the use of ICDs was first issued, it was described as the single biggest risk to PCT budgets from a NICE decision, yet last year the NHS spent £60 million on the devices and some £1 billion on statins to reduce cholesterol. Faced with the choice of approving a drug which might cost £10,000 over five years or a device that costs £10,000 today, we believe PCTs will discriminate against the device, even if the cost was a one off payment that effectively represented five years treatment. Primary care organisations need greater support to implement guidance when it relates to specialist services or requires the explicit and rapid reallocation of resources.

11. We believe that the implementation of NICE guidance is not a significant enough priority for NHS organisations, and implementation could be improved by a greater emphasis being placed on it by the Healthcare Commission.

RECOMMENDATIONS

- The topic selection process should be independent of NICE.
- No part of the Institute's work should rely solely on submissions from manufacturers.
- Primary care organisations should be given bespoke support for guidance issued relating to specialised technologies and/or those requiring a significant up front investment.
- Monitoring the implementation of NICE guidance should be an absolute priority for the Healthcare Commission.

Richard Devereaux-Phillips
Medtronic Ltd

March 2007

[Mr Devereaux-Phillips serves as a member of the Health Technology Assessment Advisory Committee of NICE]

Evidence submitted by Merck Serono (NICE 77)

EXECUTIVE SUMMARY

On behalf of Merck Serono we wish to provide our experiences of working with the National Institute for Health and Clinical Excellence (NICE). We wish to draw your attention to a number of issues that we have observed from our work with NICE and communication with the NHS:

- *Applicability of NICE guidance to the NHS*; When NICE state that a particular technology is “not recommended” this guidance generally covers routine practice and does not state “exceptional case criteria”. In the absence of NICE guidance in this area, implementation in the NHS is inconsistent and proves to be time consuming for both patients and physicians.
- *Relevance of NICE guidance once it is published*; Innovative medications often collect a broader set of information in the period after marketing authorisation has been received. On many occasions given the timing of appraisal initiation, length of the appraisal process and the short time frame in which new data is considered, often new data can make published NICE guidance out of date.
- *Independence of NICE appeals*; In appeals to NICE, the appeal committee contains members of NICE which does not make it an independent and neutral environment for assessment.
- *Grounds of NICE appeals*; The grounds for appeal are based on procedure rather than a difference of scientific opinion. The second ground for appeal is, “the decision is perverse in light of the evidence submitted”. When decision making is based upon uncertain economic estimates, “reasonability” is a much more appropriate assessment.
- *Public confidence in NICE*; Public confidence in NICE has been questioned due to recent decisions denying patients access to the only licensed treatment available for their condition for, “cost effectiveness” reasons. This is the case with regards to bortezomib for multiple myeloma, pemetrexed disodium for malignant pleural mesothelioma, and cetuximab for the third line treatment of metastatic colorectal cancer.
- *Inconsistent NHS implementation of guidance*; A number of factors contribute to this, the most important being poor NHS financial management, clinical resistance, and lack of sanctions against poor implementation.

RECOMMENDATIONS

- When NICE issue a guidance which states that a technology should not be used routinely in the NHS, it should define, “non routine use”, then a set of, “exceptional case” circumstances to be included in guidance. This will ensure consistency of use and decrease the current postcode prescribing which occurs through “exceptional case” decisions at the present. In addition, this will reduce the number of patients being disadvantaged and aid clarity as to when, “non-routine use” of technology should or should not be used.
- When important new information becomes available within the timeframe of a NICE MTA appraisal then it should be considered by NICE. This will reduce the number of decisions being made with the use of old, out of date information.
- The constitution of the NICE appeal panel should be reassessed to increase impartiality and independence of such decisions. The Appeal panel itself should be more independent with a decreased role for members of NICE.
- The second grounds for a NICE appeal are limited to the assessment of “perversity” of the decision. This criteria should include the possibility to discuss differences in opinion and interpretation of scientific evidence and should be assessed on grounds of “reasonability”, and not “perversity”. This wording should be revised to read, “the decision is unreasonable in the light of the evidence submitted”.
- When NICE is reviewing the only licensed treatment available for a disease state then cost effectiveness should not be the overruling driver of the decision making process. In these circumstances other factors such as whether the condition is life-threatening or whether there are any other direct treatment alternatives should be given equal consideration.
- A review of NICE guidance implementation should be carried out with recommendations that result in clear action, but in particular, that NICE approved medicines are automatically included in local formularies.

INTRODUCTION

1. Merck Serono understands and values the objectives of NICE to improve the quality of care in the UK NHS. We are sure, if the system is modified, that the institute can be of even greater benefit to patients and the NHS.

APPLICABILITY OF NICE GUIDANCE TO THE NHS

The institute's evaluation process—and whether particular groups are being disadvantaged in the process

2. Guidance issued by NICE falls into a set list of definitions: recommended, not recommended or for use in clinical trials. A guidance of, “not recommended” can be most often found in recent decisions for oncology in particular, and is dissimilar to guidance issued in mental health, neurology and dermatology where guidance may provide criteria for which patients may receive a particular treatment. Absence of “non-routine use” and, “exceptional case criteria” is a major issue that impacts upon how NICE recommendations are implemented. Each hospital has its own procedure and definitions for what may be termed an “exceptional case”, and this can vary from symptomatology, patient personal circumstance and the disease knowledge of the hospital appeal committee.

3. For a patient to receive treatment under the, “exceptional case” procedure, it is dependant upon their particular physician, and the physician’s motivation/time to fight for the particular treatment. At present, the time taken for a physician to forgo normal practice to prepare and attend an “exceptional case” meeting is significant and negates the efficiencies that NICE are trying to promote. Additionally, the strain on the patient is significant, by focusing their energies on fighting for treatment, when they should be using their energy to fight their illness. To add a further variable, the success of a patient being determined as an “exceptional case” and granted treatment can be increased through having legal representation.

4. This failure to define “exceptional case” criteria within NICE guidance only increases inequalities and promotes post code prescribing. It is relatively easy for the NHS to implement positive and negative criteria for a broad group of patients, however the way the NHS defines “exceptional case criteria” is variable and depends upon a number of factors. To make guidance more applicable and aid implementation, NICE should, as standard, include “exceptional case criteria” in their guidance to increase NHS efficiency and promote common standards across the country. This will also promote greater efficiencies for physicians in prescribing and guide them further, in defining when a patient may be determined as an “exceptional case” and reduce the number of patients being disadvantaged.

RELEVANCE OF NICE GUIDANCE ONCE IT IS PUBLISHED

Why NICE's decisions are being challenged more frequently

5. Innovative medications often collect a broader set of information in the period after marketing authorisation has been received. This can mean that NICE guidance can be irrelevant or out of date once it is published. This is found mostly in the Multiple Technology Assessment (MTA), because of the length of such an appraisal and the short window of time in which new data is considered. When important information becomes available within the timeframe of a NICE MTA appraisal then it should be considered by NICE to reduce the number of decisions being made with the use of old, out of date information.

6. This whole issue falls within the inflexibility of the NICE process for assessment of data. NICE will only consider evidence for a technology appraisal within a given timeframe. However if the technology appraisal takes 18 months (typical for an MTA) from first manufacturer submission to guidance granted then there is a very strong likelihood that further key evidence may become available within this timeframe, but outside of the technical assessment group’s window of data assessment.

7. In the case of oncology this is especially a concern since new data is constantly being published, and in some cases the new evidence can significantly inform decision making, and health economic calculations. Within such health economic calculations there is often a high degree of uncertainty for the final result. This is caused by uncertain variables used due to the lack of information available to make more considered judgement. In such cases it is not uncommon for a manufacturer to have a different opinion to NICE with regards to a crucial element of the calculation which significantly impacts on decision making. In many cases NICE make uncertain areas certain and will only consider their opinion of the data. A major problem arises when new data does become available which proves that NICE were wrong in their assessment, but this data becomes available outside of the data assessment window. In this circumstance such data will not be considered by NICE which means that decision making is flawed and published guidance is incorrect.

8. It is clear that NICE cannot constantly reassess the public domain for new information, however failure to show flexibility in the procedure to take into account significant new evidence during the appraisal leads to guidance which is unreasonable in light of the total information available in the public domain. As standard, such information will not be heard at NICE appeal hearings even if it proves that one party was correct in making an assumption of data.

9. An example of such a decision can be found in technology appraisal 118 for bevacizumab and cetuximab in the treatment of metastatic colorectal cancer. NICE announced it would assess these drugs in April 2005 with a closing date for evidence submission by August 2005. A technical assessment group (ScHAAR) were commissioned to organise evidence and report to NICE by February 2006 and a closing date for all submissions was set for the end of April 2006. In August 2006 draft guidance (Appraisal Consultation Document (ACD)) was published giving a negative decision for both drugs, stating that

guidance would not be reviewed before May 2009. An appeal for cetuximab was heard in November 2006 but no new evidence was allowed to be presented at this meeting. The NICE appeal committee rejected this appeal at the end of January 2007 and guidance was published.

10. In September 2006 new evidence became available for cetuximab which validated the use of particular assumptions within its economic modelling. However this information could not be assessed by NICE. Therefore a total of 21 months elapsed with no possibility of any new evidence being considered for nearly 18 months. This new evidence could mean that drugs originally given negative guidance might be given a positive guidance.

11. With the creation of the new Single Technology Appraisal (STA) process this problem should be minimised, however such appraisals are not as rapid as those performed by the Scottish Medicines Consortium (SMC) in which an appraisal is complete in four months from submission of a manufacturer dossier. This greatly decreases the possibility that new vital information may become available during the appraisal and alter the context of guidance issued.

12. In addition, SMC allow resubmission based upon new data becoming available. Such a flexible system promotes the use of the best medicine recommended based on the best available information. How does this compare to the NICE STA process? An STA can be significantly longer than an SMC submission. In the experience of Merck Serono it has been greater than eight months. In addition, NICE only re-reviews its guidance every four years.

INDEPENDENCE OF NICE APPEALS

The appeal system

13. In appeals to NICE there are concerns over the independence of the constitution of the Appeal Panels. NICE's procedures envisage that two or three members of the five person Appeal Panel (including the Chairman of the Panel) will be members of NICE's own Board (one of those three persons may instead be an NHS representative). The constitution of such an appeal panel may consequently have an inherent interest in supporting the decision previously reached by NICE's Appraisal Committee. Hence, this may not make a NICE appeal an independent and neutral environment for re-assessment of the technology appraisal.

14. The constitution of the NICE appeal panel should be reassessed to increase impartiality and independence of such decisions. The Appeal panel itself should be more independent with a decreased role for members of NICE.

GROUNDS OF NICE APPEALS

The appeal system

15. The stated grounds for a NICE appeal are based on the procedure of the technology assessment rather than a difference of scientific opinion. The second ground for appeal is, "the decision is perverse in light of the evidence submitted". This criteria is very stringent and presents a very high bar to prove the, "perversity" of a decision made. NICE procedures explain that it is theoretically possible for two Appraisal Committees to be given the same facts, yet to reach different conclusions, without either being perverse. This greatly reduces the possibility for any successful challenge of an Appraisal Committee conclusion. While a finding may be termed as incorrect, this may still not be termed as perverse.

16. This particular issue is highlighted in the assessment of health economic information when, in the absence of compelling data, informed assumptions must be made to overcome uncertainty and complement harder scientific information. Hence, in many areas information utilised may not be perverse but termed as, "unreasonable". A test of "reasonability" is a much more appropriate assessment of such data. With the use of such wording this allows differences in opinion and interpretation of scientific evidence to be discussed.

17. The "perversity", ground of appeal also prevents the discussion of new data which may greatly inform and potentially change decisions made. As previously mentioned, in health economic modelling, uncertainty is handled by making assumptions. However if evidence becomes available which greatly invalidates an assumption, this should be considered. The present system of decision making and review is one in which there is no opportunity to have relevant material and up to date facts considered in any appeal. A more robust appeal process would allow consideration of the best available evidence.

18. There is a fear that such an appeal system could lead to a "never ending" process. NICE should consider appeals in other legal fields such as immigration or housing where these bodies continue to function and do not suffer from a "never ending" process by considering new data.

PUBLIC CONFIDENCE IN NICE

Whether public confidence in NICE is waning and if so why

19. Recently public confidence in NICE has been questioned due to decisions denying patients access to the only licensed treatment available for their condition for “cost effectiveness” reasons. This is the case with regards to bortezomib for multiple myeloma, pemetrexed disodium for malignant pleural mesothelioma, and cetuximab for the third line treatment of metastatic colorectal cancer.

20. The objectives of NICE to improve the quality of care are clearly defined in, “Social Value Judgements: Principles for the development of NICE guidance”.⁹⁴ This report clearly states; “*social value judgements relate to society rather than basic or clinical science; they take account the ethical principles, preferences, culture and aspirations that should underpin the nature and the extent of care provided by the NHS*”⁹⁴.

21. In a Health Technology Assessment, NICE assess the, “cost-effectiveness”, of a technology by means of quality adjusted life years (QALYs) and relationship to cost. The QALY is a simple concept which takes into account quantity and quality of life, however this method is limited and does not capture the broad objective of the aforementioned NICE report or the added value of new innovative treatments. In addition the Cost/QALY calculation does not take into account the actual treatment setting such as at the end of life in which quantity and quality of life is already limited, but nonetheless valuable.

22. In an area such as oncology, if an expensive new treatment allows a terminal cancer patient to live three months longer, then it seems intuitively unfair that this should be ascribed the same low value-for-money rating (ie cost per-QALY threshold) as a treatment that gives three additional months of life to those with a non-life threatening disease. For patients with a poor prognosis, the absolute level of life-saved will likely be relatively low. The concept of ascribing higher cost-effectiveness thresholds to patients with lower life-expectancy is consistent with the “rule of rescue”, which applies greater value to therapies for patients with poor prognosis and where there are few available alternatives which are life prolonging. Given that in the UK, cancer survival is an established national health priority (NHS Cancer Plan) it is reasonable to accept a higher threshold of cost effectiveness for this patient group.

23. When NICE is reviewing the only licensed treatment available for a disease state then cost effectiveness should not be the overruling driver of the decision making process. In these circumstances other factors such as whether the condition is life-threatening or whether there are any other direct treatment alternatives should be given equal consideration.

INCONSISTENT NHS IMPLEMENTATION OF GUIDANCE

The method in which NICE recommendations are implemented—both in technology appraisals and clinical guidance—and the reasons why guidance is acted upon or not

24. NHS implementation of NICE guidance is inconsistent across the UK. A number of factors contribute to this, the most important being poor NHS financial management, clinical resistance, and lack of sanctions against poor implementation. This is despite considerable efforts to improve this situation from the NICE Implementation team.

25. If such guidance from NICE is not followed, one could question the significant resources required to fulfil its function and meet its requirements. Implementation will be improved by stronger sanctions and in particular automatic inclusion of NICE approved medicines on local formularies.

Stephen J Ralston

Manager of Health Economics and Health Technology Assessment

Merck Serono

March 2007

Evidence submitted by the MS Society (NICE 65)

EXECUTIVE SUMMARY

The MS Society welcomes this inquiry. We are the largest charity dedicated to supporting people living with MS. Our most recent involvement with a NICE appraisal has been the Tysabri STA which is ongoing at the time of writing.

In our submission we draw attention to the tension between NICE’s economic and utilitarian principles and patient representative groups’ duty to support the individual in accessing the best treatments, regardless of how much these cost. We also raise concerns about the accountability of NICE and the lack of

⁹⁴ Social Value Judgements: Principles for the development of NICE guidance. Section 1.1 Page 7. Thursday 8 December 2005. <http://www.nice.org.uk/page.aspx?283494>

transparency in some of its processes. We urge NICE to enter into genuine engagement with patient groups and to take into greater consideration the wider cost impact treatments may have on NHS and social care demands.

We contributed to a previous Health Select Committee session on NICE in 2002. Many of the points we made at that time with regard to the transparency of the NICE process and a lack of clarity about its operations still apply.

At the end of our submission we make the following recommendations:

- There should be greater clarity and transparency in NICE’s decision making process. This would include revising the appeal system to ensure it is truly independent. This would go some way to restoring faith in NICE.
- Greater weight should be given to improvements in patients and carers’ quality of life arising from new treatments. Other costs associated with a disease should be included in the cost model used by NICE.
- NICE should either publicly inform patient groups it is not interested in their input, or should try to engage more constructively with them. The current mood of hostility does no-one any good. We would welcome a patient organisation seminar with NICE and with other charities so that they can clearly set out what they see as our role. We would then undertake to communicate this to our members so that their expectations of NICE were more clearly informed.
- Central government should take more responsibility for ensuring that the laudable MS guideline from NICE is not let down at local implementation level.

ABOUT MULTIPLE SCLEROSIS AND THE MS SOCIETY

1. Multiple sclerosis (MS) is an autoimmune disease in which the central nervous system comes under attack from the immune system. This causes damage to myelin (the coating on nerve fibres), leaving scars known as lesions or plaques. This myelin damage disrupts messages travelling along nerve fibres, slowing and distorting them if they get through at all.

2. The damage caused in MS leads to a range of symptoms, including loss of sight and mobility, pain, fatigue and depression. While life expectancy with MS is close to normal, the quality of life with the condition is often very poor. There is no cure for MS and few effective treatments, but living with MS can be made more bearable with proper information and support.

3. Our annual income is £27.8 million, with three-quarters of our income from voluntary donations. In 2005, we received £329k from the pharmaceutical industry (1.2% of our total income), principally to fund the MS nurse scheme which we manage at the request of the Association of British Neurologists. Our role is to act as an independent conduit for these funds to ensure they are put into MS nurse posts in the most appropriate locations. We declare all donations of more than £10,000 in our Annual Report and Accounts.

Why NICE’s Decisions are Increasingly Being Challenged

4. One of the key principles underlying NICE appraisals is that they should:

“Assess the clinical and **cost effectiveness** of treatments or management approaches” [our emphasis]. The Single Technology Appraisal, which is designed for the appraisal of a single product, device or other technology, “considers evidence on the health effects, costs and cost effectiveness of a health technology in comparison with current standard treatment in the NHS in England and Wales”. Health effects include both benefits and harms (side effects). This includes the impact on health-related quality of life (for example, relief of pain and disability), and the probable effects on mortality. It also considers estimates of any associated costs, concentrating particularly on costs to the NHS and Personal Social Services.⁹⁵

5. This basis for NICE’s decision-making process flies in the face of government rhetoric about patient choice in health care. For example:

“Giving people more choice and control over the treatment and services they receive will . . . remain a key priority as we continue to develop health and social care services that put the patient first” (Choice Matters, 2006).⁹⁶

6. The concept of patient choice puts the individual at the centre of their health care. It suggests an entitlement for an individual to be involved in their health care decisions and to have some control of the treatment and services they receive.

⁹⁵ NICE, *Guide to the single technology appraisal (STA) process* (2006). Available at <http://www.nice.org.uk/page.aspx?o=STAprcessguide>

⁹⁶ Department of Health, *Choice Matters: Increasing Choice Improves Patients’ Experiences* (2006).

7. But in reality, treatment choice is often limited by NICE guidance on drugs. This is a particular problem in complex conditions like MS where drug treatments are expensive, and where efficacy data is far from overwhelming or clear cut.

8. As a result, we have NICE using economic and utilitarian principles to assess the viability of drug treatments in direct tension with choice in health care reform. You can only choose what is available to you; if the only drug treatments that suit your condition are ruled out on cost, you have no choice at all.

9. Mixed signals are also sent out about NICE's independence. In theory, it can make its decisions outside of the current political agenda. But political interventions, such as the Secretary of State for Health's comments on Herceptin, suggest that NICE does respond to political pressure. This strengthens the perception that NICE's decisions are influenced by external factors and encourages organisations like ourselves to challenge NICE. The Herceptin case (and the beta interferon campaign in MS) suggests that if you shout loud enough, NICE will listen.

10. Several of the high profile challenges to NICE have been led by or included patient representative charities. We suggest that this is because organisations like us believe our individual members have an intrinsic value. We believe each of them, as a person living with MS, deserves the best possible treatment and that cost should not be an issue. We do not accept that a person with MS should be condemned to a lower quality of life because of the cost of a drug.

11. We understand that NICE helps the NHS take a rationing approach, and that this is necessary in an environment with limited funds. But while government policy encourages patient choice, and while we are mandated by our members to fight on behalf of individual people with MS who need expensive treatments, we cannot accept NICE's cost-based decisions without challenge if they result in MS treatments being limited.

12. Despite being able to sign up as stakeholders, patient representative groups are often marginalised during NICE's appraisals. The MS Society found its engagement in the recent Tysabri STA confusing and our attempt to have reasonable discussions with NICE was fruitless. The attitude we experienced was one of hostility and we are aware other charities have met with a similar response. There is also no clear process for patient representative groups to follow to express concerns about a NICE decision, other than through a public challenge.

13. The tight criteria used by NICE when reviewing evidence means that the collective qualitative experiences which patient groups can provide are often disregarded. Combined with the lack of a truly independent appeal process, this means that patient groups may feel excluded from the official process, encouraging public lobbying against NICE.

14. One key problem may be that NICE might not actually be interested in patient groups' opinions, but is not prepared to say this publicly. In the Tysabri STA, we felt as though our input was a token gesture by NICE rather than a two-way consultation. We were concerned that when we urged NICE to time its appeals process to ensure the consultation over Tysabri did not clash with Parliamentary recess. NICE was not prepared to take this into consideration.⁹⁷ It was our opinion that MPs should be able to contribute on behalf of their constituents living with MS. This experience of NICE does not suggest an institution with any commitment to stakeholder engagement.

15. We would urge NICE to either strive to enter into genuine engagement with patient groups—we have 44,000 members who mandate us to speak out on their behalf, and we can also be a channel for information about drugs to our audience—or to state openly they are only interested in peer reviewed research. This would save us the extensive effort and cost involved in taking part in an STA and would allow us to focus our research and policy priorities to contribute in a way that NICE could use.

16. The MS Society shares the concerns of the Alzheimer's Society over the lack of transparency in NICE's decision making process. The failure of NICE to provide full explanations for decisions and the difficulty in engaging in a dialogue with NICE can leave no option but to follow the appeal process. This is a costly process for charitable patient groups and one that any organisation would want to avoid if at all possible. However, when a NICE decision is believed to be counter to patient needs and the decision has not been justified, then it becomes the patient group's duty to challenge it.

17. We share the Alzheimer's Society's belief that more transparency in the decision making process could help to reduce the number of appeals and would recommend the following to enable this:

- Representatives of patient groups should be able to act as non-speaking observers at appraisal committee meetings at which a relevant technology is discussed.
- A full minute of the meeting should be available, with sufficient detail so that it is possible to understand how decisions were reached.
- Fuller explanations should be provided as to how a decision was reached in FADs and ACDs. "Considered not appropriate" is not good enough. The provision of a summary version and more detailed document would allow people to choose the level of detail they want.

⁹⁷ Email from Meindert Boysen, Associate Director STA at NICE, to MS Society 1 March 2007.

Whether Public Confidence in the Institute is Waning, and if so Why

18. The public's perception of NICE is influenced by the press and by communications from charities like ourselves. A series of decisions by NICE to reject treatments for vulnerable groups, such as those with dementia, and which are decisions perceived to be based on cost grounds, contribute to a negative perception of the Institute. High profile campaigns by established patient representative groups also contribute to a drop in confidence in NICE. There is also a risk that such justifiable campaigns will result in a damaging perception of charities competing with each other.

19. The lack of clarity as to the accountability of NICE also damages public confidence. As mentioned above, the Institute does appear to respond to pressure, whether from patient groups or high-profile politicians. This is despite NICE's own assertion that it is an independent organisation.⁹⁸ Charities have to take some of the responsibility for this, but as we have set out above we are acting in the interests of our members and we cannot ignore that duty.

Comments on NICE's evaluation process, and whether any particular groups are disadvantaged by the process; the speed of publishing guidance; the appeal system

20. We believe the NICE evaluation process fails to take due consideration of the views of patient representatives and carers. The economic model is too narrow in its scope, failing to consider sufficiently wider savings a new treatment might bring. Benefits from effective treatments to a person with MS, their family and carers, stretch extensively beyond the health service. For example, caring for someone with severe MS can effectively be a full time job. This means two people are out of work, claiming benefits, paying less tax and so on. Early, effective interventions can support people's independence and maintain their ability to contribute (financially and otherwise) to society.

21. While NICE does acknowledge that benefits to carers and so on should be considered, we believe this aspect of a treatment is undervalued in their assessments. It would surely be possible for the evaluation to look at, as a minimum, other governmental costs incurred by a condition like MS, particularly as paid out through the benefits system. NICE bases all of its argument on an economic footing, but the model ignores massive and obvious costs associated with conditions like MS.

22. It should also be noticed that there is a risk that NICE's evaluation process, with a perceived rise in negative decisions, may discourage research investment in the UK and in conditions like MS in general. If a pharmaceutical company invests tens of millions in an MS treatment, only to see it rejected on cost grounds in England and Wales, the disease area becomes less attractive (for example, spending on HIV and cancer treatments massively outweighs spending on neurology; why, then, should a company invest in MS when there are better returns elsewhere?) This could have a knock on effect on UK clinical trials, and this will in turn have a detrimental impact on early patient access to new therapies.

23. There is the wider issue of UK drugs pricing, which falls outside the scope of this investigation. But we would draw the Committee's attention to the Office of Fair Trading's recommendation that the Pharmaceutical Price Regulation Scheme (PPRS) should be reformed to deliver better value for money.

The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this).

24. We would refer the Committee to the MS Trust/Royal College of Physicians audit of the NICE guideline for MS.⁹⁹ The guideline is an excellent toolkit and we warmly welcome it; along with the NSF for long term conditions, government policy on the care of MS is praiseworthy. We are, however, concerned about implementation. Central policies need to be enacted locally, but local management of NHS trusts and strains on budgets mean expensive long term conditions often struggle to get adequate support.

25. The Department of Health has said that implementation of NICE guidance "does not fall to any single body; rather, what is needed is a broad partnership to ensure that patients get ready access to the quality of care recommended by NICE."¹⁰⁰ The MS Society agrees that partnership working is integral to the implementation of NICE. However, the lack of a single body to oversee implementation results in more examples of postcode lottery care. There are insufficient timeframes to ensure that primary care trusts do fulfil NICE guidance as quickly as possible. When challenged on implementation difficulties, the government is able to refer the matter to local commissioners who are in turn able to point to NHS deficits. We would urge the government to take more responsibility for ensuring that laudable national policies are not let down at local implementation level.

⁹⁸ NICE, *A Guide to NICE* (2005). Available at <http://www.nice.org.uk/page.aspx?o=guidetonic>.

⁹⁹ Royal College of Physicians, MS Trust. *NHS services for people with multiple sclerosis: a national survey*. London: RCP; 2006.

¹⁰⁰ Lord Warner, Department of Health. *Implementation of NICE guidance* Available at http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Dearcolleagueletters/DH_4083904 Accessed 20 March 2007.

 RECOMMENDATIONS FOR FUTURE ACTION BY THE GOVERNMENT

We recommend that:

- There should be greater clarity and transparency in NICE's decision making process. This would include revising the appeal system to ensure it is truly independent. This would go some way to restoring faith in NICE.
- Greater weight should be given to improvements in patients and carers' quality of life arising from new treatments. Other costs associated with a disease should be included in the cost model used by NICE.
- NICE should either publicly inform patient groups it is not interested in their input, or should try to engage more constructively with them. The current mood of hostility does no-one any good. We would welcome a patient organisation seminar with NICE and with other charities so that they can clearly set out what they see as our role. We would then undertake to communicate this to our members so that their expectations of NICE were more clearly informed.
- Central government should take more responsibility for ensuring that the laudable MS guideline from NICE is not let down at local implementation level.

Matthew Trainer
MS Society

March 2007

Evidence submitted by the Motor Neurone Disease Association (NICE 25)
BACKGROUND

- MND is the name given to a group of related diseases affecting the motor neurones (nerve cells) in the brain and spinal cord. As the motor neurones die, the muscles stop working.
- MND is a rapidly progressive and fatal disease that can affect any adult at any time. The cause of MND is unknown and there is no known cure.
- Every year 1,600 people die from MND in the UK. It affects over 5,000 people in this country at any one time, with a prevalence of around seven per 100,000.
- On average it takes 17 months from first symptoms to diagnose MND. Half of those with the disease die within 14 months of diagnosis.
- MND leaves people unable to walk, talk or feed themselves, but the intellect and the senses usually remain unaffected.

EXECUTIVE SUMMARY

1. The MND Association welcomes the Health Committee's inquiry into the National Institute for Health and Clinical Excellence (NICE). We have a particular concern about the length of time it takes for topics to be selected for appraisal by NICE.

2. The MND Association suggested non-invasive ventilation (NIV) for MND to NICE as a topic in January 2006. However, we are concerned at the length of time it is taking for NIV to be selected for appraisal. The Association has estimated that if NIV is selected as a topic, guidance on its use would not be issued until 2009 at the earliest—three years after we suggested it. Nearly 5,000 people with MND will have died in this time, many without access to this beneficial treatment.

NON-INVASIVE VENTILATION FOR MND

3. During the course of the disease, most people with MND develop respiratory muscle weakness and respiratory failure is frequently the cause of death.

4. Research published in 2006 showed that NIV can significantly improve quality of life and extend survival for people with MND.(1) For people without severe bulbar dysfunction, NIV extended life by a median of 205 days (around six months). This is significant on a median survival of 14 months.

5. A survey of consultant neurologists carried out in 2002 showed that only 5.5% of people with MND under review were using NIV (an estimated 2.6–3.5% of all people with MND).(2) The survey showed that most neurologists (172 out of 265) had referred no patients for NIV in the preceding year, while three neurologists made 30% of all referrals nationally. This variation in clinical practice is clearly unacceptable.

6. The only drug treatment licensed to treat MND—riluzole—was recommended by NICE in January 2001. It has shown to extend life by an estimated three to six months, so NIV compares favourably to it.

NICE SELECTION PROCESS

7. We formally suggested NIV to NICE in January 2006. This was about the same time that the topic selection procedure was being reviewed, ironically to make it faster.

8. Fourteen months later, we understand that NIV may be considered at the Consideration Panels in July. If it is successful at this stage and later stages of the process, it will be at least another nine months before any appraisal would start (spring 2008). This would mean that guidance would be issued sometime in 2009—three years after the Association suggested it as a topic. Sixteen hundred people die from MND every year, so over this period of time nearly 5,000 people with MND will have died, many without access to NIV.

REFERENCES

(1) Bourke SC, Tomlinson M, Williams TL, Bullock RE, Shaw PJ, Gibson GJ Effects of non-invasive ventilation on survival and quality of life in patients with ALS: a randomised controlled trial. *Lancet Neurol* 2006; 5:140–47.

(2) Bourke SC, Williams TL, Bullock RE, Gibson GJ, Shaw PJ. Non-invasive ventilation in motor neuron disease: current UK practice. *ALS and other motor neuron disorders: official publication of the World Federation of Neurology, Research Group on Motor Neuron Diseases* 2002 Sep; 3 (3): 145–9.

Alison Railton
MND Association

21 March 2007

Evidence submitted by Myeloma UK (NICE 30)

1. EXECUTIVE SUMMARY

- NICE are increasingly giving negative decisions to new treatments. There is also growing recognition of the fact that their recommendations are not lining up with current clinical practice or translating into fair and sensible treatment availability for patients.
- Public confidence in NICE is waning after several high-profile negative decisions. Only 11% of 131 people surveyed by Myeloma UK were confident that NICE generally makes the right decisions when assessing treatments for use on the NHS, compared with 70% who disagreed or strongly disagreed with this statement. There is a strong perception of government interference in NICE decisions that are deemed more ‘worthy’ than others.
- It is the opinion of Myeloma UK that patients with rare cancers, who could be treated with highly effective orphan medicines, are disadvantaged by the NICE process. We supply evidence to this effect.
- There must be faster and timely decisions made on new and novel treatments because for patients, time is of the essence. It is nonsensical that different bodies exist across the UK duplicating efforts in appraising drugs.
- There is no independent appeal process to NICE’s appraisal system, the appeals process is lengthy and the timelines for appellants are unrealistic.
- There continues to be both widespread inequity in access to cancer treatments and confusion out in the Service as to the protocol when awaiting final NICE guidance.

RECOMMENDATIONS FOR ACTION

- NICE should place greater emphasis on: transparency and willingness to share methods of working, greater public and patient involvement, improving public perception of political and financial motives behind their decisions.
- A complete review of the NICE appraisal methodology and in particular the arbitrary cost per QALY is required so that NICE can assess orphan, higher-cost treatments within relevant and appropriate parameters that can then translate into fair and sensible treatment availability on the NHS.
- One body should be created that produces the guidance for the whole of the UK. In lieu of having a truly national body, where the SMC or the AWMSG have already assessed a drug, let their recommendations be applied in the interim in England.

- Establish an independent Appeals Panel, put measures in place to speed up both the publishing of guidance and the appeals process, and a more realistic turnaround should be granted to appellants to submit their appeal evidence.
- PCTs should be directed with clearer guidance, both as to their obligations during an ongoing NICE appraisal process, but also as to what the guidance does and does not mean.

MYELOMA UK

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma and its related disorders. We have been involved with two NICE technology appraisals—erythropoietin for cancer treatment-induced anaemia and bortezomib (Velcade) for treatment of relapsed/refractory myeloma. Evidence presented in this submission derives from our extensive knowledge of patient issues; submitting evidence to NICE appraisals and appeals; and ongoing organisational research into the role and workings of NICE and how new drugs are accessed in the UK.

Why NICE's Decisions are Increasingly being Challenged

1. Primarily, NICE's decisions are increasingly being challenged because there is growing recognition of the fact that NICE's recommendations frequently do not translate into the clinical excellence they are striving for, or even reflect current clinical practice. The limitations of NICE's appraisal methods when interpreting evidence (for example using data in their analyses that was never intended to provide answers of clinical and cost effectiveness that can be extrapolated to the wider NHS, and only reviewing drugs within the limits of their licensed indication) means that their recommendations are out of kilter with current UK practice and can perversely subject patients to treatments that lack the gold standard evidence base which they insist scrutinised drugs possess. Consequently there is a real possibility that the NHS is wasting money on less effective treatments rather than investing in treatments backed by sound clinical evidence.

2. The recent brunt of negative decisions cannot be ignored: NICE are increasingly giving negative recommendations to new treatments. Examination of the eleven published NICE recommendations for cancer medications since January 2006 and the further eleven technology appraisals currently in development with a published ACD or FAD indicates that more than half (13 out of 22) have received a negative decision. Ten of the eleven preliminary decisions are negative at time of writing¹ (Appendix 1). The majority of these are for less common cancers and conditions: head and neck cancer, glioma, myeloma, lymphocytic leukaemia, mesothelioma and cancer-treatment induced anaemia. Whilst these recommendations are still in draft format, it does not seem unreasonable to construe that the future looks uncertain for patients with less common cancers awaiting guidance on new treatments. This is neither right nor sustainable, thus NICE decisions are being publicly challenged.

3. Each negative decision inevitably breeds anger in the affected patient sectors which catalyses further dispute with the Institute's decisions, and it is evident that unless reform is initiated particular groups of patients will continue to be disadvantaged with regard to access to novel treatments.

Whether Public Confidence in the Institute is Waning, and if so Why

4. Public confidence is waning after several high-profile negative NICE decisions. As part of our ongoing work and to help substantiate our views, we surveyed the opinions of those who visit Myeloma UK's website (including patients, families, healthcare professionals and the general public) on the role and workings of NICE. 131 people completed the survey (a full transcript of the responses can be made available if the Committee wish to see it). The following views were collected:

- Only 11% of the 131 respondents were confident that NICE generally makes the right decisions when assessing treatments for use on the NHS, compared with 70% who disagreed or strongly disagreed with this statement.
- 70% of respondents disagreed or strongly disagreed that NICE operates as an independent organisation free from political intervention. Our experience from talking with patients is that there is a strong perception of government interference in NICE decisions that are deemed more 'worthy' than others; the Herceptin example and Patricia Hewitt's intervention is frequently cited by patients.
- 63% believed cost considerations to be the most important consideration in NICE analysis, compared to 19% believing that equal consideration is given to both cost and clinical effectiveness evidence. Patients consider that the principles underlying NICE decisions, namely the role that cost and government funding of the NHS play in the evaluations, should be made explicit and communicated honestly to patients and the wider society. There is a lack of transparency within the appraisal process which generates suspicion of the motives behind the process.
- 64% disagreed or strongly disagreed that NICE should decide which treatments are made available on the NHS. 46% believed that it should be doctors responsible for patient care that should be making the decisions. If a drug is not approved by NICE, then it is down to the tenacity of the

patient to either get themselves on a trial, persuade their PCT to pay for the drug or finance their own care privately. This causes immeasurable stress, worry and frustration. Having similar bodies in Scotland and Wales reaching different conclusions about the same drugs further diminishes public confidence in the decisions of NICE.

NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process

5. As outlined in section 2 above, there has been a recent wave of negative decisions assigned to treatments for less common cancers (Appendix 1). It is the opinion of Myeloma UK that patients with rare diseases, and in particular rare cancers, who could be treated with highly effective orphan medicines, are disadvantaged by the NICE process.

6. NICE, in a formal response to the Department of Health in March 2006ⁱⁱ, wrote that they did not consider that any changes are required to its methods for the appraisal of orphan drugs (those for treatment of an orphan disease with a prevalence of < 5 per 10,000). NICE state that orphan drugs referred to the Institute have been appraised successfully "suggesting that for these drugs it was possible to apply NICE methodology". The Institute does, however, advise adoption of different methods for appraising their self-appointed "ultra-orphan" drugs as they "encompass all products that appear, both now and in the foreseeable future, to be particularly problematic".

7. There are important issues to raise in response to this assertion:

- Analysis of Appendix 1 of the NICE responseⁱⁱ reveals a considerable number of errors and omissions (including erroneous inclusion of products which are not for rare diseases, erroneous classification of EMEA and FDA orphan designation, and omitted orphan medicines) (see Appendix 2). These are misleading to their overall recommendation to the Department of Health. Furthermore, the incremental cost effectiveness ratio (ICERs) for each drug was provided and those that were considered to be cost ineffective (and thus not recommended) are highlighted in bold text. The inference is that the remainder of the products were considered cost effective and were recommended for usage. However, 6 (46%) of the 13 medicines inferred as cost-effective and recommended were in fact recommended for use by a restricted subgroup only (see Appendix 2 of this submission).
- Independent research undertaken by the Office of Health Economics (OHE) reveals that as of January 2007, NICE had appraised 16 EMEA/FDA designated orphan medicines, of which it has rejected 4 (25%), recommended 9 (56%) for restricted use and only recommended 3 (19%) for general use. By way of comparison, of the 116 non-orphan drugs appraised by NICE only 7 (6%) were rejected, 56 (48%) were recommended for restricted use, and 53 (46%) were recommended for general use. There is statistically significant difference between the outcomes of NICE appraisals for orphan and non-orphan medicines (p value 0.013)ⁱⁱⁱ.
- Further 6 of the 8 orphan medicines currently under NICE appraisal have reached a preliminary decision (as of January 2007). All 6 are orphan medicines for the treatment of rare cancers; myeloma (bortezomib), mesothelioma (pemetrexed disodium), head and neck cancer (cetuximab), malignant glioma (temozolomide and carmustine implant). Of these appraisals 5 (83%) were rejected, 1 (17%) was recommended for use in a restricted subgroup only, none were recommended for general use (Appendix 3). For bortezomib and pemetrexed disodium, the negative recommendations were based primarily on cost-effectivenessⁱ. It should also be pointed out that 4 of the 5 that have reached the FAD stage have been subject to lengthy appeals, which further delays access to effective treatment for patients with high unmet need.
- Thus, NICE have no basis on which to make their claim that orphan drugs have been appraised successfully. Indeed, compelling evidence exists to support our position that patients with rare diseases who could be treated with highly effective orphan medicines are disadvantaged by the NICE process.

8. It is illogical that after measures are put in place by EU licensing legislation (which safeguards research and development of orphan drugs) patient access is stymied by NICE assessing their cost effectiveness in the same manner as "conventional" therapies. Indeed the slow uptake of orphan medicines in the UK is of concern to the EMEA (Appendix 4). Many EU countries have special arrangements to facilitate fast patient access to orphan medicines. For example, in the Netherlands orphan medicines can be exempt from economic evaluation.

9. It is artificial to apply the same quality-adjusted life years (QALY) parameters to treatments for rarer and more common diseases. Indeed, this approach is at odds with the fundamental NHS principle of equity of access to treatments for all patients based on clinical need:

- The existing parameters of cost effectiveness do not make allowance for the smaller financial burden on the NHS from fewer patients accessing the treatment, or indeed the higher per-patient costs in developing novel drugs for rarer illnesses and the frequency with which these development opportunities arise.

- The cost per QALY threshold has been untouched by inflationary uplifts let alone the much higher NHS inflationary uplifts: extra investment in the NHS is growing by an average of 7.4% a year; drugs costs are rising even faster yet the QALY threshold has stayed unaffected.
- The QALY does not capture all that is valued in a health outcome eg it cannot adequately and sensitively capture improvements in quality of life, much to the disadvantage of those with debilitating and incurable diseases to whom this is a precious outcome.
- By the Institute's own admission, many orphan drugs have ICERs at the "high" end of what the appraisal committee consider to be cost effectiveⁱⁱ. Patients with rarer diseases are being disadvantaged as a result of an inappropriate costing exercise.

The Speed of Publishing Guidance

10. The introduction of the rapid Single Technology Appraisal process in November 2005 set out to improve the NICE approval system. Bortezomib (Velcade), a myeloma treatment, was one of the first drugs to be appraised by this rapid assessment process. At the time of writing, 16 months on, the outcome is still subject to an appeal decision and patients remain exposed to discretionary access to an effective drug. There must be faster and timely decisions made on new and novel treatments because for patients, time is of the essence.

11. It is nonsensical that different bodies exist across the UK applying the same efforts and resource to interpreting the same evidence for the effectiveness of a treatment. This represents a massive duplication of effort. It is also disheartening for patients to feel like a second-rate citizen to their neighbour across a UK border.

The Appeal System

12. There is no independent appeal process to NICE's appraisal system. Engaging with a process where the deciding body is both judge and jury limits confidence in the end result.

13. Whilst stakeholders have 14 days to submit their appeal evidence after the release of a Final Appraisal Determination (substantially encroaching on staff time and resource for smaller organisations) the ensuing appeals process can take months. A lengthy appeal process exacerbates the delay in access to effective medicines for patients that may have already high unmet need.

Comparison with the Work of the Scottish Intercollegiate Guidelines Network (SIGN)

14. Myeloma UK has no comment to make on this sub-section.

The Implementation of NICE Guidance, both Technology Appraisals and Clinical Guidelines (Which Guidance is Acted On, Which Is Not and the Reasons For This)

15. It is difficult for us to comment fully on this section as with regards to specific myeloma guidance, the Velcade appraisal has not yet reached completion so has not been distributed out to the Service for implementation. However, we have started a scoping exercise to obtain ongoing snapshots of how the provision for patients is being affected by draft guidance:

- In an ongoing survey^v of 39 haematology doctors working in the field of myeloma in England, 56% have experienced a lack of consistency among Primary Care Trusts when seeking funding for the myeloma treatment Velcade. 46% have found it more difficult to obtain Velcade for NHS patients since its negative FAD was made public on the Institute's website in October 2006. This indicates that there is both widespread inequity in access to this treatment and confusion out in the Service as to the protocol when awaiting final NICE guidance, both of which disadvantage patients.
- We know from other published reviews that there is still considerable variation of spending on cancer drugs by PCTs^{vi} and in the implementation of NICE guidance^{vii}. This knowledge, coupled with the existing variation in access to drugs in use pre-1999 and the establishment of NICE, stresses the urgent need for reform.

16. The December 2006 *Good Practice Guidance on Managing the Introduction of New Healthcare Interventions* makes strides to consolidate the advice in HSC 1999/176 which seeks to explain the responsibilities of PCTs throughout the NICE appraisal process. More could be done, however, to clarify that when guidance is draft or subject to appeal it should not be used to inform local decision making.

Eric Low

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- ii <http://www.nice.org.uk/page.aspx?o=286850>.
- iii OHE Working paper by the OHE : “HTA for orphan drugs: A review of the Issues and of NICE and SMC Decisions.
- iv http://ec.europa.eu/health/ph_threats/non_com/docs/EMEA_chart_en.pdf accessed March 2007.
- v Independent study carried out on behalf of the myeloma community by Dr Mehta, Royal Free Hospital, London.
- vi Local variations in NHS spending priorities, King’s Fund Briefing, August 2006.
- vii Usage of Cancer Drugs approved by NICE, Report of Review by the National Cancer Director, September 2006.

Evidence submitted by UK Myeloma Forum (NICE 96)

EXECUTIVE SUMMARY

1. Delays by NICE in identifying and assessing novel treatments is adding further to preventing UK patients from access to effective treatment.
2. Orphan drugs are being disadvantaged by the NICE process because the remit of NICE is structured in such a way that conventional cost effective thresholds act as a barrier due to higher per patient and incremental costs of orphan medicine. The quality thresholds should be re-evaluated for these rare disease.
3. A clinical specialist in the field under assessment should be involved at the initiation of the process and throughout the evaluation of the drug to ensure that the public and the profession retains confidence in the Institute.
4. Clinical trial design should be re-evaluated to ensure that appropriate evidence is presented to NICE by facilitating closer interaction between the Institute and clinicians before drugs come to market.

Multiple myeloma has an incidence of four to five per 100,000 of the population and is defined internationally as an orphan drug. In the course of the last 50 years, the treatment of myeloma has been advanced, initially by the discovery of Melphalan as a chemotherapy agent in the early 1960s and then in the 1980s and 1990s by the identification of high dose combination chemotherapy with the addition of an autologous stem cell transplant for haemopoetic support. A third advance has been discovery of novel agents that has evolved from our greater understanding of the biology of the disease. Currently, there is one drug with a licence namely Velcade and a second drug that is looking for an EMEA licence in the second or third quarter of this year, namely Revlimid. In addition there are some 30+ novel agents that are in early stages of clinical and pre-clinical development. These agents are working through an entirely different mechanism of action to conventional chemotherapy and represents a major advance in the management of myeloma and indeed other malignancies. At the present time, patients in the UK are being denied access to these agents due to the NICE evaluation process, disadvantaging rarer cancers and the speed with which the process is undertaken.

NICE PROCESS

1. Because of the rarity of orphan diseases, large randomised phase III trials are not able to be conducted in timely manner and NICE will only accept evidence from phase III trials. This policy needs to be revisited for orphan disease.
2. Property confidence in the institute is waning because “expert” clinical advice to the committee is only sought at a late stage in the process and there is a feeling that the committee decision making occurs ahead of any input from specialists in the particular area under consideration.
3. NICE’s decision process lags behind clinical progress and the scope of application needs to reflect current and possibly future use of the drug. This was highlighted in the evaluation of Velcade where its use as a single agent was brought into question at a time when clinicians are using the drug in combination with steroid plus or minus other chemotherapy agents which has had a dramatic effect on responses and time to progression and survival. Because this was outside the scope of the NICE review, evidence for its use in this setting was not considered and was major reason for the NICE provisional findings being challenged and confidence in the system being undermined.
4. It is clear that patients with rare diseases have poor outcomes following NICE reviews than in any non-orphan conditions. Review of the NICE process has shown a biased outcome against orphan drugs as has evidenced by the working paper of the OHE and a review of the NICE website. The latter has shown that six drugs, where there was a preliminary decision available in January 2007 for orphan drugs in development, none of the six agents was recommended for use as per licensed indication. This suggests either a failure on the part of the clinicians to conduct appropriate clinical trials, which identical to those conducted for non-orphan drugs or alternatively, to look at the process by which NICE conducts its approval process

for orphan drugs. A major issue for the latter is the evaluation of the cost effectiveness (QALY) thresholds. Consideration should be given to changing the threshold for orphan drugs in line for what is currently identified as “super orphan” drugs. This latter appeared to be arbitrarily defined without regard to conventionally epidemiological criteria or referenced to international agreed standards. Implementation of NICE guidance is very often delayed and patchy throughout the country. This is due to the fact that Trusts, in particular Foundation Trusts, feel they are under no obligation to use these agents and a further process needs to be undertaken locally through PCTs, cancer networks and Trust’s formulary and/or clinical directorate budgetary committees. All of these further delay the prescribing of drugs to patients.

Dr Stephen Schey
Chairman, UK Myeloma Forum

March 2007

Evidence submitted by the National Childbirth Trust (NICE 27)

EXECUTIVE SUMMARY

The National Childbirth Trust welcomes this inquiry into the work of NICE and is very pleased to be able to contribute towards it. We support the work of NICE and believe that it carries out vital functions, however we also recognise its shortcomings and appreciate this opportunity to improve its effectiveness.

In summary the principle recommendations made by the NCT regarding the operation of the National Institute for Health and Clinical Excellence are as follows:

1. Job descriptions and personal specifications should be drafted for each member of guideline development groups (GDG) to ensure that recruitment establishes a team with the necessary skills to carry out the functions required.
2. Stakeholders participating in guideline development should be free to discuss elements of the consultation with their constituent groups and participate with any registered stakeholder in consultations.
3. Formal working relationships between NICE and the UK Cochrane Collaboration should be established.
4. NICE should provide further formal training for all members of GDG.
5. Each GDG should contain at least one epidemiologist or appropriate research methodologist.
6. The Chair of the GDG should therefore be selected for their leadership and negotiation skills, as well as their knowledge of the subject. They should be able to approach questions from an informed service-user perspective.
7. We favour the reintroduction of the two stage consultation process for guideline development.
8. The strength of evidence presented should be assessed by several experienced peer reviewers in addition to general stakeholders in respect of its strength and limitations.
9. Guideline scope should be limited to ensure that its assessment is manageable in the allotted time.
10. An iterative process during the development phase would ensure that the questions are clinically as relevant as possible and address service users’ concerns.
11. Establish a more rigorous policy on good practice points and a more robust process for developing them.
12. Service users views and preferences should be explored and acknowledged as important in guidelines. They should influence the recommendations made, alongside clear assessment of clinical outcomes.
13. An independent appeals panel should be establish with a much greater degree of autonomy from the Institute.
14. We would welcome a more robust system of audit to establish the extent to which recommendations on “demedicalising” care, as well as those for new clinical interventions, have been implemented.

INTRODUCTION

1. The National Childbirth Trust (NCT) welcomes the Health Select Committee’s inquiry into the work of NICE. As an organisation we support the principle of a national organisation tasked with evaluating medical technologies, procedures and activities and producing evidence based guidance.

2. However, we also recognise the need for continued vigilance and accountability to ensure that any evaluation undertaken is of the highest possible standard. In the NCT’s experience there are a number of ways in which the processes could be improved. We shall limit our response to those aspects of NICE’s operations that directly impact upon the NCT’s experience and sphere of activity.

Why NICE's Decisions are Increasingly Being Challenged

3. NICE publishes clinical appraisals of whether particular treatments should be adopted by the NHS, based primarily on criteria of cost-effectiveness. As medical treatment is an extremely emotive subject for those personally involved it is to be expected that decisions will be questioned from time to time. The NCT has had no direct involvement in any recent challenges to NICE decisions; however we are aware of decreased levels of satisfaction with the outcome of appraisals. It is possible to surmise a number of reasons for this:

- (i) Appraisals can be seen as taking too long to publish findings.
- (ii) The public perception of NICE appraisals is that they are often based primarily on criteria of cost-effectiveness rather than medical efficacy.
- (iii) Scope of some recent guidelines has been very wide leading to the conclusion that some issues are not receiving the specialised attention that they require. For example the forthcoming Intrapartum Care Guideline, when published in draft, was an extremely long document covering a great number of issues that could, perhaps, have been better analysed if approached individually.
- (iv) Guideline Development Groups (GDG) have arguably not been entirely representative of the professions involved in the provision of care. It is important to have clinicians with relevant experience and knowledge. In addition, since the main task of the GDG is to interpret research evidence, some of which is very complex, then the expertise of research methodologists are also needed on the GDG.
- (v) In the last few years members of GDGs have been instructed not to discuss details of the guidelines that they are developing with their respective organisations and not to be involved in the stakeholder consultations. Unfortunately this presents the possibility that members may feel isolated, unable to confirm or refute their understanding of certain issues with people they know to have the necessary expertise, and they may lack the support needed to appropriately review many of the extremely complex matters that they are tasked with.

Whether Public Confidence in the Institute Is Waning, and if so Why

4. As a body initially created to combat the perceived postcode lottery within the NHS, it is no surprise that NICE has always generated a certain degree of controversy. Similarly the areas within which NICE must operate are particularly emotive and do not easily lend to objective reasoning on the part of the public or media. Recent media coverage pertaining to decisions involving medical technology such as beta-interferon for multiple sclerosis, imatinib for leukaemia, trastuzumab for breast cancer and various pharmacological treatments for Alzheimer's disease have negatively affected the public perception of the agency. It has been alleged by the media that NICE are overly concerned with the cost-effectiveness of new technologies rather than their ability to treat patients. From an individual's perspective it can sometimes seem that NICE is denying access to a potentially life-saving treatments based primarily on economic concerns which can conflict with the best interests of patients' health.

5. The media has also highlighted concerns that powerful pharmaceutical companies possess too much influence over the NICE decision making process. It is alleged that said companies are able to exert excessive pressure on the media to precipitate a ground swell in public opinion against negatively judged appraisals by the agency, for example in the case of the use of Herceptin[™] for the treatment of breast cancer. Additional ways of involving patients and the public, giving them more influence and of using qualitative research evidence on patients' views might be helpful.

NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process

6. The system that NICE has developed for the production of guidelines demonstrates a number of valuable strengths:

- (i) The scope is published and subject to consultation before the process of production begins.
- (ii) There is a face-to-face meeting to discuss the scope between the stakeholders and NICE.
- (iii) There is a multi-disciplinary guideline development group.
- (iv) NICE provides guidance on how the evidence should be evaluated and whether it is of high enough quality to form the basis of a recommendation.
- (v) The draft guideline is distributed for stakeholders' consultation in good time for consideration.

7. However, whilst NICE has many favourable attributes there are numerous weaknesses with their process, some of which have serious consequences. We have attempted to order these putting the most important points first:

- (i) NICE guidelines are so important that the knowledge, research evaluation skills, commitment and team working abilities of the Guideline Development Group (GDG) members are crucial to quality of the GDG. It is important to have clinicians with relevant experience and knowledge. When a guideline covers a broad series of related questions, as is the case currently with the

Intrapartum Care Guideline, it is important, for example, to have on the group midwives who have experience of birth in community settings (home birth, birth centre birth) as well as in hospital settings. They need to be confident in using and appraising research, and able to express their views in a multi-disciplinary group. NCT recommendation: draft a job description and person specification for the various GDG members, advertise in relevant journals and interview to establish a team with the necessary skills and attributes.

- (ii) In recent years, members of GDGs are all told that they must not discuss the draft guideline or the draft recommendations with anyone outside of the GDG and that they cannot be involved with their organisation in the stakeholder consultation. This is problematic, as the questions to be answered are often complex and interpretation of the evidence is challenging. Members can feel isolated and be in need of further support from their stakeholder group. **NCT recommendation: We believe that the various stakeholders should be able to discuss the deliberations with their constituent groups and participate with any registered stakeholder in consultations.**
- (iii) At present there is no system for formal liaison with the UK Cochrane Collaboration, which was established at the end of 1992, by the National Health Service Research and Development Programme, “to facilitate and co-ordinate the preparation and maintenance of systematic reviews of randomised controlled trials of health care”. Closer liaison would potentially cut down on duplication of effort and improve the quality of reviews carried out by the NICE national collaborating centres and GDGs. It is clear that the thoroughness with which the Cochrane Collaboration undertakes its systematic reviews cannot be replicated by the NICE research fellows because of time constraints (though duplicate assessment at each stage of the process could be implemented). It would seem extremely beneficial if the NICE Collaborating Centre contacted the relevant Cochrane groups a year before the guideline commences, to get new reviews underway that may be needed in the guideline, and to get current reviews updated. NCT recommendation: Establish formal working relationships between NICE and the UK Cochrane Collaboration.
- (iv) At present there is an induction process but little on reviewing evidence for GDG members. More input at the beginning of the process would provide agreed processes to follow to help answer difficult methodological questions and resolve disputes within the GDG. A short “Listening skills” session would also be valuable. NCT recommendation: NICE to provide further compulsory training for all members of the GDGs, and any new national collaborating centre staff, on the NICE appraisal of evidence process. In addition, voluntary mentoring should be available to assist and develop members, supporting them if differences of interpretation or opinion become difficult to resolve on the GDG.
- (v) The GDGs do not necessarily include people with appropriate research knowledge and skills to interpret the evidence accurately. The members of the GDG need to judge whether the staff from the collaborating centre have followed the searching processes, abstracting policy and summarising of findings to an acceptable standard, and have drawn appropriate conclusions, as the recommendations are based on this synthesis. NCT recommendation: In our view it is also vital to have at least one epidemiologist or appropriate research methodologist on each GDG, as few clinicians or user representatives have the detailed methodological knowledge to assess the appropriate balance of evidence from the pooling of results from studies of widely differing design and quality.
- (vi) The important role played by the chair of each GDG is currently underestimated. If the chair is not seen to be impartial and is not able to arbitrate between different strongly held view points, the business of developing the guideline may be hampered. Some training in group skills and consensus building might be helpful. NCT recommendation: The Chair of the GDG plays a vital role in steering the deliberations of the GDG and should therefore be selected for their leadership and negotiation skills, as well as their knowledge of the subject. They should be independent minded and be able to approach questions from an informed service-user perspective. Some further training may be beneficial.
- (vii) There are too few checks and balances in a system that will determine clinical guidance for the whole health service for the foreseeable future. In 2006, NICE changed from a two stage consultation process to a one stage process. This has been particularly problematic during development of the Intrapartum Care Guideline. In our experience of maternity-related guidelines, the drafts circulated for first consultation guidelines are sometimes either “rough and ready” or seriously flawed in their approach. By second consultation stage they have necessarily changed very considerably. NCT recommendation: If a single consultation is to remain in future, it is vital that the guideline is well crafted when it is disseminated, having been through several drafts with the GDG to bring it up to an acceptable standard. A two stage consultation remains the ideal from the perspective of the quality of the guideline.
- (viii) There is often a fine line between “evidence of no improved (or less good) outcomes with X” and “no evidence of different outcome”. In the latter case there is insufficient research evidence to make a sound judgement, but sometimes a small study with insufficient power to find a difference may be mistakenly interpreted as showing that a particular promising treatment or model of care is no

better than a previous approach or even more harmful in some way. NCT recommendation: Advice is needed from several experienced professional peer reviewers as well as general stakeholders on the strength of the evidence and its limitations.

- (ix) The Intrapartum Care Guideline has been too broad in scope to be manageable as one guideline, particularly in the time available. If the GDG and the national collaborating centre staff have a too heavy workload in the time available the quality of the guideline suffers. As the impact of a NICE guideline is very considerable, affecting commissioning, delivery of care and users/patients choices and quality of life, there is a clear responsibility not to rush to judgement. If mistakes are made, the wrong messages will be disseminated very rapidly and affect thousands, if not millions, of individual care pathways and potentially health and well-being outcomes. NCT recommendation: The scope of any one guideline should be limited so that the work is manageable within the allocated time. The time period for guideline development should not be unduly restricted; quality is more important than quantity of throughput.
- (x) There is no opportunity to add to or revise the scope of the guideline if new questions or issues emerge as part of an iterative process of discussing the guideline and emerging evidence. In addition the members of the GDG are not involved with the development of the scope and are required to work with the scope given to them and this is not always satisfactory. Sometimes the key questions become clearer once the development group have begun their work. For example, one of the “inherited guidelines”, on “electronic foetal monitoring” was too narrow in focus. To make sense from a woman’s point of view, it needed to be a guideline on all methods of foetal monitoring or there seemed to be an assumption that electronic monitoring was the norm and intermittent auscultation might be overlooked entirely. At the time (in 2002) we persuaded the GDG to expand the scope but the rules seem to be more rigid now. NCT recommendation: allow for a more iterative process during the development phase to be sure that the questions are clinically as relevant as possible and address service users’ concerns.
- (xi) There are many “Good practice points” in some guidelines, such as the Intrapartum care draft guideline. This can lead to a guideline that is highly opinion-based, than an evidence-based, undermining the purpose of NICE. Currently, “Good practice points” are based on the opinion of members of the GDG only, maybe a dozen people. Using a Delphi process would be one way to involve more people with relevant experience and expertise. NCT recommendation: establish a more rigorous policy on good practice points and a more robust process for developing them. Also only to have “Good practice points” where they seem really necessary.
- (xii) In the maternity related guidelines, there is insufficient attention paid to women’s views because qualitative evidence is considered lower level evidence than quantitative evidence. Women’s views reported within an RCT are usually included in guidelines, but this is not as rich and meaningful data as that comes from good quality qualitative research studies. NCT recommendation: There need to be questions asked on women’s views alongside the clinical questions set at the beginning, and these need to be addressed using good qualitative research as an integral part of the process.

8. On the whole, we would suggest that user groups tend to be disadvantaged by the process of guideline development as they are in a minority on the GDG, outnumbered by health professionals and officials of various kinds who have a vested interest, in getting through the guideline development process quickly. For service users/patients who will be on the receiving end of the final recommendations, a more carefully considered review of the evidence and recommendations is usually preferable.

The Speed of Publishing Advice

9. Whilst we recognise the benefits of up-to-date guidance published in a timely manner, it is our view that it is preferable to wait for carefully considered guidance than rush the outcome of judgements.

The Appeal System

10. Although there is a relatively clear process of appeals for technical appraisals we feel that clarity regarding appeals procedures could be improved, particularly in the case of guideline development. There is, to our knowledge, no fully independent appeals process available to stakeholders with concerns over the validity of NICE decisions as currently “independent appeals panels” are constituted by three non-executive directors of the Institute and only two third party representatives. Should stakeholders therefore disagree with the findings of NICE appraisal their only method of recourse is a process dominated by the Institute itself. NCT recommendation: We would welcome the introduction of a truly independent appeals panel who could operate outside of the NICE process entirely with this ability to critique findings and require further reconsideration.

Comparison With the Work of the Scottish Intercollegiate Guidelines Network (SIGN)

11. SIGN and NICE operate from different methodologies with regards to guideline development however certain comparisons are possible. In the experience of the NCT SIGN does not tend to embark on producing such complex or extensive guidelines as NICE has recently, for example the NICE Intrapartum Care guideline. As such our members with experience of both procedures have reported that contributing to SIGN consultations is a more manageable task than the English equivalent.

The Implementation of NICE Guidelines, Both Technology Appraisals and Clinical Guidelines (Which Guidance is Acted on, Which is not and the Reasons for This)

12. In our experience, implementation of the NICE guidelines can be slow, particularly if there are financial implications or the recommendations conflict with current practice and belief. Anecdotally, it seems that adoption of some acute maternity services recommendations may be happening more quickly in recent years and this seems to be linked to the requirement of Clinical Negligence Scheme for Trusts (CNST) that delivery suite protocols are in place and reviewed regularly. We welcome the maternity services audit being conducted by the Healthcare Commission this year and commend their commitment to involving a service user perspective. NCT recommendation: We would welcome a more robust system of audit to establish the extent to which recommendations on “demedicalising” care, as well as those for new clinical interventions, have been acted upon.

Chris Norris
National Childbirth Trust

March 2007

Evidence submitted by the National Infertility Awareness Campaign (NICE 44)

EXECUTIVE SUMMARY

NICE fertility guideline

1. NIAC welcomed the publication in February 2004 of a clinical guideline by NICE which aimed to address the inequalities in access to NHS funded treatment for infertility by setting a national standard of service that all patients should expect to receive across England and Wales.¹⁰¹ Amongst other recommendations, the guideline stated that three full cycles of *in vitro* fertilisation (IVF) should be made available on the NHS to all those meeting agreed clinical criteria. On its publication, the then Secretary of State for Health, Rt Hon Dr John Reid MP, asked Primary Care Trusts (PCTs) to make at least one full cycle of IVF available to all those eligible by April 2005, with the expectation of progress being made towards full implementation of the guidance in the longer term.¹⁰² It was the first time that Government had issued such an announcement on the implementation of a NICE guideline.

Implementation of NICE fertility guideline

2. In March 2005, NIAC conducted a survey of PCTs in partnership with the All Party Parliamentary Group on Infertility to assess progress being made across England towards implementing the NICE guideline and meeting the April 2005 deadline.¹⁰³ The results showed that significant inequalities in access to NHS funding continued to exist, including wide variations in the eligibility criteria set by individual PCTs. Since then, NIAC has also been made aware of a number of PCTs that have decided to reduce or suspend funding for infertility treatment altogether.

Central guidance to PCTs

3. In Scotland, Wales and Northern Ireland, guidance on the provision of NHS funded infertility treatment was accompanied by centrally set eligibility criteria. NIAC welcomed these efforts to ensure that patients received equal access to treatment, regardless of where they lived. However, in England, PCTs are able to set their own eligibility criteria for access to NHS funding, over and above the clinical criteria recommended in the NICE guideline. This has perpetuated the inequality of access and NIAC would call on the Government to set the criteria centrally in order to remove this unfairness.

¹⁰¹ Department of Health press release, *Working Towards Ending The Postcode Lottery Of Infertility Treatment*, 30 November 2000.

¹⁰² Department of Health press release, *Health Secretary welcomes new fertility guidance*, 25 February 2004.

¹⁰³ NIAC/All Party Parliamentary Group on Infertility PCT Survey, March 2005.

Single Embryo Transfer

4. A potential move towards single embryo transfer (SET) has now made full implementation of the NICE guideline of paramount importance, both in terms of funding the three full cycles of IVF that NICE recommended, and in ensuring they are funded as quickly as possible. In October 2006, an independent expert group set up by the Human Fertilisation and Embryology Authority (HFEA) to look at reducing the number of multiple births from IVF, recommended the introduction of SET.¹⁰⁴ However, they also concluded that failure to implement the NICE guideline was the single greatest obstacle to its introduction in the UK. NIAC would welcome a move towards SET for appropriate patients, but would call on the Government to issue a clear direction to PCTs to implement the NICE guideline in full as quickly as possible and ensure that three full cycles of IVF include both fresh and frozen embryo transfers.

KEY POINTS

Why NICE's decisions are increasingly being challenged

5. The publication in February 2004 of a clinical guideline by NICE on assessment and treatment for people with fertility problems aimed to address the inequalities in access to NHS funded infertility treatment that existed across England and Wales.¹⁰⁵ Amongst other recommendations covering a full range of infertility treatments, the guideline stated that three full cycles should be made available on the NHS to all those meeting agreed clinical criteria.

6. On its publication, the then Secretary of State for Health, Rt. Hon Dr John Reid MP, asked PCTs to make at least one full cycle of IVF available to all those eligible by April 2005 with the expectation of progress being made towards full implementation of the guidance in the longer term.¹⁰⁶ It was the first time that Government had issued such an announcement on the implementation of a NICE guideline. At the same time, the Welsh Assembly Government also announced that one cycle of IVF would be made available to eligible patients in Wales by April 2005.¹⁰⁷

7. However, unlike technology appraisals, it is not mandatory for NICE clinical guidelines to be implemented by PCTs. In the case of the fertility guideline, this means that it is up to individual PCTs to prioritise the commissioning of infertility services for their population, alongside a range of competing health needs.

8. NIAC is concerned that in some cases, the low prioritisation of infertility, coupled with PCT deficits, have led to a lack of progress in implementing the guideline. Yet it is important to note that the NICE guideline defines infertility as a disease process worthy of investigation and treatment.¹⁰⁸ It is crucial that PCTs recognise the status of infertility as a disease and prioritise the implementation of the NICE guideline accordingly, in order to ensure patients have access to the treatment they were promised.

9. Furthermore, the publication of the NICE guideline was met with some concern in the media that it would be very costly for PCTs to implement and possibly divert resources away from other health needs.

10. To coincide with the publication of the guideline, the All Party Parliamentary Group on Infertility (APPGI) published a report looking at the structures needed to implement the guideline on the NHS in the most cost-effective way. The report recommended that considerable cost savings could be made in implementing the guideline if services were commissioned effectively and unnecessary or inappropriate investigations and treatment were avoided.¹⁰⁹

Whether public confidence in the Institute is waning

11. When the Government first referred infertility treatment to NICE, it was with the aim of helping to "ensure that in future, infertile couples get fairer, faster access to clinically, cost effective and appropriate treatments".¹¹⁰ It is fair to say therefore, that patients' expectations around the publication of the guideline were high, and that these expectations were raised further upon publication of the guideline when the former Secretary of State called for at least one full cycle to be funded by April 2005. The Prime Minister too announced that he hoped to see over the next couple of years "at least very substantial progress towards implementation of the full NICE guidelines".¹¹¹

¹⁰⁴ Expert Group on Multiple Births after IVF, *One child at a time*, October 2006.

¹⁰⁵ Department of Health press release, *Working Towards Ending The Postcode Lottery Of Infertility Treatment*, 30 November 2000.

¹⁰⁶ Department of Health press release, *Health Secretary welcomes new fertility guidance*, 25 February 2004.

¹⁰⁷ Welsh Assembly Government press release 2004.

¹⁰⁸ NICE Fertility Guideline, February 2004.

¹⁰⁹ All Party Parliamentary Group on Infertility, February 2004.

¹¹⁰ Department of Health press release, *Working Towards Ending The Postcode Lottery Of Infertility Treatment*, 30 November 2000.

¹¹¹ Prime Minister's Questions, 25 February 2004.

12. However, three years' on from its publication, and PCTs are still far from implementing the guideline in full and, in some cases, are even failing to meet the one cycle called for by the Government. It is therefore understandable that patients and health professionals might start to lose confidence in the NICE guideline's ability to overcome the inequalities in access to NHS funded infertility treatment that it was intended to achieve.

13. Moreover, the 2005 PCT survey showed that the PCTs that were funding infertility treatment were interpreting NICE's own recommendations in different ways.¹¹² For example, a number were setting their own female age ranges outside the 23–39 range recommended by NICE. NIAC is also concerned that some PCTs may not be clear as to the definition of a full cycle of IVF, which should include both fresh and frozen embryo cycles.¹¹³

14. In Scotland, Wales and Northern Ireland, guidance on the provision of NHS funded infertility treatment was accompanied by centrally set eligibility criteria. NIAC welcomed these efforts to ensure that patients received equal access to treatment, regardless of where they lived.

15. However, in England, PCTs are able to set their own eligibility criteria for access to NHS funding, as well as prioritise whether to fund at all. This has perpetuated the inequality of access and NIAC would call on the Government to issue central guidance to PCTs on the number of cycles that should be provided and the eligibility criteria to access those cycles. In fact, NICE itself commented in a press release issued at the time of the guideline's publication, that:

“A consistent approach by the NHS to the treatment of fertility problems is long overdue . . . We have therefore suggested to the Department of Health that they consider giving advice to NHS organisations on how they should approach putting our recommendations into practise.”¹¹⁴

16. Last year, the British Fertility Society issued a number of recommendations on national eligibility criteria for NHS funding and implementation of the NICE Guideline. They were supported by NIAC as a means of providing a framework for centrally set criteria that could be applied to patients across England, regardless of where they lived.¹¹⁵

The implementation of NICE guidance

17. In March 2005, NIAC conducted a survey of PCTs in partnership with the All Party Parliamentary Group on Infertility to assess progress being made across England towards implementing the NICE guideline and meeting the April 2005 deadline.¹¹⁶ The results showed that significant inequalities in access to NHS funding continued to exist, including wide variations in the eligibility criteria set by individual PCTs and the fact that some PCTs were funding nothing.

18. They also highlighted unacceptably long waiting lists in some parts of the country and evidence that some PCTs were intending to reduce the current number of cycles they funded down to one, where they were previously funding more than one. Since then, NIAC has also been made aware of a number of PCTs that were funding treatment, but have subsequently decided to reduce or suspend it altogether.

19. Unfortunately, patients have little recourse available to them if their PCT decides not to implement the NICE guideline, as it is not mandatory. However, the Government has made a clear statement of its expectations with regard to meeting NICE's recommendations and PCTs should be showing progress towards achieving them. It is therefore important not only for the Government to take action to ensure that progress is made, but also for PCTs to be involving both patients and clinicians in the decision-making process when allocating resources for local services.

20. A potential move towards single embryo transfer (SET) has now made full implementation of the NICE guideline of paramount importance, both in terms of funding the three full cycles of IVF that NICE recommended, and in ensuring they are funded as quickly as possible. In October 2006, an independent expert group set up by the Human Fertilisation and Embryology Authority (HFEA) to look at reducing the number of multiple births from IVF, recommended the introduction of SET.¹¹⁷ However, they also concluded that failure to implement the NICE guideline was the single greatest obstacle to its introduction in the UK.

¹¹² NIAC/All Party Parliamentary Group on Infertility PCT Survey, March 2005.

¹¹³ NICE Fertility Guideline, February 2004.

¹¹⁴ NICE press release, *New NHS guidelines on fertility treatment*, 25 February 2004.

¹¹⁵ *Implementation of the NICE Guideline—Recommendations from the British Fertility Society for National Criteria for NHS funding of assisted conception*; R Kennedy, C Kingsland, A Rutherford, M Hamilton, W Ledger, August 2006.

¹¹⁶ NIAC/All Party Parliamentary Group on Infertility PCT Survey, March 2005.

¹¹⁷ Expert Group on Multiple Births after IVF, *One child at a time*, October 2006.

RECOMMENDATIONS

21. It is incredibly frustrating for the one in seven couples affected by difficulties in conceiving that more than three years after the publication of the NICE fertility guideline, huge inequalities in access to NHS funded treatment continue to exist. This is not what patients were promised and many feel let down. They want to see the NICE guideline fully, not geographically, implemented.

22. NIAC remains committed to raising awareness of the need for the Government to take action to address these areas of concern. It therefore calls for a clear direction to be issued to PCTs to implement the NICE guideline in full, ensuring that a full cycle of IVF includes the transfer of both fresh and frozen embryos.

Clare Brown

Chair, National Infertility Awareness Campaign

March 2007

Evidence submitted by the National Osteoporosis Society (NICE 69)

1. Executive Summary

1.1 The National Osteoporosis Society (NOS) is closely involved, as an active stakeholder, in the development process of the clinical guideline on osteoporosis and the technology appraisals on the primary and secondary prevention of osteoporotic fragility fractures in postmenopausal women since their inception. This written evidence is therefore limited to the NOS' experiences of NICE, drawing on the development of NICE guidance for osteoporosis to illustrate our points where possible.

1.2 The development of the technology appraisals for osteoporosis has been a lengthy process and is now entering its sixth year. The NOS has some concerns about the transparency of the methodology that NICE has used in its economic modelling to reach its conclusions in this particular case. We are also concerned that since being actively involved in the development of the scope for the technology appraisals, it has changed significantly during the long development process. At the present time, much of the remit of the appraisals has been transferred to that of the clinical guideline on osteoporosis, which does not have mandatory status.

2. Introduction

2.1 The NOS is the only national charity dedicated to improving the prevention, diagnosis and treatment of osteoporosis. The charity provides a range of services in support of people with, and at risk of, osteoporosis. Drawing on the unrivalled expertise of the numerous health and social care disciplines involved in this disease area, together with our members, volunteers and staff, the NOS works for the improvement of treatment options and care for patients throughout the country.

2.2 Osteoporosis is a chronic disease which can result in painful and debilitating fractures, particularly in the hip and spine (in a similar way to high blood pressure which is a chronic condition that can lead to a stroke). Almost half of all women and 1 in 5 men over the age of 50 will break a bone due to osteoporosis. A range of drug treatments exist to both prevent and treat osteoporosis, some of which can reduce the risk of breaking a bone by almost a half. The provision of these drugs on the NHS is currently being reviewed by NICE, for which the NOS is an active stakeholder organisation. However, the NOS is concerned that the final guidance will fall short of the standards required to make a difference to people with, and at risk of, osteoporosis.

2.3 The NOS has been closely involved, as a stakeholder, with the development of NICE guidance relating to the care and treatment of people with osteoporosis. We have also inputted into the development of the clinical guideline on falls and we are an active stakeholder in a number of other clinical guideline and public health guidance programs.

2.4 It was therefore with great interest that we read the terms of reference for the Committee's inquiry, particularly given the NOS's concerns about the ongoing development of NICE guidance for this disease area, and in light of recent developments, which we allude to in our submission. We have taken the opportunity of submitting this brief response setting out our comments on this inquiry. The comments are in order of the inquiry's terms of reference.

3. *Why NICE's Decisions are Increasingly Being Challenged*

3.1 The NOS was actively involved in developing the scope for the technology appraisals on the prevention and treatment of osteoporosis in 2002, but since that time it has changed significantly. NICE have published a series of consultation documents, which have differed greatly despite little change in the evidence. The length and complexity of this process has led to our members becoming disillusioned and frustrated at the lack of progress.

3.2 The NOS has some concerns about the methodology used by NICE to reach its latest draft recommendations on the use of drugs for osteoporosis. In particular we are concerned about the transparency of the economic modelling. On the basis of these concerns, the NOS is inclined to challenge the Institute's findings on behalf of our members, in order to seek justification for the conclusions they have reached in the case of guidance for osteoporosis treatments and services.

3.3 In its draft guidance NICE has made decisions about the age of women who will be eligible to receive treatment that appear to be perverse in light of the evidence. We are therefore seeking clarification from NICE to understand fully the reasoning behind its recommendations in this particular case.

3.4 The processes used by NICE are extremely complicated. Further to this, we are being asked more and more strongly by our members to challenge NICE's decisions on osteoporosis.

4. Whether Public Confidence in the Institute is Waning, and If So Why?

4.1 As a national charity with over 24,000 members, the NOS represents patients with, and at risk of, osteoporosis around the country who are affected by the decisions made by NICE. Throughout the technology appraisal and guideline development process, the NOS has kept its members fully updated with the situation, and has received overwhelming support from both members of the charity and members of the public for the points it has taken up with NICE. During individual consultations we have received thousands of letters of concern from our members which would suggest that public confidence, in this inquiry at least, is waning.

4.2 The NOS believes that NICE have become increasingly more conservative in their consideration of osteoporosis and that this has been perceived by our members as a questioning of the importance of osteoporosis as a disease.

4.3 Recent examples of challenges against NICE appear to have captured the imagination of the public, encouraging some people to be more active in voicing their objections. Media exposure of challenges to NICE's decisions has opened and exposed arguments around cost effectiveness of treatments to the general public. Many of our members do not understand why an osteoporosis treatment which costs just 27 pence per day is not being made available more widely, when herceptin has been made widely available for the treatment of breast cancer.

5. NICE's Evaluation Process, and Whether Any Particular Groups are Disadvantaged by the Process

5.1 In section 3.1 we have referred to the significant change to the published evaluation process over the course of five years. Three separate sets of guidance on osteoporosis appear to have been allowed to be developed without NICE monitoring that they were working in parallel with each other, this being the original intention.

5.2 The NOS is concerned that older people may be disadvantaged by the NICE process. In terms of simply accessing information, many of the NOS' members have commented that they had difficulties using the NICE website, which is the primary public access point for information on the Institute's work. We are concerned that this facility is not as "user friendly" for the older population, who, broadly speaking, do not have the same access to, or ability to use, the Internet. As a result, when the NOS encourages its members to register their views on NICE's recommendations via the website, many older people are less able to input into this process.

6. The Speed of Publishing Guidance

6.1 Development of osteoporosis guidance has been ongoing for over 5 years, which is significantly longer than most other technology appraisals.

6.2 We are concerned that the delay in publishing osteoporosis guidance may have impacted upon the levels of implementation for existing mandatory guidance. The original technology appraisal for the assessment of drugs in the secondary prevention of osteoporotic fractures (TA87) was published in January 2005. This appraisal is now under review to include a new drug, strontium ranelate, and to incorporate emerging research from the World Health Organisation with regard to risk assessment. However, our evidence suggests that the existing TA87 is not being implemented as it should be, as doctors await the outcome of the NICE review process. To this end, we believe that the length of time it has taken NICE to develop this particular guidance may have contributed to the general lack of progress in improving services for patients at risk of osteoporosis.

7. The Appeal System

7.1 As a stakeholder, the NOS welcomes the opportunity to challenge the proposed recommendations put forward by NICE through the consultation process, and has exercised this right in relation to the development of guidance on the use of drugs for osteoporosis. We further recognise that the appeals facility is an important facet of the guidance development process.

7.2 The NOS is currently awaiting the outcome of the consultation on the draft recommendations for the use of drugs in primary and secondary prevention of osteoporotic fractures. If there is insufficient movement on the issues of particular concern to the charity in the final recommendations we will consider mounting an appeal against them. However, we do have some reservations about the composition and independence of the Appeals Panel that will give consideration to our objections.

7.3 More recently, over the last 12 months, it has been necessary for many of the most senior officials of NICE to become closely involved with the development of the different guidance on osteoporosis to ensure that they become realigned and work in parallel. It is our understanding that these very same officials will appoint an appeal panel and for this reason, we are concerned that the panel may lack impartiality. We would therefore question whether or not such a system could accommodate a truly independent consideration of an appellant's objections.

7.4 The NOS would welcome the introduction of an independent, impartial panel to consider appeals.

8. *Comparison with the Work of the Scottish Intercollegiate Guidelines Network (SIGN)*

8.1 The NOS works closely with NHS Quality Improvement Scotland as the umbrella organisation under which the Scottish Intercollegiate Guidelines Network (SIGN) and the Scottish Medicines Consortium (SMC) work as independent bodies. The NOS was represented on the guideline development group for the SIGN guidance on the Management of Osteoporosis and the Management of Hip Fracture in Older People. We have also responded to consultations on the use of osteoporosis drugs by the Scottish Medicines Consortium.

8.2 As a nationwide organisation, the NOS campaigns to ensure that patients throughout the UK have access to the same standards of care and treatment for osteoporosis. However, it is difficult to draw direct comparisons between NICE and SIGN given that they have different roles within their respective health services.

8.3 It is however notable that the outcome of SIGN guidance appears to gain a higher degree of buy-in from its stakeholder organisations than has been the experience of NICE.

9. THE IMPLEMENTATION OF NICE GUIDANCE, BOTH TECHNOLOGY APPRAISALS AND CLINICAL GUIDELINES (WHICH GUIDANCE IS ACTED ON, WHICH IS NOT AND THE REASONS FOR THIS)

9.1 We alluded to the difficulties we have observed in the implementation of TA87 in point 6.2 above. We are now extremely concerned that if TA87 has not been implemented in full it stands to reason that the recommendations made by the non-mandatory clinical guideline will also not be implemented. This is of particular concern in the field of osteoporosis, as much of the original scope of the technology appraisals has been transferred to the clinical guideline during the development process.

9.2 We also believe that it is important that the clinical guideline and technology appraisals are fully complementary. To this end, we would argue that all guidance, both the technology appraisals and clinical guidelines, must be implemented in order for it to be fully effective. In addition, given the longevity of the development process for the osteoporosis guidelines, it would be an entirely inefficient use of NICE's time and resources for health bodies not to act on the final guidance and to ensure it is adhered to.

9.3 We are also concerned that the implementation of NICE guidance also has consequences for the implementation of other national guidance. Once finalised, the NICE guidance will form an important part in a set of national standards for osteoporosis services, including the National Service Framework for Older People. It is necessary for all of these services to be in place in order to provide the optimal benefits for patients.

Heidi-Mai Warren
National Osteoporosis Society

March 2007

Evidence submitted by the National Rheumatoid Arthritis Society (NICE 82)

EXECUTIVE SUMMARY

We are all healthcare professionals, patient officers of the National Rheumatoid Arthritis Society (NRAS) and volunteer patient members of NRAS, working in the field of rheumatology. We all have personal and direct experience of the National Institute for Health and Clinical Excellence (NICE); as participants in the NICE Health Technology Appraisal (HTA) and Clinical Guidelines programmes.

NICE has an important role to play in ensuring that patients gain access to the medicines they need to treat or manage their condition, as well as developing and supporting best clinical practice. Our experience suggests that this role is increasingly being dominated by economics arguments rather than an evaluation

of the therapeutic benefits (short and long-term), with innovative and effective licensed medicines not being recommended by NICE on predominantly cost-effectiveness grounds. The input and needs of patients (and, to a lesser extent, clinicians) has been marginalised. This is a particular cause for concern for us.

For inflammatory arthritis, there is a rapidly developing armamentarium of novel and highly effective treatments. There is a lag however, between studies demonstrating safety and efficacy and the more complex studies required to provide evidence of real world clinical- and cost-effectiveness. We are concerned that the existing evaluation process does not take this into account adequately.

We are concerned about the inequities that persist between England and Scotland, both in terms of the absolute decisions being made and in terms of delay in reaching decisions. It is well documented that the NICE Multiple Technology Appraisal (MTA) process takes a minimum of 54 weeks in theory, and often much longer in practice. By contrast, the Scottish Medicines Consortium's review process takes only 4-6 months. We are hopeful that the NICE Single Technology Appraisal (STA) process will reduce delays and that decisions about new, potentially beneficial, treatments can be made much more quickly.

Whilst a NICE decision is pending, patients are further disadvantaged as a consequence of the phenomenon known as "NICE blight". We are seeing many examples where, in spite of reminders from the Department of Health that Health Service Circular 1999/176 remains in force, Primary Care Trusts are refusing to fund a particular drug on the grounds that it has not yet been endorsed by NICE.

We are particularly concerned by the undue weight being given to the health economic aspects of NICE HTAs, at the expense of clinical, therapeutic and quality of life issues, which are arguably of more importance to patients. The incremental cost per QALY is increasingly becoming the sole determinant of NICE recommendations; rather, the cost per QALY should be just one of the many factors that the Appraisal Committee takes into account in reaching its conclusions about the use of a particular technology.

Health economic models should not be construed by the NICE Appraisal Committee as definitive "evidence" in the same way that data from a well-designed, randomised clinical trial is evidence. Relying upon the cost per QALY as the preferred measure of health outcome disadvantages those people needing treatment for chronic, long-term conditions—such as inflammatory arthritis. The paradox arises because measures used to derive QALYs tend to be weighted towards conditions resulting in death or a reduced life expectancy. In conditions like inflammatory arthritis, there may be short term gains that have long standing accrual over the lifetime of the person that are not captured using existing measures of utility.

So far as the actual Appraisal Committee meetings are concerned, the Committee rarely includes anyone with specialist clinical knowledge of the therapy area or condition under consideration. Appraisal Committee meetings can be intimidating and confusing for nominated patient experts. Meetings can be dominated by technical discussion on the health economic aspects. The anecdotal experience of the patients who are actually using these medicines is rarely listened to or, if the decisions are indicative, taken into account. Patient and clinical experts are required to leave the meeting before the Appraisal Committee starts to discuss its recommendations.

Overall, we feel that an overly "tokenist" approach is being taken to patient evidence, in particular, and the quality of life issues that are key to us.

Finally, we suggest that the process for bringing a successful appeal is neither fair, independent nor transparent and needs to be reviewed.

INTRODUCTION

1. The undersigned are all members of a standing advisory board to the National Rheumatoid Arthritis Society (NRAS). NRAS provides the secretariat support to the All Party Parliamentary Group on Inflammatory Arthritis and we act as advisers to NRAS in respect of its parliamentary work.

2. We welcome the opportunity to make this short submission to the Health Committee, based upon our collective personal experience and observations of NICE processes and procedures.

3. We are all healthcare professionals or patients (patient officers of the charity and volunteer patient members of NRAS) working in the field of rheumatology and we all have personal and direct experience of the National Institute for Health and Clinical Excellence (NICE); as participants in the NICE Health Technology Appraisal (HTA) and Clinical Guidelines programmes, as clinicians trying to secure funding to implement NICE guidance; or as patients. Five members of our advisory board have contributed to NICE decision-making, either as nominated clinical or patient experts attending NICE Appraisal Committee meetings, or as members of Guideline Development Groups.

4. We have experience of participating in the following NICE technology appraisals and Clinical Guidelines:

- Cox II inhibitors—Osteoarthritis and rheumatoid arthritis TA027
- Anakinra—Rheumatoid arthritis TA072
- Etanercept and infliximab—Rheumatoid arthritis TA036
- Etanercept—Juvenile Idiopathic Arthritis TA035

- Etanercept and Infliximab—Psoriatic Arthritis TA104
- Adalimumab, etanercept and infliximab—Ankylosing spondilitis (appraisal in development)
- Adalimumab, etanercept and infliximab—Rheumatoid arthritis (appraisal in development)
- Abatacept—Refractory rheumatoid arthritis (Single Technology Appraisal in development)
- Rituximab—Refractory rheumatoid arthritis (Single Technology Appraisal in development)
- Osteoarthritis (guideline in development)
- Rheumatoid Arthritis in Adults (guideline in development)—Ailsa Bosworth has applied to join the Guideline Development Group

5. In our opinion, NICE has an important role to play in ensuring that patients gain access to the medicines they need to treat or manage their condition. Sadly, our experience suggests that this role is increasingly being sacrificed in favour of pure economics, with innovative and effective licensed medicines not being recommended by NICE on predominantly cost-effectiveness grounds. As a result, the input and needs of patients (and, to a lesser extent, clinicians) has been marginalised. This is a particular cause for concern for us.

INEQUITIES ACROSS COUNTRIES

6. We are concerned about the inequities that persist between England and Scotland, both in terms of the absolute decision being made and in terms of the delay in reaching decisions. For example, in December 2003 the Scottish Medicines Consortium accepted adalimumab for use in the NHS in Scotland, soon after it had received a marketing authorisation for the UK. Over three years later, NICE has not yet issued final guidance on the use of adalimumab, or completed its review of the other anti-TNF inhibitor treatments etanercept and infliximab. NICE's final recommendations are currently the subject of an appeal from 6 different appellants. This is despite evidence for the excellent clinical efficacy of these therapies in rheumatoid arthritis.

7. Similarly, adalimumab was accepted for use in NHS Scotland for people with ankylosing spondilitis in 2006. Despite having first added this appraisal to its work programme three years ago, the NICE Appraisal Committee has not yet been able to reach a conclusion on whether adalimumab should be recommended for use in England and Wales for this indication.

8. It is well established and well documented that the NICE Multiple Technology Appraisal (MTA) process takes a minimum of 54 weeks in theory, and often much longer in practice. By contrast, the Scottish Medicines Consortium's review process takes only 4–6 months. We are hopeful that the NICE Single Technology Appraisal (STA) process will reduce delay and would urge that a strictly enforced timetable is attached to this process.

9. Whilst a NICE decision is pending, patients are disadvantaged as a consequence of the phenomenon known as "NICE blight". Blight occurs when Primary Care Trusts decline or refuse funding for a particular drug, on the grounds that it has not yet been endorsed by NICE. Although Health Service Circular 1999/176 prohibits Primary Care Trusts from refusing make a treatment purely on this basis, we are aware of many practical examples where this is taking place.

10. For example, Addenbrookes Hospital in Cambridge has refused to fund rituximab therapy, yet this drug is being made available to patients in Leeds and Plymouth, for example. Camden Primary Care Trust in London has also refused to fund rituximab at present, and this is particularly problematic because Camden is the lead PCT for University College Hospital (UCLH). This means that any patient referred to UCLH from anywhere in the country will be bound by Camden's policy. People with rheumatoid arthritis, who have been successfully treated with rituximab as part of a long-term clinical trial and are responding well, are now being taken off treatment pending NICE's decision. In our view that is unethical.

INCREASING RELIANCE ON HEALTH ECONOMIC ASPECTS

11. We are particularly concerned by the undue weight being given to the health economic aspects of NICE HTAs, at the expense of clinical, therapeutic and quality of life issues. Not only are these issues arguably of more importance to patients, but they also have the potential to impact on the wider societal costs and benefits of a long-term condition, such as affecting a person's ability to return to work or their reliance on the welfare system.

12. It seems to us that the incremental cost per QALY is starting to become the sole determinant of NICE recommendations; rather, the cost per QALY should be just one of the many factors that the Appraisal Committee takes into account in reaching its conclusions about the use of a particular technology.

13. Health economics is an art, not a science. It is very easy to manipulate the incremental cost-effective ratios (ICERs) for a particular technology, simply by changing the inputs or the assumptions in the model. In that sense, the health economic analyses undertaken by the academic centres are nothing more than a series of simulations; they should not be construed by the Appraisal Committee as definitive "evidence" in

the same way that data from a well-designed, randomised clinical trial is evidence, unless the model has been validated by an independent third party to identify the strengths and weaknesses of the assumptions used, inputs and robustness of model design.

14. As noted previously, cost effectiveness studies lag behind emerging evidence including some of the industry-funded safety and efficacy studies and require specific utility measures. The existing utility measures intended for capturing quality of life for cost effectiveness in conditions like inflammatory arthritis are lacking maturity and sophistication rendering QALY measures flawed. “Disutility” factors which are particularly pertinent to long-term conditions—such as disability, pain and morbidity—are not captured, disadvantaging patients affected by decisions based on these data.

15. As a representative patient organisation, it is very difficult for us to generate or collate the sort of evidence which NICE is looking for, particularly for new technologies where the evidence of clinical and cost effectiveness is limited, despite evidence of excellent efficacy, and where patient experience is small.

COMPOSITION OF THE NICE APPRAISAL COMMITTEE

16. Again, in our collective experience of several HTAs, the composition of the Appraisal Committee is problematic. Firstly, the Committee membership—and the meetings themselves—can be dominated by the health economists. Secondly, there is rarely a clinician on the Appraisal Committee with a specialist’s understanding of the therapeutic area under consideration. When NICE was reviewing the use of etanercept for use in Juvenile Idiopathic Arthritis, there was no paediatrician sitting on the Appraisal Committee. This contrasts with the Guideline Development Groups, which are charged with developing best practice guidance for the management of a particular condition, and which do include appropriate clinical expertise.

APPRAISAL COMMITTEE MEETINGS

17. The Appraisal Committee relies on two patient and two clinical experts to attend the meetings and give oral evidence of a particular condition, how the drug performs in clinical practice and what it is like to live with a particular condition. Whilst we are very grateful to have the opportunity to present our case to the Appraisal Committee in person, we cannot help but feel that a very “tokenist” approach is being taken to patient evidence, in particular and the quality of life issues that are key to us.

18. Our experience is that Appraisal Committee meetings can be intimidating and confusing for nominated patient experts. The meetings are heavily influenced by technical discussion on the health economic aspects. As a result the anecdotal experience of the patients who are actually using these medicines is rarely listened to or, if the decisions are indicative, taken into account.

19. The inclusion of patient representatives in NICE’s decision-making processes is—at the moment—chiefly tokenism in our view; the way in which data and results are presented are challenging—even for healthcare professionals—and this makes it very hard for patient organisations and representatives to interpret and respond appropriately. In our view, NICE needs to provide a greater level of support and guidance to patient groups if their expertise and experience is to be meaningful and used appropriately.

20. Patient and clinical experts are required to leave the meeting before the Appraisal Committee starts to discuss its recommendations. It is often very difficult to understand how and why a particular decision has been arrived at, and we do have concerns about the transparency and fairness of the NICE decision-making process.

APPEALS PROCESS

21. Finally, when one considers the desirability of having a NICE process that is fair, independent and transparent, the anomalies of the appeal process should not be overlooked. It strikes us as perverse that the Chair of NICE should also review the merits of whether an appeal should be allowed to proceed, and then go on to Chair one of the Appeal Panels himself. In essence, we are required to appeal to the same body of people who made the original decision. In no sense can that be characterised as an independent, robust appeals process.

CONCLUSION

22. We would like to thank the Health Committee for the opportunity to submit our comments and we would be very pleased to provide the Health Committee with any additional information or clarification that it might require.

National Rheumatoid Arthritis Society

March 2007

Evidence submitted by the NHS Confederation (NICE 73)

The NHS Confederation is a membership body that represents over 90% of all statutory NHS organisations across the UK. Our role is to provide a voice for the management and leadership of the NHS and represent the interests of NHS organisations. We are an independent organisation.

The NHS Confederation welcomes the opportunity to give evidence to the Health Select Committee on NICE. This evidence sets out our views, based on feedback from a cross section of our member forums.

EXECUTIVE SUMMARY

- The NHS Confederation supports the role of NICE and regards it as a successful organisation that has proved responsive to the view of stakeholders and has a high reputation for the quality of its work.
- Many of the issues relating to NICE are less about the Institute itself and more about associated government policy. This includes the selection of topics and the mandating of funding of NICE decisions.
- There seems to be a view in some quarters that NICE is able to provide a solution to the difficult problems of how resources should be allocated and how new technologies and treatments can be afforded and prioritised. This was not the intention and it is not reasonable to expect NICE to be able to do this.
- There are a number of measures that could be taken to support organisations in implementing guidance and ensuring effective uptake.

1. *Why NICE's decisions are increasingly being challenged and 2. Whether public confidence in the Institute is waning, and if so why?*

1.1 NICE has raised the public understanding of how health interventions are introduced into practice. This includes understanding of the need to consider treatments according to their effectiveness.

1.2 NICE does appear to have made genuine efforts to engage all stakeholders in reaching its recommendations.

1.3 NICE have approved more treatments than they have refused. This has received very little coverage and the media have tended to portray NICE as a rationing body.

1.4 Even so media coverage at the time of newly published NICE guidance can be associated with concerns from professional /care provider agencies, and may create a perception that NICE exists to ration care rather than make judgements of cost-effectiveness. MORI polling suggests that the public are not sympathetic that access to drugs should be restricted on the basis of cost and some are even not clear that effectiveness should be a criteria. The problem therefore, may be less about NICE and more about how the public perceive the issues.

2. *Whether public confidence in the Institute is waning, and if so why?*

2.1 There has been some coverage showing that post code differences in the uptake of NICE appraisals guidance have persisted—albeit that the level of variation has been reduced. This is not in fact NICE's responsibility but reflects the problem of the diffusion of changes in clinical practice. The existence of NICE has certainly reduced the overall level of this problem.

3. *NICE's evaluation process, and whether any particular groups are disadvantaged by the process and 4. speed of publishing and 5. the appeal process*

3.1 Our members do not question the quality of NICE's appraisal processes, however, there are a number of aspects of the way that NICE is currently required to operate that do cause some concern.

3.2 At present NICE examine individual treatments or technologies referred to them by the DH. The assessment is made difficult by a lack of good quality cost effectiveness data. Even where it may do this NICE is not mandated to make judgements about how best to allocate limited resources to the new treatment. Many of the treatments that NICE examined have been at the margins of cost effectiveness. As a result the paradox arises that NHS funding is mandated for a marginally cost effective drug and local NHS organisations may have to achieve this by not spending on treatments which may be very much more effective and could benefit more people.

3.3. The development period for NICE Clinical Guidelines and technical appraisals has been lengthy. We recognise the very technical nature of the process and the need for complex models to be developed or validated. Delays can be absolutely legitimate, for instance where the development process is suspended if the scope needs to be redefined.

3.4. The more recent faster technology appraisals seem a sensible approach to dealing with concerns from patients and NHS for guidance on new interventions immediately after market availability. There is however, a trade-off to be made between speed and the availability of reliable data creating the risk that decisions will subsequently be reversed. Rapid appraisals are more likely to have to rely on data provided by the developer than more independent sources,

4. *The appeal system*

4.1 The appeals process is clear and appears to be effective.

5. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)*

5.1 The Scottish Intercollegiate Guidelines Network (SIGN) established in 1993, has concentrated on the development of Guidelines considered by each of the seven specialty subgroups. There is an emphasis on not duplicating any work already commissioned by NICE.

5.2 Although topics can be submitted to NICE from a range of sources (eg professionals, public, NICE), the recommendations made by the consideration panels are submitted to the DH, to make the final decision on which topics are referred to the NICE work programme.

5.3 In contrast, topics that are submitted to SIGN are considered by an Executive team for appropriateness, before a full proposal and scoping process commences. Proposals referred to the appropriate clinical subgroup are prioritised and included within a list of potential topics for the Programme Advisory Group. The SIGN Council ratifies which topics are selected.

5.4 It seems the topic selection process adopted for NICE TAs & CGs is potentially more influenced by DH priorities compared to the CG model adopted by SIGN.

5.5 More thought needs to be given to how the areas that NICE should be examining are chosen. This is a genuinely difficult area as the knowledge of what areas would replay examination is not widely spread. Some investment in investigating new methodologies to improve the selection of candidate would be useful. At present this is not NICE's responsibility and it might be appropriate if they were involved in developing such methods.

6. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this).*

6.1 NICE has concentrated on decisions about whether to start using new technologies and much less on which treatments could be stopped although there are new measures to improve this. It may be that some of the expectations that this will lead to large scale savings are over stated.

6.2 There is a general problem that the methods for dissemination and implementation of guidance are not as well understood as they might be and work and NHS management would benefit more research on influencing clinical practice.

6.3 Recommendations frequently involve several provider agencies/teams, which can delay progress with the implementation of service specific and/or overall implementation. Departmental expectations of implementation for NICE products needs to consider how organisations such as a NHS trust and its PCT partner(s) can prioritise which guidelines and within individual guidelines which recommendations to implement first and where business planning is required to progress new or additional resource.

6.4 There is an understanding that the clinical guidelines are developmental in nature and that organisations will therefore need time to plan resources for and to implement any one of them, but given the number of different guidelines now available some direction about how to look at them as a group and to prioritise within them overall might be helpful.

6.5 The Interventional Procedure Programme (from 2003) supports healthcare professionals involved in the introduction of new procedures and patients themselves, by publishing guidance on the safety and efficacy of the procedure. Trusts take these NICE recommendations and integrate within local policies for implementing new procedures which is vital for local ownership of changes in practice but can also appear as a delay.

6.6 The DH requirement to fund NICE treatments may lead to in-year financial pressures flexibility becomes increasingly limited. The publication of NICE appraisals throughout the year does not fit with the annual allocation of resources to NHS organisations although NICE have introduced a forward planner which can assist with this. The introduction of fast track appraisals could potentially reduce the ability of PCTs to plan for significant NICE recommendations. The DH policy of developing contingency funds could assist with this.

6.7 The argument made by Ministers in the past that this is good for patients or that it eliminates post code prescribing may not fully reflect the reality of how decisions are implemented. By definition insisting on funding a less cost effective treatment will be at the expense of other patients who would have benefited

more. It may eliminate post cost prescribing in the treatment that NICE have examined but, as the funding government provides for NICE decisions is in general allocations and not earmarked, different NHS organisations will find the money in different ways producing variation elsewhere.

RECOMMENDATIONS FOR ACTION

- NICE has been successful and should be supported in its role. Further work on opportunities for disinvestment and advice on cost minimisation is required. NICE will need access to data on utilisation and research on health technology assessment in order to do this. Unsurprisingly, manufacturers do not tend to sponsor research which produces data that can inform this.
- Methods for topic selection could be improved. It is welcome that NICE has been given more responsibility for this. Developing new methods for doing this might be of value.
- It is not reasonable to expect NICE to provide the answer to the difficult question of how to allocate resources. This is a decision for PCTs, and NICE can assist with this. An expansion of the NICE programme would help this. However, there is a need for a debate with the public about some of the difficult resource allocation decisions that need to be made, how priorities are set, and how scarcity should be managed.
- The policy of mandating of funding of technology appraisals should be evaluated in terms of its impact on other services.
- There would be merit in further research and tool development for the dissemination of appraisal and guidelines. Making these available on the desk top of NHS clinical computer systems would be helpful.

NHS Confederation

March 2007

Evidence submitted by Novartis Pharmaceuticals UK Ltd (NICE 59)

EXECUTIVE SUMMARY

- Public confidence in NICE is being eroded owing to a growing perception that it is an arm of Government to cut costs rather than a force for improving clinical care: This perception has been reinforced by some recent decisions that appear to be incompatible with common sense, eg the decision not to recommend pharmacological treatment for patients with mild Alzheimer's disease but to let them progress to a moderate to moderately-severe disease state before offering treatment.
- The perception that NICE decisions are driven by economics is supported by its apparent over-reliance on cost-QALY as the over-arching decision-making variable: Whilst cost/QALY values are useful, they should be used as an aid, and not the sole basis for decision-making with regard to patients' access to medicines. Other factors, such as clinical need and availability of other effective treatments should be given relevant weight in the decision-making process. We would welcome a broader debate on exactly how the value of medicines should be assessed.
- Flaws in the quality of evidence assessment have resulted in the need for further analysis and unnecessary delays. Two examples have been provided which relate to Novartis products.
- Some patient groups are disadvantaged by the methods used by NICE: in particular those who derive quality (rather than quantity) of life benefits from treatment, eg the elderly, people at the end of life, or with chronic conditions and those with rare conditions. This is contrary to the increasing attention of Government on management of long-term conditions and the focus on care and dignity for the elderly and equality of access to care.
- The perspective taken by NICE in assessing value is perhaps incompatible with that of the public. NICE examines value to the NHS, whereas the public may feel it should look at value to patients, carers and wider society.
- These factors are leading to an increasing number of appeals using an appeals process that is seriously flawed and which is weighted heavily against appellants achieving any significant changes to guidance.
- Implementation of NICE guidance is highly variable, with differing interpretations of what implementation means. Technology appraisal guidance is often perceived as a necessary evil that contributes to cost pressures, although evidence has shown that good financial planning removes funding as the major barrier to implementation. "Wait-for-NICE" policies are common and often written into local policy documents.
- Collaborative and constructive dialogue with industry is lacking thereby preventing significant information and arguments on patient benefit from forming part of the appraisal process.

Novartis recommends that:

- Factors other than cost/QALY are given sufficient weight by NICE when making decisions and it makes clear how these factors have been balanced in its guidance.
- NICE works with industry to broaden this definition of value and to adopt a more holistic approach to evaluation of benefits and costs of treatment, to include societal benefits and costs beyond NHS and personal social services.
- is given direct accountability for the quality and consistency of the assessments of evidence it receives from the academic centres commissioned to provide Assessment/ERG Reports.
- NICE; academic centres and companies engage in a truly constructive dialogue throughout the appraisal on such issues as identifying the most appropriate population for whom treatment would be deemed cost effective, methods and assumptions to be used, data quality and modelling techniques.
- A root-and-branch review of the appeal process is conducted.
- Implementation of NICE guidance is given more attention in the Healthcare Commission's Annual Health Check and that an implementation component is included in the Quality and Outcomes Framework.

INTRODUCTION

1. Novartis Pharmaceuticals UK Limited has a long track-record of researching, developing and supplying innovative medicines in areas of major unmet medical need. In the past five years, we have launched more chemical entities than any other major pharmaceutical manufacturer, including significant advances in the fields of medicine which include cancer, ophthalmic medicine, transplantation and asthma. Furthermore, our interactions with NICE are likely to increase in the coming years with an unprecedented programme of new launches planned.

2. During this period, we have been involved in 15 NICE appraisals and 1 review for products which include imatinib (Glivec®), verteporfin (Visudyne®), rivastigmine tartrate (Exelon®), letrozole (Femara®), clozapine (Clozaril®) and ranibizumab (Lucentis®). We therefore have considerable experience of working with NICE, of its processes and its effects on patient care. Whilst NICE does much good work, we feel that there is scope to improve the consistency and quality of some assessments conducted by the independent assessment groups.

Why are NICE decisions increasingly being challenged?

3. There are a number of factors that may contribute to the increasing number of challenges to NICE guidance. The first is that there is an impression that NICE is increasingly focusing its decision-making on the cost/QALY and whilst the cost/QALY is a useful measure, it should not be used as the sole basis for decision-making. Although we recognise that QALYs provide a useful measure to compare cost-effectiveness across a wide range of different treatments, it is important that all relevant factors are given due consideration to ensure fair, balanced and evidence based guidance to the NHS. Cost/QALY as it is today is too narrow, excluding such factors as societal costs and some of the qualitative costs to the patient.

4. An area that appears to have diminishing importance when reaching a decision is the opinion of patients, carers and clinicians. These stakeholders have direct experience of living with and managing the condition in question, yet it appears that their opinions are often given relatively less emphasis in comparison to economic considerations. Such an approach undermines the confidence of NHS staff and patients in the quality of guidance produced, resulting in increased challenges to guidance as well as poor implementation.

5. NICE's policy on the use of QALYs was outlined in 2005 in its valuable paper on social value judgements. NICE states "*that while it endorses the use of cost-utility analysis in the economic evaluation of particular interventions, such information is a necessary, but not sufficient, basis for decision-making*". We believe that if this policy were fully implemented that a more well informed and patient focused decision making process would be the result.

6. Another reason for NICE decisions increasingly being challenged is the sometimes questionable quality of the work undertaken for it by the academic centres commissioned to produce Assessment Reports and Evidence Review Group Reports. Whilst economic models submitted by manufacturers of technologies are criticised heavily during the appraisal process, NICE is reluctant to accept any criticism of the models developed by the ERGs. This situation is further exacerbated by not allowing manufacturers access to fully working versions of the models developed by the ERGs. For example, in the case of Alzheimer's disease, the economic model developed by SHTAC¹¹⁸ only used two disease states (plus death)—full-time care and pre-full-time care—contradictory to the medically recognised and identifiable stages of the disease (mild,

¹¹⁸ Southampton Health Technology Assessment Centre.

moderate, moderately severe, severe, as measured by MMSE¹¹⁹ scores). The criteria used to define these states were taken from a small US study, where clinical practice and availability of full-time care are substantially different from the UK. Moreover, drug treatment is licensed for use dependent on MMSE scores, not on care setting.

7. In the COX-II appraisal in 2004, concomitant use of aspirin was included in the meta-analyses for COX-II users but not in users of NSAIDs. Given that the benefits of COX-IIs reside in their ability to reduce gastro-intestinal side-effects, which can be found with aspirin, this decision immediately biased the results of the meta-analyses and subsequent economic models against the use of COX-IIs.

8. In both cases further cost-effectiveness analyses were required resulting in major delays to guidance and patients' access to the medicines.

9. The work from Assessment/Evidence Review Groups is commissioned via the National Coordinating Centre for Health Technology Assessment. This puts NICE in a difficult position in that it is not directly accountable for the quality of the work upon which it relies for its decision-making. It is also difficult for NICE to ensure consistency of methods, standards and approaches across, in particular, the different Evidence Review Groups, who wish to exercise some degree of academic freedom.

10. We believe the degree of challenge to NICE decisions would be reduced considerably if a more inclusive approach were taken during the assessment process, enabling a dialogue from the beginning on the appropriate patient population in whom treatment may be cost effective, on methods, on assumptions, on data quality and on modelling techniques. Currently interaction is generally limited to the manufacturer's submission of its dossier. We believe that such an approach is not incompatible with NICE maintaining its independence.

11. In contrast, it is not uncommon to collaborate with other Health Technology Appraisal bodies as the assessment progresses on such issues as the assumptions to be used and appropriate patient populations. This type of approach enables a more rigorous and robust evaluation of the evidence base thus more effectively serving the needs of the patient. Importantly, it assures that misunderstandings in a submission are removed, thereby ensuring a more balanced judgement.

12. We would therefore recommend that NICE considers constructive dialogue throughout appraisal, to clarify issues and prevent unnecessary misunderstandings. This would also seem a sensible means to reduce the number of appeals.

Are any particular groups disadvantaged by the NICE evaluation process?

13. Uncertainty in cost-effectiveness calculations is particularly marked when estimating quality of life. Quantity of life is more tangible, but quality of life measurement is highly subjective and approximate, and the generic instruments preferred by NICE to measure quality of life are relatively simplistic and insensitive to incremental changes.

14. Over-reliance on cost/QALY as the major decision-making criterion therefore disadvantages patients where treatment benefits enhance rather than lengthen life, eg in the elderly, end-of-life therapies and chronic diseases where small improvements can make a big difference to patients.

15. Patients suffering from rare conditions are another group disadvantaged by the NICE process. Development costs for therapies in such conditions are relatively high, and the price per patient appears to be high (while the budget impact is often relatively low). It can therefore be difficult to make the economic case using the criteria required by NICE. Proportionately fewer orphan medicines receive a positive recommendation than non-orphan medicines. Patients are therefore being denied effective treatments for severe, often life-threatening conditions, simply because those conditions are rare.

Is public confidence in the Institute waning and if so why?

16. We believe that public confidence is waning because NICE's role appears to be moving away from clinical excellence to cost containment. The decisions referred to above, eg denying access to drug treatment for patients with mild Alzheimer's disease, runs counter to what most people would deem as common humanity and sense. Such decisions lead to a perception that NICE exists as an arm of Government to cut costs, rather than to promote good patient care. The current attention given to NHS deficits only strengthens this view.

17. A contributing factor to lack of confidence is that the balance of factors taken into account by NICE in deciding on guidance is not made clear. We believe that a clear rationale for how NICE reached its decisions should be given when guidance is issued.

18. One question the Committee may wish to explore is what is meant by value when NICE makes its decisions—value to whom: the NHS, the patient, or wider society? NICE's remit is to focus on the costs and benefits to the NHS and Personal Social Services. However, medicines can confer benefits and savings

¹¹⁹ Mini Mental State Examination.

beyond the health budget, eg in social services costs (for which people with mental health problems account for a significant proportion) in improved educational outcomes in children, enabling them to contribute to society through adult life, and in reduced disability enabling people to continue to work.

19. Calculations of such benefits and costs can make a significant difference to cost-effectiveness assessment: in the Alzheimer's disease appraisal, 30% of the costs of institutionalisation were attributed to carers. The exclusion of this 30% from the costs of NHS care artificially inflated the cost/QALY estimates of the medicines under review.

20. Costs and benefits beyond the health system are included in the assessment of clinical and cost effectiveness in HTA systems in Sweden and the Netherlands. In Sweden LIF economic evaluation guidelines state ". . . *all relevant costs and revenues for treatment and ill health, irrespective of the payee (county council, local authority, state, patient, relation) should be considered*". Whilst we understand this is challenging, we would call on NICE to work with industry to improve its methodology in this respect.

The speed of publishing guidance

21. The aim of the NICE Single Technology Appraisal (STA) process was to address concerns that the Multiple Technology Appraisal process was too long and delaying patients' access to important new medicines. Regrettably, only two of the 10 STAs commenced to date have been completed within the target six months. Whilst early teething problems are inevitable, it appears that very few STAs will not be subject to consultation, which is initiated when the Appraisal Committee's preliminary recommendations are "substantially more restrictive than the terms of the licensed indication being appraised".

22. A further delay is being caused by a disproportionate number of appeals resulting from NICE appraisals and the numbers and rates of appeals appear to be increasing.

The appeal system

23. Embarking on an appeal against a Final Appraisal Determination is not to be undertaken lightly because the chances of any significant change to NICE decisions are minimal. Appeals are costly, taking a significant amount of management time on the one hand and delaying market access on the other.

24. The majority of appeals are the result of disagreement with the interpretation of the evidence and the resulting evaluation of cost-effectiveness. NICE procedures do not allow for challenge on the basis of a differing view of the interpretation of evidence, unless the appellant can show that the NICE decision was "perverse," which is defined as "*to be obviously and unarguably wrong, to be in defiance of logic or so absurd that no reasonable Appraisal Committee could have reached such conclusions*". This is a very high hurdle. It is not helped by the fact that there is no health economics expertise on the Appeal Panel.

25. The NICE appeal process is not independent: the Chairman of the Appeal Committee undertakes the initial scrutiny of appeals to assess admissibility (which appears in many cases to constitute an early assessment of the merits of the appeal) two or three members of the Appeal Panel (including the Chairman) are members of the NICE Board and following an upheld appeal the same Appraisal Committee is asked to review the original decision. NICE is therefore acting as judge and jury over its own guidance.

26. The lack of success in appealing NICE decisions is a barrier to companies—but it is an even bigger barrier to other stakeholders, in particular patient groups, who are deterred from making appeals by the highly legalistic nature of the process, the complexity and expense and who, in many cases, do not have the resources available.

27. For all these reasons we would support the ABPI's call for a root-and-branch review of the appeal process.

The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)

28. In common with most other stakeholders, our experience is that implementation of NICE guidance is highly variable. Whilst some NHS organisations have well-developed systems to horizon scan, plan for and implement NICE guidance, this is far from the general picture. Some organisations "cherry pick" parts of guidance, especially where they conform with their existing practice or audit programmes.

29. The interpretation of what "implementation" means varies—in some organisations it means circulation of the guidance and the allocation of funding (without necessarily effectively communicating the existence of that funding) to others it means identifying a clinical lead and project manager who work with colleagues to draw up a plan and reconfigure services in order to deliver the guidance with appropriate funding to support it.

30. Implementation of NICE technology appraisal guidance is more straightforward and more developed than implementation of clinical guidelines and has been subject to more focus as it is associated with mandatory funding. It is our belief that understanding of how guidelines are implemented is universally poor and a lot of research needs to be done to get a clearer picture before the Committee's questions can be answered.

31. NICE technology appraisal guidance is often perceived by PCTs and Trusts to be a necessary evil that has to be funded and adds to cost pressures, rather than a means to improve patient care. However, the Audit Commission Study, *Managing the Implementation of NICE Guidance* (September 2005) showed that where good financial planning systems are in place, funding is not the major barrier to implementation.

32. "NICE blight" is a common phenomenon. The inclusion of a medicine on the NICE work programme frequently triggers processes whereby funding is only released on a case-by-case basis, necessitating individual "business cases" to be generated by clinicians for patients. This is bureaucratic and time-consuming and increases the problem of post-code prescribing. To quote one PCT's Local Development Plan for 2007–08: "*The PCT will not fund any drugs that are not NICE approved unless prior agreement has been reached. Drugs handling costs, overhead costs, admin and packaging costs will also not be funded unless prior agreement has been reached.*"

33. The major drivers for effective implementation are good financial and project planning, clinical engagement, clear lines of accountability and a commitment at senior level to the importance of NICE guidance as a means to improving patient care. The major influence to ensure that implementation is effective is Healthcare Commission assessment, and we would call for the Commission to put in place measurement and inspection systems that provide a clear picture of both the quality and extent of implementation. A further lever in primary care would be to include implementation of guidance as a component in the Quality and Outcomes Framework.

Novartis Pharmaceuticals UK Ltd

March 2007

Evidence submitted by Pfizer (NICE 47)

RECOMMENDATIONS

1. The Health Select Committee needs to critically evaluate the impact of health technology assessment (HTA) as currently practised by NICE on the sustainability of pharmaceutical innovation in the UK.

2. NICE should commit to establishing a process for defining the evidence, expected to be necessary at the time of approval, to demonstrate cost-effectiveness and value. That process must include the pharmaceutical company and allow for collaborative interaction in defining the target evidence for promising new technologies.

3. Pharmaceutical companies should be permitted to attend appraisal committee meetings with the same rights as all other stakeholders.

4. Appraisal committee hearings should be held in public and all calculations and models should be made available to stakeholders in advance in a format that enables full and proper independent audit.

5. NICE should revise its appeal process so that it considers the merit of the decision, as well as the process, and the appeal process should be conducted and chaired by an independent panel.

6. NICE needs explicitly to recognise the inherent limitations of using quality adjusted life years (QALYs) to measure the value of medicines.

7. Further research is required to develop more robust, inclusive and transparent methodologies for valuing medicines. These need to acknowledge the variations in patient response to medicines and the limitations of applying population level models to individuals.

8. NICE needs to broaden the perspective of appraisals so that they include costs and savings that accrue to patients, caregivers, and wider society.

9. NICE needs to recognise the inherent uncertainty in all economic evaluations and not to place undue emphasis on these results when developing guidance.

INTRODUCTION

1. The National Institute for Health and Clinical Excellence (NICE) was created in 1999, and has established a reputation as one of the leading HTA organisations in the world. Pfizer supports the objective of NICE to raise the standards of health care in the UK and its stated aim of supporting the diffusion of innovation.

2. NICE has appraised approximately one hundred technologies, of which, approximately 70% have been medicines. However, despite the often high profile and controversial nature of these appraisals, they cover a relatively small percentage of annual NHS spending or activity.

3. Pfizer has been involved in over a dozen NICE appraisals, including the ongoing assessments of treatments for Alzheimer's disease and age-related macular degeneration.

4. The theory of Health Technology Assessment (HTA) has intuitive appeal—the NHS clearly needs to use its resources wisely, and Pfizer recognises that NICE can play an important role in guiding healthcare professionals towards treatments that offer the most value to patients and the NHS.

5. However, there remains a significant gap between the theoretical benefits of HTA and the reality of medicines' development. Indiscriminate application of HTA has the potential to have a significant and adverse impact on public health and pharmaceutical innovation in the UK.

6. Pfizer welcomes this opportunity to contribute to the Committee's inquiry. In this short submission, we outline reasons why Pfizer believes that NICE's decisions are often contentious, outline significant ongoing concerns and make proposals that would better safeguard the interests of patients, the National Health Service (NHS), taxpayers and the research based pharmaceutical industry.

REMOTE DECISION MAKING AND LACK OF ACCOUNTABILITY

7. The allocation of public money will always have a significant political dimension. In healthcare, where the consequences of treatment being provided or withheld can have profound implications for individuals, these decisions are often highly emotive.

8. Historically, treatment decisions in the UK were made by physicians, often with input from patients. The approach that NICE has introduced makes greater use of population level assessments of health gain, predominantly undertaken by health economists. While population assessments can be useful, they do have significant limitations including their failure to reflect the specific needs of individual patients.

9. NICE attempt to include the views of patients and doctors in their appraisals. However, the processes for doing so have been regularly criticised as being insufficient (Milewa, 2005; Bridges 2007). Importantly, it is often difficult for patients to present information in a form that is able to be fully incorporated into highly data driven methods adopted by NICE appraisal panels. As a result, concerns have been raised that decision making relies too heavily on the academic assessments. This has an adverse impact on the relationship between patients and their doctors who are charged with implementing NICE guidance.

10. Another concern with over-reliance on economic assessments is that wider implications of decisions about which groups of patients to treat are not formally scrutinised through any political process. Lines of accountability are unclear and are a cause of frustration when patients are denied access to treatments.

IMPACT ON INNOVATION

11. Pfizer believes that given the substantive costs and time required to develop new medicines, any system of medicines assessment should be stable and lead to predictable outcomes. Despite NICE being in existence for eight years, many of its appraisal decisions remain contentious and unpredictable; leading to high levels of frustration for patients, professional groups, patient groups and pharmaceutical companies.

12. One of the principles of HTA is to compare new medicines with current standards of care. New classes of medicines must bear significant research and development costs in order to satisfy the requirements of regulatory and HTA organisations. Generic medicines have no such requirements and therefore, can be provided to the NHS at a significantly lower price. Thus, in disease areas where current practice is a relatively cheap, off patent medicine, such as in many areas of cardiovascular disease, mental health and respiratory illness, HTA discriminates against pharmaceutical innovation.

13. One argument put forward for this approach is that it creates incentives for pharmaceutical companies to concentrate their research efforts in areas of unmet clinical need rather than in areas where cheaper older medicines are already available. This thinking appears to have underpinned recommendations in the recent Cooksey Report into Medical Research in the UK as well as the Office of Fair Trading's market study into the Pharmaceutical Pricing and Regulation Scheme (PPRS). However, it is flawed for two reasons and, as such, risks damaging the future of medical innovation to the detriment of both industry and patients.

- First, the notion that if treatments exist within a given disease area, then there is no longer clinical need, is simply false. Cardiovascular disease is still the biggest killer in the Western world—and is increasingly a major problem in the developing world—and yet, treatments exist. We need more and better treatments in cardiovascular medicine, not fewer.
- Second, associating value only with breakthrough pharmaceutical innovation is fundamentally flawed. History shows that disruptive pharmaceutical innovations are rare and that medicines normally evolve incrementally over time (Wertheimer, 2005; Williams 1999). Furthermore, and perhaps most importantly, within a new area of medical innovation, the first medicine is rarely the best.

14. Unless this is addressed, then there is a real prospect that no new medicines will be introduced in the UK into disease areas where common practice is to use off patent medicines. By 2020, this could realistically extend to all disease areas.

Recommendation 1

NICE EVALUATION PROCESS

15. The credibility of NICE guidance relies on there being open, transparent decision making during the appraisal process that involves all stakeholders. Pfizer recognises the appraisal process has evolved considerably in recent years, for which NICE should be commended. We do believe that despite these changes, there remain a number of areas where further improvements should be made. These include:

EARLY ENGAGEMENT WITH PHARMACEUTICAL COMPANIES

16. Unlike the regulatory authorities, NICE does not engage with pharmaceutical companies in early dialogue concerning the data needed to conduct a NICE appraisal. Without this dialogue, there remains a risk that NICE will reject a medicine because the pharmaceutical company did not collect data required by NICE.

17. We welcome the indication from NICE that it may be willing to engage in early discussions with pharmaceutical companies to clarify future data needs in the event of a NICE evaluation. We strongly urge NICE to implement this change in order to help reduce the likelihood of negative recommendations due to different expectations of required data. It should also lead in return to faster decision-making and a more timely issue of appraisals.

18. NICE needs to recognise that it may not always be possible to conduct clinical trials to meet their specific information requests, especially before and around the time the medicine is licensed. NICE, therefore, needs to adopt a pragmatic approach to assessing new medicines, and not unduly punish a pharmaceutical company if these data are not forthcoming.

19. Given the limited scope of clinical trials, the real value of a medicine to the NHS can only be confirmed after launch following sufficient and appropriate use in a real world setting. There is clearly a trade-off between the need for NICE to provide early advice on new medicines, and our ability to provide the type of data required to make such decisions. We believe that earlier engagement between NICE, pharmaceutical companies and other key stakeholders such as patients, carers and clinicians, would enable a more informed dialogue about the optimal time to conduct any appraisal given that the evidence base for new medicines evolves over time.

Recommendation 2

PHARMACEUTICAL COMPANY PARTICIPATION IN APPRAISAL COMMITTEE MEETINGS

20. Pharmaceutical companies are currently the only stakeholder group not represented at appraisal committee hearings, despite knowing most about the medicine under review. We believe this is fundamentally wrong and increases the chances of arbitrary decision making by NICE. Addressing this shortcoming would also have a number of practical benefits, including quicker responses to any questions or uncertainties about submitted data, and reducing the likelihood of decisions going to appeal as a result of factual errors and omissions.

21. We note that other HTA agencies, including the All Wales Medicines Strategy Group, have managed to successfully include pharmaceutical companies in their meetings and would request NICE consider this option.

Recommendation 3

TRANSPARENCY

22. Pfizer believes the NICE appraisal process should be fully transparent. We note that other HTA agencies, including the All Wales Medicines Strategy Group, hold their hearings in public. We believe NICE appraisal committee hearings should adopt this approach.

23. We remain particularly concerned that NICE does not make available to stakeholders its cost effectiveness calculations in a format that enable independent audit. This is unreasonable and in contrast to the requirement of pharmaceutical companies to provide all of their calculations with unlocked, fully operational versions of the models that are developed as part of their submission.

Recommendation 4

THE APPEAL PROCESS

24. The current NICE appeal process focuses almost exclusively on whether the appraisal process has been followed correctly. It provides insufficient opportunity to review whether the appraisal decision is fair and balanced in light of the available evidence. The range of data chosen to be included, and the fundamental assumptions in the cost-effectiveness model are not subject to appeal, yet these are likely to be at the heart of flawed guidance. The consequences of flawed guidance can be profound for patients and their carers. As such the development of a fair appeal process, where the evidence reviewed and value judgements adopted by the panel can be critically examined, is long overdue.

25. Failings of the current appeal process include:

- The definition of perversity adopted by NICE serves no practical use as no guidance could realistically meet the NICE definition of “perverse”.
- The current appeal process is conducted by NICE itself with no external consultation as to its form or judgements. Essentially, NICE members act as judge and jury on their own decisions.
- The level of input from affected stakeholders appears to be arbitrary.
- Certain groups of stakeholders such as patients may be excluded by the complexity of the process.

Recommendation 5

METHODOLOGICAL ISSUES

26. Pfizer remains concerned that the methodological approaches adopted by NICE systematically underestimate the value of medicines to patients and the NHS. This is primarily due to the failure of currently available tools to capture the full value of medicines to patients along with the systematic exclusion of important costs and benefits for appraisals. Pfizer is also concerned that NICE fails to publicly recognise the wide range of plausible cost-effectiveness estimates that exist in many appraisals and instead, places undue emphasis on individual estimates.

LIMITATIONS OF EXISTING TOOLS FOR ASSESSING HEALTH GAIN

27. NICE has adopted the quality-adjusted life year (QALY) as the standard basis for assessing the value of medicines. It is widely acknowledged that the QALY has very significant limitations and does not produce reliable estimates of health gain (McDonough, 2007). For example, NICE recommends the use of a generic tool for assessing health gain, the EQ-5D, for incorporation in QALY analyses. This instrument is simplistic and relatively insensitive to important changes in quality of life that are important to patients (Krahn-Murray et al, 2007).

28. In practice, the tendency to under-report the impact of a medicine on a patient’s quality of life actively disadvantages those medicines where the benefit is in improving quality of life rather than extending life expectancy, such as medicines for pain relief and neurological conditions. By implications, patients with chronic conditions and elderly patients are most likely to be disadvantaged (Harris, 2005).

Recommendations 6 and 7

FAILURE TO INCLUDE THE FULL COST AND SAVINGS ATTRIBUTABLE TO MEDICINES FROM A TOTAL HEALTHCARE SYSTEM PERSPECTIVE

29. NICE currently only includes the financial impact of medicines on NHS and social services budgets. It excludes the impact on social security payments and costs borne by patients and carers. For example, residential care costs borne by patients were excluded in the appraisal of medicines for the treatment of Alzheimer’s disease, which has the effect of systematically under-estimating the value of these medicines. In addition, focusing on new technologies and medicines in isolation risks ignoring the potential implications for increasing costs elsewhere in the system.

30. Pfizer believes NICE appraisals should reflect the full value of medicines to UK society, rather than the NHS alone. An approach would be to focus on “episodes of care” as a way to recognise the full cost and value of an intervention, the overall patient outcome, and the corresponding costs and benefits incurred across the healthcare system. By expanding the perspective from one of evaluation in isolation to a broader systemic look, it is possible to better integrate the cost and value of medicines and focus the comparison of all treatment options on their ability to affect overall outcomes. Hence, NICE needs to review how the perspective taken in its cost effectiveness analysis can be broadened to allow additional relevant costs and benefits delivered outside the NHS to be formally taken into account.

 Recommendation 8

OVER-RELIANCE ON ECONOMIC ASSESSMENTS

31. Pfizer is concerned that NICE does not fully respect the limitations of current economic analyses methodologies and resulting imprecision of these assessments. Economic modelling often results in a wide range of plausible cost-effectiveness estimates, depending on which data and assumptions are used. Despite this uncertainty NICE appraisal committees appear to place undue weight on the certainty of economic analyses when developing guidance.

32. The complexity of evaluation methods employed by NICE have increased considerably in recent years. However, despite adding the appearance of advanced science, these methods do not obviate the need for pragmatism in handling data, particularly those derived from recently launched products.

33. While economic assessments can legitimately generate a wide range of plausible value for money estimates, these should be seen as contributing to the decision making. Pfizer believes NICE places undue emphasis on a single result within this range and does not adequately recognise the high degree of variability of these results.

Recommendation 9

FUTURE ROLE OF HTA

34. Despite the progress NICE has made since 1999, there remain a number of important areas where NICE reform is required to ensure that it properly fulfils its current role. However, even if these issues are addressed, the fundamental limitations of HTA will remain—it provides only one of a number of perspectives on the value of health technologies, it is conducted at a distance from the vital conversations between patients and their doctors, and it cannot foresee how medical advances will develop in practice.

35. Sir David Cooksey's report on medical research in the UK and the Office of Fair Trading's market study into the Pharmaceutical Pricing and Regulation Scheme (PPRS) suggest far wider roles for HTA in priority setting and pricing. The range of problems with these ideas are out of the scope of the Committee's current inquiry, but the suggestions are worth noting since they reflect an over-enthusiasm for what can be achieved by bodies like NICE. We have advocated greater pragmatism and more realistic expectations throughout this submission; this applies with even greater force to any suggestions about extending NICE's remit into these areas.

36. Pfizer notes that the current focus of NICE activities accounts for a relatively small proportion of NHS activity and expenditure. If NICE is truly to realise its role in achieving a better use of NHS resources, then it needs actively to consider broadening its current assessments beyond a narrow subset of medicines and other technologies. One possibility would be to look more broadly at the effectiveness and efficiency of the NHS and how it delivers care.

Pfizer

March 2007

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Evidence submitted by The British Psychological Society (NICE 81)

The British Psychological Society welcomes the opportunity to contribute to the committee's inquiry into the Aspect of Work of the National Institute for Health and Clinical Excellence (NICE). The British Psychological Society has a keen interest in the work of NICE and along with the Royal College of Psychiatrist jointly sponsors the National Collaborating Centre for Mental Health which produces clinical practice guidelines on behalf of NICE. The Society's comments will address the work of the Collaborating Centre its particular focus on mental health and also the specific areas of interests that are raised by the committee in its invitation to submit comment.

The Society is the learned and professional body, incorporated by Royal Charter, for psychologists in the United Kingdom, has a total membership of over 45,000 and is a registered charity. The key Charter object of the Society is "to promote the advancement and diffusion of the knowledge of psychology pure and applied and especially to promote the efficiency and usefulness of members by setting up a high standard of professional education and knowledge".

SUMMARY

- NICE guidance has have brought significant benefit to patients and practitioners and in particular has effectively promoted evidence based psychological interventions.
- We doubt whether NICE guidance has been increasingly challenged but recognise that some guidance has attracted significant adverse publicity.
- Public confidence is difficult to estimate but professional confidence and patient support for guidance particularly in mental health remains strong.
- The evaluation process seems methodologically rigorous but questions about the evidence base and the applicability of measures like QALYs to mental health and the needs of carers need further development.
- Speed of publication of NICE guidance has been slow but his could be address by narrowing of the scopes and a focus on "how to do" as well as condition focused guidance.
- The appeal system seems to be fairly robust and works well.
- NICE compares favourably with SIGN but could learn from some aspects of the SIGN method.
- Implementation remains the major challenge and there are concerns that mental health generally, and psychological interventions particularly, are being disadvantaged by current commissioning and funding systems in the NHS.

INTRODUCTION

The British Psychological Society's interests lie in the promotion and public understanding of psychological science and in the case of NICE its application to the health care field. Overall the Society take the view that the work of NICE over the past 5 or more years has made a significant contribution to the effective the use of psychological theory and practice in the effective delivery of health care. The Society believes that this has been achieved in a number of ways but principally through the promotion of psychological interventions, and psychological understanding in the treatment of mental disorders. The large majority of NICE mental health clinical guidelines place psychological interventions as priorities for implementation. In addition of other NICE guidance, for example the Technology Appraisals and more recently Public Health Guidance, the importance of psychology in promoting health for example in the development of effective interventions for at risk children, or in using psychological theory and practice to promote health behaviour change across a range of disorders has also been recognised. We very support the National Collaborating Centre for Mental contribution to the work of NICE and believe that it has not only made a major contribution to the promotion of the general health and wellbeing of the population but has also make a significant contribution to the setting of standards and development and education of a broad range of health care professionals including applied psychologists.

The committee raised a number of questions in its invitation to submit evidence which we address below.

WHY ARE NICE'S DECISIONS INCREASINGLY BEING CHALLENGED?

We are aware and have indeed commented on a number of controversial pieces of guidance from NICE, for example the recent TA on the cholinesterase inhibitors in dementia or Heceptin in breast cancer. Whilst it is clear that some decisions by NICE have been controversial and have indeed attracted significant adverse comment we are unconvinced that the number of decision NICE makes are in fact increasingly being challenged. Our understanding is that the level of challenges issued to NICE are broadly in keeping with the number of guidelines issued over the years.

IS PUBLIC CONFIDENCE IN NICE WANING?

As a professional body our comments primarily reflect the interests of the profession and the implications for psychological science. We have two comments to make in this area. First, NICE guidance has been broadly welcomed and supported by psychologists working in health and social care and they have seen it as a key element in raising standards and promoting psychological interventions. In addition in relation to the work on psychological interventions, NICE guidance has gained considerable credibility and support from the wider service user movement who for some years have been arguing for more extensive psychological interventions not just in mental health but across a wide range of disorders. If there has been any waning in public confidence in NICE guidance we would speculate that the occasional and adverse publicity attracted by a small subset of guidance and its biased presentation in the media may have had an adverse effect but others may be better placed to judge this.

IS NICE'S EVALUATION PROCESS EFFECTIVE AND ARE ANY GROUPS DISADVANTAGED BY IT?

We think that the methods chosen by NICE are rigorous, transparent and stand scrutiny by any international standards. We feel that these evaluation methods apply best to studies of the effectiveness of interventions but are less well developed when looking at prognostic or diagnostic indicators and we would think that further development is required in this area. There is also some difficulty in application of some NICE methods to the evaluation of certain health care interventions. For example, many of the quality of life measures developed for general health care do not operate, we believe, as well in the area of mental health and we think that they are also not as effective or well developed more generally for certain groups, for example carers.

THE SPEED OF PUBLISHING GUIDANCE

The speed of publishing guidance as at time caused significant difficulties. In part we understand that some delays have arisen from the appeals procedure or the requirement for more detailed analysis of the evidence than was envisaged in the original scope but in other instances for example in the development of clinical practice guidelines, there have been delays due to extended development times. In part we suspect that this has arisen from the very broad scope of some of the guidance, for example depression or multiple sclerosis. We think that the process may have speeded up and we understand that the refinement of existing procedures, for example the adoption of Single Technology Appraisals, will have contributed to this. Further improvements may be obtained by the adoption of more limited scopes, for example focusing on an aspect of depression such the treatment of depression in primary care or treatment resistance depression. Alternatively using an approach based not on a condition or diagnosis specific approach but looking at the application of a suit of technologies such as NICE recently did when looking at psychosocial interventions in the treatment of drug misuse may also help. Crucially to the success of such approaches will be a more refined process for the identification and specification of the scopes.

THE APPEAL SYSTEM

We have had very limited involvement in the appeal system. Our impression is that this system is well run and seems in our opinion to give a fair view to all sides involved in the appeal.

THE COMPARISON WITH THE WORK OF SIGN

Our experience of both organisations is limited to the production clinical guidelines. There have been relatively few guidelines in the same area. Our comment would be that whilst the two processes are broadly similar, that there are aspects of the SIGN process that, for example their formal consultation meeting with stakeholders in the development phase that could potentially be adopted by NICE. However, our overall view is that on average the general rigor and thoroughness of the methods which NICE has adopted confers some advantage in terms of the final product.

THE IMPLEMENTATION OF NICE GUIDANCE

This is our major area of concern. NICE has produced a considerable body of compelling evidence which we believe has major implications for health care. However, from the point of view of the Society aimed at promoting psychological practice we have a number of concerns. These could be broadly summarized as follows:

- (a) Mental health guidance appears not to have had the same general support for implementation as other health guidance. In part this make stem for the fact that mental health guidance has been disproportionately represented in clinical guidelines as opposed to technology appraisal but we believe it may also it also reflect weaknesses in the commissioning and funding of mental health services. It is our impression that overall structures and supports systems for mental health commissioning are somewhat weaker than those for general healthcare commissioning.
- (b) It is noticeable that some criticism of NICE guidelines refers to the possible negative consequences of NICE recommendations acting as inviolable mandates on practitioners. In the field of mental health, NICE guidelines routinely call for psychological interventions, which are often not available in NHS Trusts. This disparity is not lost on the users of mental health services, who already feel they are the recipients of "Cinderella services".

- (c) The lack of a mental health tariffs under PBR may also have further reduced the incentives to support guideline implementation in mental health.
- (d) We welcome the recent work by the Healthcare Commission focusing of the implementation of the schizophrenia guideline which focused in part about psychological interventions but we are very concerned that despite the emphasis given to psychological interventions on NICE guidance and is supported by other initiatives such as the DH programme on Improving Access to Psychological Therapies implementation of guidelines remains weak. There are a number of reasons for this and these include the reluctance of healthcare commissioners and services to adopt the proper services delivery structures to support effective implementation; the lack appropriate training (funding for clinical psychology training this year has been reduced) and the lack of appropriate supervision and support structures for postgraduate training. We believe that these represent a significant impediment to the implementation of NICE guidelines.

The British Psychological Society

23 March 2007

Evidence submitted by Rarer Cancers Forum (NICE 34)

EXECUTIVE SUMMARY

1. Research and development of treatment for rarer diseases, including cancers, should not be compromised by NICE preventing access to new, innovative medicines through standard appraisal processes. A separate appraisal process should be set up for treatments of rarer diseases, including cancers, to ensure that innovation is encouraged.

2. All treatments for rarer diseases, whether designated as “orphan medicines” or not should be appraised through a separate process where the criteria are adjusted to account for clinical efficacy, unmet need, and total cost to the NHS, over and above cost-effectiveness.

3. The informal sub-category designated by NICE as “ultra-orphan diseases” should be removed as the facts used to define the need for this sub-category are fundamentally flawed (ie the assumption that most treatments for rarer diseases are not disadvantaged by using standard appraisal criteria is unfounded).

4. The time to issue appraisals through NICE has improved but is still not optimal. Patients with rarer diseases, including cancers, are still waiting too long for access to new treatments once they have been shown to be effective in clinical research or have received Marketing Authorisation.

5. Improving Outcomes Guidance should be issued by NICE as soon as possible for Rarer Cancers. Guidance should include clear recommendations for commissioners on funding treatments for rarer cancers, whether they have been appraised by NICE through the HTA or will not be appraised.

6. Clear guidance should be issued by NICE to commissioners in the interim period before final HTA appraisals are issued where treatments are already available in the NHS. This should also include clear guidance where treatments are already available in the NHS for an unlicensed indication of a medicine on the market that has not yet been appraised. This is common in cancers where initial licenses are usually gained in late stage disease and there is a time delay before Marketing Authorisation of a new indication and again before NICE Guidance. In addition, for rare diseases, guidance is required for commissioners for treatments that will not be reviewed at all by NICE.

7. There should be a clear link between guidance from NICE and the work done by the National Specialist Commissioning Advisory Group (NSCAG) and Regional PCT Specialist Commissioning Groups to ensure that treatments for rarer diseases, including cancers, are funded equitably across the UK, based on patient need as opposed to where a patient happens to live.

NICE'S EVALUATION PROCESS DISADVANTAGES PATIENTS WITH RARER CANCERS

1. Thousands of diseases and conditions exist that affect so few people that without special support it would be unlikely that any company would find it financially viable to develop a treatment or cure for them. Legislation on orphan medicinal products, Regulation (EC) No 141/2000 of the European Parliament and of the Council and Commission Regulation (EC) No 847/2000 entered into force in January 2000 and April 2000 respectively. This introduced a Community procedure for the designation of medicinal products as orphan medicinal products and incentives for their development and placement on the market. The European Commission was concerned about the equality of access to orphan medicines in the Member countries, and commissioned a survey (conducted by Alcimed) in 2004¹²⁰. They perceived that there was a lack of homogeneity in:

- Time between obtaining the Marketing Authorisation and commercialisation of these drugs.

¹²⁰ http://ec.europa.eu/enterprise/pharmaceuticals/orphanmp/doc/pricestudy/final_final_report_part_1_web.pdf

- Funding (reimbursement) of these products by each Member State.

The European Agency for the Evaluation of Medicinal Products (EMA), which has set up the Committee for Orphan Medicinal Products (COMP) to implement and monitor the regulations, published a chart commenting on individual country access to orphan medicines, which labelled the UK access as “slow” compared to other member states, and non-orphan medicines¹²¹ (Appendix 1).

2. NICE claim that their current Health Technology Assessment (HTA) process is appropriate for the majority of treatments for rarer diseases, and that only a small percentage of these diseases (defined by NICE as an informal sub-category called ultra-orphan diseases) require a different process. However, evidence compiled by the Office of Health Economics (OHE) shows that appraisals of treatments for rarer diseases, including cancers, are statistically more likely to be rejected by NICE than standard treatments.

	<i>Recommended</i>	<i>Restricted Use Only</i>	<i>Not Approved</i>
16 EMA/FDA* designated orphan medicines reviewed	3 (19%)	9 (56%)	4 (25%)
116 non-designated medicines	53 (46%)	56 (48%)	7 (6%)

The distribution of the decisions made for orphan and non-designated medicines are statistically different ($p = 0.013$).¹²² In addition, there are six orphan designated medicines currently under review, with five not approved in the preliminary assessment released. Four of these appraisals have been appealed leading to further delaying patient access to highly effective medicines.

3. In November 2004, the NICE Citizen’s Council considered and reported on access for patients to orphan medicines. NICE then made recommendations on the appraisal of orphan medicines in March 2006.¹²³ NICE suggested that there would only be problems with the appraisal of medicines for “very rare diseases” (defined as an informal sub-category by NICE as “ultra orphan drugs”) having a prevalence of less than 1 in 50,000, and proposed to develop a process to evaluate these through an “Ultra-Orphan Drugs Evaluation Committee”. The data provided by NICE upon which part of this decision was made is fundamentally flawed. For example:

- Cancer medicines were included in the NICE analysis which are not for a rare disease (irinotecan, oxaliplatin, capecitabine and tegafur uracil for metastatic colorectal cancer).
- Cancer medicines were included which NICE claimed are classified by the EMA as orphan designated but are not on the register (topotecan, gemcitabine, temozolomide).
- Cancer medicines were included which NICE claimed are classified by the FDA as orphan designated but are not on the register (topotecan, gemcitabine, irinotecan, oxaliplatin, capecitabine, tegafur uracil).
- There are many other examples which are not specific to cancer. The analysis by the OHE shows that medicines for rare diseases, including cancers, are less likely to be approved by NICE than standard medicines, and therefore a separate appraisal process should be considered for these cases which are being disadvantaged. The rationale for a separate appraisal process for “ultra orphan diseases” is based on a flawed assessment and therefore should not be recommended as an informal sub-category.

4. It is important that all medicines for rarer diseases, whether they have applied for EMA orphan designation or not, are assessed by a different set of criteria to medicines for common diseases. For example, Velcade, which is currently being assessed for multiple myeloma, is not designated as an orphan medicine as the company did not apply for this status, but the disease itself can be categorised as rare. Applying the same cost-effectiveness criteria will lead to most orphan medicines being denied to patients due to the high price. The price of orphan medicines may appear expensive when compared to other therapies. This needs to be put into context in terms of research and development costs. For example:

- Clinical development costs are still high, even with fewer patients, as patients are more difficult to recruit and a wider number of centres may be needed.
- Costs of research, pharmacovigilance, medical information and manufacturing are generally at least as high as for other medicines as there are less economies of scale.
- There are small patient numbers, which make it more difficult for companies to earn a return on investment.

In order to continue to encourage research and development into treatment of rarer diseases, the criteria for approval of innovative treatments should be adjusted to account for clinical efficacy, unmet need, and total cost to the NHS, over and above cost-effectiveness. This would meet with the requirements of the European Commission to encourage access to medicines for rarer diseases.

¹²¹ http://ec.europa.eu/health/ph_threats/non_com/docs/EMA_chart_en.pdf

¹²² OHE Working paper by the OHE : “HTA for orphan drugs: A review of the Issues and of NICE and SMC Decisions”.

¹²³ <http://www.nice.org.uk/page.aspx?o=296850>

THE SPEED OF PUBLISHING GUIDANCE CAN BE IMPROVED

5. The time to issue appraisals through NICE has improved, particularly with the development of the Single Technology Assessment (STA) process, but is still not optimal. Patients with rarer diseases, including cancers, are still waiting too long for access to new treatments once they have been shown to be effective in clinical research or have received Marketing Authorisation. For example:

- Velcade for multiple myeloma was initially granted Marketing Authorisation in April 2004, and received positive opinion for the expanded indication in March 2005, and the NICE guidance on the expanded authorisation has still not been issued. In the meantime, patients are dependent on decisions made by local PCTs based on budgets only which has led to inequality of access across the UK.

6. In the UK, high per-patient costs for medicines for rarer diseases, including cancers, can produce budget issues for local providers. This can be dealt with through specialist commissioning or top-sliced funding which works well through the National Specialist Commissioning Agency (NSCAG) for very rare diseases where a centralised budget is maintained. However, there is no guidance for the majority of treatments of rare diseases, which are decided at PCT level through local commissioning processes leading to inequality of access for patients.

Improving Outcomes Guidance should be issued by NICE as soon as possible for Rarer Cancers. Guidance should include clear recommendations for commissioners on funding treatments for rarer cancers, whether they have been appraised by NICE through the HTA or will not be appraised.

Clear guidance should be also issued by NICE to commissioners in the interim period before final HTA appraisals are issued where treatments are already available in the NHS. This should also include clear guidance where treatments are already available in the NHS for an unlicensed indication of a medicine on the market that has not yet been appraised. This is common in cancers where initial licenses are usually gained in late stage disease and there is a time delay before Marketing Authorisation of a new indication (eg Herceptin) and again before NICE Guidance. In addition, for rare diseases, guidance is required for commissioners for treatments that may not be reviewed at all by NICE. (for example Sutent for Gastro Intestinal Stromal Tumors and late stage kidney disease.

Penny Wilson-Webb
Rarer Cancers Forum

March 2007

Evidence submitted by Roche Pharmaceuticals (NICE 55)

1. INTRODUCTION

1.1 *Roche in the UK*

1.1.1 Roche aims to improve the health and quality of life of people in the UK through the research, development and supply of innovative medicines and services for the early detection, prevention, diagnosis and treatment of disease. As part of one of the world's leading healthcare groups, Roche in the UK employs over 2,000 people in pharmaceuticals, diagnostics and clinical development.

1.1.2 Our portfolio of medicines includes treatments for cancer, rheumatoid arthritis, osteoporosis, obesity, anaemia and virology. Further information about Roche in the UK can be found at www.rocheuk.com

1.2 *Roche and NICE*

1.2.1 Roche fully supports the aims and objectives of NICE. Over the course of the past eight years, Roche UK has submitted 24 technology appraisal dossiers to NICE on almost all of our key medicines. This record of engagement is substantially more than most other pharmaceutical companies. Details of these appraisals are provided in the accompanying Appendix.¹²⁴ Of these, four have been undertaken using the new Single Technology Appraisal (STA) process through which NICE intends to appraise most medicines in the future. At present, Roche therefore has a greater level of experience of the STA process than other manufacturers.

1.2.2 The first ever STA which was conducted for Herceptin in early breast cancer was described by the Chair of the Appraisal Committee which reviewed it as "setting the gold standard for all subsequent STA appraisals".

¹²⁴ Not printed here.

1.2.3 Roche has continuously engaged with NICE, the ABPI and other key stakeholders in sharing learnings and experiences of undertaking health technology appraisals in the UK from both NICE and the Scottish Medicines Consortium (SMC) and would be pleased to provide further evidence in this regard at an oral hearing of the Committee.

2. EXECUTIVE SUMMARY

2.1 As part of one of the world's leading healthcare groups, Roche in the UK employs over 2,000 people in pharmaceuticals, diagnostics and clinical development. Our portfolio of medicines includes treatments for cancer, rheumatoid arthritis, osteoporosis, obesity, virology and anaemia.

2.2 Roche fully supports the aims and objectives of NICE. Over the course of the past eight years, Roche UK has submitted 24 technology appraisal dossiers to NICE. Of these, four have been appraised using NICE's new Single Technology Appraisal (STA) process through which most medicines will be reviewed in the future. At present, Roche therefore has a greater level of experience of the STA process than other manufacturers and we would therefore be pleased to provide further evidence in this regard at an oral hearing of the Committee.

3. SUBMISSION

3.1 *Whether public confidence in the Institute is waning and if so why?*

3.1.1 NICE has recently declined to give a number of innovative medicines approval and these cases have received high profile and significant media attention. When drugs are rejected by NICE, significant negative publicity often follows with generalised media statements being made about NICE being overly focussed on cost. Whether this is true or not, these perceptions may be serving to undermine the confidence of the general public and patients alike that NICE is simply an organisation put in place to contain NHS costs. However, the reasons that NICE reject drugs are varied and often not related to matters of cost at all. For example, perceived issues with the evidence base may often mean that a particular medicine might not be endorsed. This was the case recently for example with Roche's oral medicine Tarceva for non-small cell lung cancer. It may therefore be helpful for NICE in the future to be more specific about its precise reasons for rejecting medicines in its dealings with both the general and medical media.

3.1.2 It does appear though that NICE's rejection rate for medicines may be increasing. The Inquiry might therefore usefully investigate whether the approval rate for drugs has changed year-on-year since NICE's inception and if so what the reasons are for this. It might also investigate what the approval rate is across the different independent Appraisal Committees (two being chaired by Professor David Barnett and one being chaired by Professor Andrew Stevens) in case different approval standards are being inadvertently applied across different Appraisal Committees.

3.1.3 Such an analysis would be particularly timely given the introduction of the new rapid STA process which is currently being used to appraise a good number of medicines and in the future will be the primary mechanism for appraising almost all medicines. There are issues with the STA process which we outline in section 3.2 below which may be contributing to the apparent increasing large number of negative NICE appraisals. It is essential that these issues are resolved quickly if all stakeholders, including patients, are to maintain faith in both NICE and the STA process overall. Due to the increasing importance of the STA process for appraising medicines, we have limited our comments in the question below to the STA evaluation process.

3.2 *NICE's evaluation process, and whether any particular groups are disadvantaged by the process?*

3.2.1 The premise of the new STA process, akin to that of the Scottish SMC, is that the manufacturer has to provide the majority of the evidence to be used in the appraisal. The role of University-based Evidence Review Groups (ERGs) being to provide a balanced critique of the manufacturers submission rather than to produce an independent assessment report or undertake additional analysis or new economic modelling as is the case with the original multiple technology appraisal (MTA) process. Many of the ERG reports which have been produced to date involving Roche drugs have been unfair and unbalanced in their perspective. Roche has significant issues with the ERG reports produced for three out of the four STAs in which we have participated to date, namely:

- MabThera for Non-Hodgkin's Lymphoma.
- Tarceva for Non Small Cell Lung Cancer.
- MabThera for Rheumatoid Arthritis.

3.2.2 Despite now being the primary evidence provider to support the STA process, manufacturers are significantly disadvantaged in the STA process as follows:

- 3.2.2.1 The manufacturer is not given sight of the ERG report to correct any inaccuracies, factual errors or major misinterpretations of the manufacturer's submission by the ERG group prior to it being seen and utilised by the Appraisal Committee for decision making. In three out of

the four STA appraisals to date involving Roche drugs (listed above) there have been issues with ERG reports which we believe could have been corrected and addressed had we been given sight of the ERG report before being utilised by the Appraisal Committee for decision making.

- 3.2.2.2 The manufacturer is excluded from being present at the first STA Appraisal Committee meeting to answer questions or provide clarification about its evidence submission. In contrast, patient groups and clinical experts are present and representatives from the ERG group are in attendance to answer questions and provide clarification. It is our understanding that often there are questions raised during Appraisal Committee meetings regarding the manufacturer's submission to which the answers are "second guessed" since the manufacturer is not present to provide any direct response.
- 3.2.2.3 The manufacturer is excluded from being present at the second STA Appraisal Committee meeting to answer questions or provide further clarification. Notably the ERG group also attends this second meeting even though it is the manufacturer which will inevitably be providing the primary response to issues raised after the first Appraisal Committee meeting.

3.2.3 As well as manufacturer attendance at Appraisal Committee meetings, Roche also believes that Appraisal Committee meetings should be held in public (as at present are meetings of the All-Wales Medicines Strategy Group (AWMSG), the NICE Board and NICE appeal hearings).

3.2.4 Furthermore, it is clear that there is significant variation in the approach being taken to critiquing manufacturer submissions across the different Evidence Review Groups. NICE should provide ERGs with clearer requirements and expectations regarding their role in the STA process in the same way that manufacturers are provided with specific and detailed guidance about the contents of their submissions. Greater quality control and quality assurance of the work undertaken by ERGs is urgently required.

3.2.5 In the current arrangements this is difficult, if not impossible, for NICE to engineer since it does not hold the direct contractual relationship with academic Evidence Review Groups nor does it fund their NICE related work directly. Commissioning of ERG work is done via the national HTA R&D Programme which is funded directly by DH and this limits the ability of NICE to properly direct the work of ERGs.

3.3 *The speed of publishing guidance*

3.3.1 The introduction of the STA process has provided NICE with the opportunity to significantly improve the speed with which technology appraisal guidance can be produced. For example, the STA appraisal of Herceptin for adjuvant breast cancer was not only one of the fastest appraisals undertaken by NICE but also one which produced guidance within weeks of EMEA licensing.

3.3.2 However, as more STAs are referred to NICE it will be important to ensure that NICE is appropriately resourced in its Technical Teams to ensure an acceptable turnaround time for appraisals. Regular performance metrics should be collected and made available detailing key milestones in the NICE appraisal process such as the time which medicines spend in the topic selection process; time in appraisal; time in appeal; and time to publish final guidance.

3.3.3 Whilst the speed of publishing and communication of NICE guidance is generally more acceptable with the STA process, the speed of implementation of guidance by the NHS remains problematic. There remain significant variations in the speed with which some NHS organisations choose to fund and implement guidance. Roche regularly audits the implementation of NICE guidance relating to its medicines and consistently we see that there remain large variations in uptake across different parts of the NHS in England and Wales. This is true for primary care medicines such as Xenical used to treat obesity; for specialist medicines such as Pegasys used to treat Hepatitis C; and for Roche's portfolio of NICE appraised cancer medicines: Herceptin for breast cancer, MabThera for Non-Hodgkin's Lymphoma and Xeloda for breast and colorectal cancer.

3.3.4 Implementation issues are described further in section 3.5 below.

3.4 *The appeal process*

3.4.1 Roche has participated in five appeals, most recently for the use erythropoetins in cancer related anaemia and for Tarceva for the treatment non-small cell lung cancer (to be heard at oral hearing in April 2007). In general though, Roche believes that the appraisal process should facilitate the early resolution of issues through dialogue and up front engagement in order to prevent lengthy, resource and time consuming appeals being lodged. At present around 30% of technology appraisals go to appeal and we believe this figure is too high; spending this level of resource on appeals does not represent good value for money for taxpayers or patients. The high level of appeals is demonstrative of the fact that the appraisal process is not sufficiently focussed on early resolution of disputes and issues emerging during the appraisal process. In the case of the STA for Tarceva for non-small cell lung cancer which Roche is presently appealing, many of the issues raised in the appeal could have been dealt with earlier in the appraisal process, had Roche, for example, been given sight of the ERG report for the appraisal before it went to Committee. Such engagement would in fact also be consistent with the recommendations made in the Cooksey Report for earlier dialogue with manufacturers.

3.4.2 Our observations and recommendations for change regarding the appeal process are:

- 3.4.2.1 Many of the issues raised in appeals relate to health economics issues and yet there is no qualified person on appeal panels to deal with such issues, ie a health economist and this deficiency should be remedied.
- 3.4.2.2 Stakeholders at appeal hearings are often in practice not treated equally, whilst all discussion at appeal hearings is directed through the Chair it is usually the case that attendees from NICE, the Appraisal Committee or academic groups working on an appraisal are permitted to engage in greater dialogue or communication than the appellants, and with less hostility, and this is unfair. This may open up the appeal process to accusations of imbalance and unfairness and should be remedied.
- 3.4.2.3 The appeal process should be administered and undertaken by an independent body unconnected with NICE. The fact that NICE can be its own “judge and jury” seems inappropriate to any outside and fair minded observer and leaves NICE open to the perception of potential bias. This is of course a long standing issue which the Committee has investigated previously in its first Inquiry about NICE.

3.5 *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)*

3.5.1 Whilst the speed of delivering NICE Guidance has improved with the STA process, the speed at which the NHS implements guidance remains highly variable across England and Wales. The establishment of the ERNI database by NICE to bring together in one place information about the uptake of NICE guidance across the NHS is very welcome.

3.5.2 Roche conducts quarterly audits into the implementation of NICE guidance relating to our medicines which show significant regional variations in uptake for Xenical (obesity), Pegasys (hepatitis C), Herceptin (breast cancer), MabThera (non-Hodgkin’s lymphoma) and Xeloda (colorectal breast cancer). We would be pleased to make the latest results of these NHS audits into the uptake of NICE guidance available to the Committee to support the Inquiry if requested to do so.

3.5.3 More needs to be done to join-up thinking to ensure that improved access to medicines follows rapidly on from the publication of positive NICE guidance. The Ministerial Industry Strategy Group’s (MISG) Long-Term Leadership Strategy makes helpful and practical recommendations on how to improve access to medicines, including those which have been appraised by NICE and the Committee may wish to review these as part of it’s Inquiry.

3.5.4 The Committee may also wish to investigate ongoing issues relating to so-called “NICE blight” where treatments are being withheld from patients and access is being denied until final NICE guidance to the NHS is published. Although DH has recently clarified for the NHS in its Good Practice Guidance that in the absence of NICE guidance, other local and national sources of evidence should be used to inform local decision making about treatment availability, this practice is not being consistently applied across the service. The issue of NICE blight is now also being reinforced through the use of “minded rejections” utilised by the Appraisal Committee in the new STA process as a mechanism to obtain further analysis to support appraisals.

3.5.5 Key factors affecting implementation and recommendations are:

- 3.5.5.1 The availability of a local NHS champion motivated to pick up and drive the local NICE implementation agenda.
- 3.5.5.2 The buy-in of clinicians to embrace and implement guidance rapidly, including the need to embrace stopping those practices and treatments which are to be replaced by the guidance.
- 3.5.5.3 The making available of timely funding by PCTs to ensure that every eligible patient (as opposed to only a locally selected sub-set of patients) is able to receive treatment when they need it (as defined in the implementation tools produced by NICE and captured in NICE Costing Templates issued at the time of guidance publication).
- 3.5.5.4 The timely, accurate and sensitive reflection of NICE guidance in payment by results tariffs such that there are no disincentives to local implementation built in through inappropriate or lower drugs costs being reflected in the tariff.
- 3.5.5.5 The removal of any disincentives in commissioning and payment systems which do not support NICE guidance. For example, NICE guidance for Xeloda in breast and colorectal cancer endorses that patient’s should be given the choice of replacing an IV treatment option with oral Xeloda (which can save pharmacy, nurse and IV infusion time) but there are sometimes local disincentives for NHS Trusts in place (eg loss of income from day case episodes) to making such switches and implement the NICE guidance.
- 3.5.5.6 Roche believes that such perverse incentives, as well as undermining NICE guidance implementation, are damaging to patients and run counter to the choice agenda, preventing patients from having access to treatment options which have been judged to be both clinically and cost effective.

3.5.5.7 Regarding NICE clinical guidelines, there is comparatively little information available to determine whether or not guidelines are being implemented by the NHS and particularly what affect they have on access to medicines in the UK and research is urgently needed in this area.

Paul Catchpole
Healthcare Management Director
Roche Pharmaceuticals

March 2007

Evidence submitted by the Royal College of Midwives (NICE 62)

The Royal College of Midwives (RCM) is the professional organisation and trade union representing 95% of all practising midwives in the United Kingdom. Virtually all practising midwives work within the NHS, and the RCM is recognised in every Trust that provides a midwifery service.

The RCM welcomes the opportunity to respond to the Health Committee inquiry into aspects of the work of the National Institute for Health and Clinical Excellence. This response represents the views of midwifery members and RCM staff.

The RCM fully supports the aims of NICE guidance to ensure consistent improvements in people's health and equal access to healthcare. The principle of one independent organisation taking responsibility for reviewing the current evidence and research and developing universal recommendations can represent optimal use of resources. However, as the topic selection is determined at government level, guideline development is increasingly seen as acting in accordance with political drivers.

1. Why NICE's decisions are increasingly been challenged?

1.1 Under the auspices of NICE guidelines clinicians, and other healthcare, have matured and are challenging the care which is solely based on research evidence may not be most effective way to provide healthcare.

1.2 Members have voiced a lack of confidence in some of the recommendations and feel they are biased towards cost reduction as opposed to clinical and cost effectiveness. An example of this is evident in the implementation of the antenatal visiting schedule as organisations have interpreted this literally and blanket apply recommendations therefore reducing individualised woman-centred care. Within the current climate of cost constraint, the NICE guidelines may be used adversely to providing quality care. There is evidence of the consequences of this namely in staff and service reduction, as it is use negatively when calculating the manpower or service resources. In cases where recommendations would support a reduction of either staff or services they are readily adopted. Interestingly if the recommendations require extra resources they are ignored, therefore, wide open for manipulative interpretation. As stated earlier they are not primarily used for improvement in clinical practice and decision-making.

1.3 The guidelines may have set out to address best clinical care however are let down by the complexities in the determinants in providing this care. In addition the narrow evidence base considered in the development of NICE guidelines ie using RCTs as the "gold standard", to the exclusion of other types of equally valid evidence, is concerning. This results in disillusioned clinicians when planning the total care as the best practices in the other determinants are not supported.

1.4 There is also concern that the slow implementation of NICE guidelines can be associated with no requirement for impact or outcome evaluation to ensure the harm and benefit ratio of its outcome.

1.5 The evidence on which the recommendations are based are also challenged as not being appropriate to the context of UK healthcare. Equally, by addressing topics in isolation, the whole impact on care and practice can be overlooked. As an example antenatal abdominal palpation in pregnancy to screen fetal growth was not recommended. However the impact of stopping this practice will result in:

- (a) Clinicians not developing the skills or competency needed for abdominal palpation, important clinical skills in the management of labour, if not practiced antenatally.
- (b) The social and educational opportunities in the interaction with the woman has been overlooked as an outcome.

2. Weather public confidence in the Institute is waning, and if so why?

2.1 The RCM would challenge whether the Institute's aims of consistent improvements in health and equal access to healthcare have materialised as anecdotal information suggests that there is selective implementation of the guidelines often driven by financial or political imperatives.

2.2 There is a lack of robust evidence to suggest that the public are aware or knowledgeable about NICE guidelines; for example amongst maternity service users, especially the socially excluded.

2.3 High profile media on the economic consideration of many treatment therapies highlights the difficulty of universal application when faced with an individual situation and also the wide variations in access that remain.

2.4 The public's expectations of having choice, continuity and control promoted by government is not the reality many are experiencing.

3. *Nice's evaluation process, and whether any particular groups are disadvantaged by the process*

3.1 NICE experiences the same challenges of engaging with and involvement of many social groups and these challenges may result that the guidelines will never truly be representative of all sections of the population.

3.2 The process is dependant on individuals having access to the internet and e-mail which excludes members of the public and some health care professionals.

3.3 Implementation of Public Health guidance requires engagement with a wider group of stakeholders. In addition to the National Health Service, schools, local government, National government, voluntary services and the public should be actively encouraged by NICE to become involved in the consultation and share responsibility for implementation.

4. *The speed of publishing guidance*

4.1 The RCM acknowledges the in-depth work involved in guidelines production and the importance of thorough literature review and consultation. Though acknowledging that NICE has recognised this, the RCM will want to be assured that the guideline is still contemporary when finally completed. However what is more concerning is the slow implementation and service commissioner's commitment to implementation.

5. *The appeal system*

5.1 The RCM have no experience of the appeal system and therefore cannot respond to this question.

6. *Comparison with work of the Scottish Intercollegiate Guidelines Network (SIGN)*

6.1 The SIGN process for guidelines development appear to be a more straight forward process however this might be reflective of the smaller population, smaller community of healthcare professionals and less bureaucracy.

7. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this*

7.1 As there is no national audit of implementation the RCM is unable to provide a specific response. However financial commitment, local political drivers, inter-professional rivalry, lack of knowledge and understanding and lack of a whole systems approach to implementation appear to be contributory factors. Anecdote suggests that guidance recommendation which appears to offer direct cost savings, eg NHS not providing certain drug therapies, are more likely to be acted on.

7.2 Due to an often narrow clinical scope approach, some clinicians fail to comply or implement recommendations as a result of conflict with their own personal opinion, values, beliefs and experience, clinicians feel professional expertise has not been considered in the evaluation of the evidence.

Royal College of Midwives

March 2007

Evidence submitted by the Royal College of Nursing (NICE 100)

1. EXECUTIVE SUMMARY

1.1 The Royal College of Nursing (RCN) welcomes the opportunity to inform the Committee's inquiry into the National Institute for Health and Clinical Excellence (NICE). The RCN performs a dual role: working collaboratively with NICE in the development of clinical guidelines through the National Collaborating Centre for Nursing and Supportive Care, which is hosted by the College; and at the same time the RCN is a statutory consultee and stakeholder with our members contributing from their experience and expertise on the frontline.

1.2 Overall, the RCN has developed a very positive and effective relationship with NICE and reflects the commitment of the College to advocating that NHS care decisions are based on the best available clinical and cost effectiveness evidence. At the same time members have identified a number of ways in which processes and outcomes can be improved which the RCN supports.

1.3 There is scope for better communication and involvement of clinicians throughout the process and reinforcing the collaborative role of the Royal Colleges in being opinion leaders and supporters of NICE.

1.4 Continue to develop involvement of patient groups in the process to ensure that the patient view is represented.

1.5 The RCN will welcome proactive processes to continue to increase the public's confidence in the role of NICE and its work, including proposals to ensure that guideline development groups include the appropriate and relevant healthcare professionals and patient representatives.

1.6 The RCN would welcome proposals for issues of diversity and inequality to become more influential and visible, particularly for community based interventions in public health and health improvement.

1.7 It should be acknowledged that NICE works hard to balance the needs of the patients and the demands on NHS resources. NICE is recognised internationally as having an inclusive and high quality guidance development process and this should be applauded. Its process is continually reviewed and it does change in the light of feedback and will continue to develop.

2. INTRODUCTION

2.1 The RCN welcomes the opportunity to make a submission to the Committee's inquiry into NICE. The RCN represents over 390,000 registered nurses, midwives, health visitors, nursing students, health care assistants and nurse cadets in the UK. This makes the RCN the largest professional union of nursing staff in the world. The College promotes patient and nursing interests on a wide range of issues by working closely with government, the UK parliaments and other national and European political institutions, trade unions, professional bodies and voluntary organisations.

2.2 The RCN is uniquely placed to provide the committee with an insight into the development of guidelines and their practical implementation on the ground. The RCN performs a dual role in relation to NICE. The RCN works collaboratively with NICE in the development of some of its clinical guidelines through the National Collaborating Centre for Nursing and Supportive Care, which is hosted by the College. This process works very well and has informed clinical practice of nurses and other health care professionals. The RCN has a very positive relationship with NICE and this is reflected in the College's commitment to advocating that NHS guidance are based on the best available clinical and cost effectiveness evidence.

2.3 At the same time the RCN is also a consultee and a stakeholder that informs the production of NICE guidance and, for this process, works with members who are situated at the clinical coal face and are nominated to contribute to the development of guidance and to support implementation. In this respect, there has been many positive experiences from members' individual involvement. Nurses are placed on advisory groups for technology appraisal and clinical guideline development. They work with staff at NICE, the National Collaborating Centres, and with other healthcare professional and patient/carer representatives to produce guidance for the NHS. Nurses also submit evidence to NICE consultations and are involved in reviewing draft documents on behalf of the College. This is focused on clinical and cost effectiveness, clinical workability and fitness for purpose.

3. *Why NICE Decisions are Increasingly Being Challenged*

3.1 NICE decisions are and should be scrutinised rigorously as part of the consultation process. However, it is legitimate for these decisions to be challenged legally by clinicians and by patient groups. Notably clinicians and patient groups have been more likely to challenge decisions. There are a number of factors which may have contributed to this.

3.2 Contemporary policy in health and social care services is to promote patient-centred approaches. Patients are encouraged to have more input in their care and are now more knowledgeable about what works for them. They are encouraged to work with healthcare professionals to determine the most appropriate care for them. If the patient's view is that the best possible treatment is denied and knows that this is available privately they will view the NICE process as inequitable.

3.3 The process for reviewing draft guidelines changed in April 2006. In the past stakeholders had two opportunities to review draft guidelines before they were signed off. As from April 2006, NICE operate a single consultation process, though longer, this does not give stakeholders the opportunity they previously had to revisit points made and some members have commented that this is a less transparent process.

3.4 Patient groups are also increasingly challenging NICE because many of the decisions being made about drugs are seen to be about cost. The method of working out the value of an individual's life is not transparent. It does not take into account the social cost of disability or death. Human life now has an upper

limit on its value. It is seen as a form of rationing and particularly when patients are aware that the drugs are available in Scotland or other countries in the EU. Patients often find it difficult to understand how improvements in their quality of life can be measured against cost effectiveness.

4. *Whether Public Confidence in the Institute is Waning, and if so Why?*

4.1 NICE has been reviewed externally by World Health Organisation (WHO) and others and is considered to be the gold standard organisation in this field internationally. The quality of the process is continually reviewed and does develop its processes in the light of feedback and organisational learning. Public confidence in NICE would be aided if professional organisations are seen to support a robust and transparent process for health care decision making.

4.2 Many of the decisions being made by NICE are increasingly viewed by the public, and portrayed in the media, as being simply about affordability. The College recognises that NICE is placed in an invidious position when it seeks to balance cost effectiveness with clinical effectiveness. As a result of this, members are aware that some patients are now required to pay for treatment themselves as a licensed drug may not be approved by NICE, impacting on Primary Care Trust commissioning and local formulary permissions.

5. *NICE Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process*

5.1 The RCN supports the NICE practice of involving stakeholders in its guideline development processes, particularly the new implementation planning process and the provision of implementation support tools. The RCN welcomes instances where guideline development groups have included a wide range of healthcare professionals, taking on board the sub-groups of the population of patients affected by a condition.

5.2 The RCN will welcome proposals for this practice to be the norm for the composition of all guideline development groups so as to ensure that each group will have input from the appropriate healthcare professionals. For instance, where a condition being considered affects adults and children it is not always the case that the condition will manifest in the same way, therefore, representation from a paediatric and an adult perspective would be recommended.

5.3 The RCN does have some concerns over the composition of some of the healthcare professionals on the guideline development groups. The College in supporting member involvement in advisory groups are strongly advocating all members of the development group have equal voice in forming recommendations through evidence reviews or consensus processes.

5.4 The RCN supports the use of 'best available evidence' by NICE, ensuring where possible, recommendations are robust. Some members have indicated that in their experience, NICE works best for surgical type interventions (ie does one hip replacement work better than another). The complexity of related social cost and benefits are not always included in evaluations. A good example of this member feedback is in relation to the management of long term conditions.

5.5 The costs to the individual of a long term condition far out weighs the costs related to healthcare. These personal costs can often have an immense impact on society and the overall economy in terms of loss of employment. There are lots of costs particularly with LTC where continuing with current treatment rather than new treatment pathways with a more expensive drug result in significant hidden costs that are not explored. This is due in part because the data is not being collected or because they come out of different budgets (ie social services rather than trust or GP costs).

5.6 Other member feedback has indicated some concerns about the use of the quality adjusted life year (QALY) which has become an established feature of health economic analysis. A perception from members is that it renders some patients, for instance older people at risk and in particular those with chronic or mental health illnesses. This is because QALY analysis focuses on physical rather than psychological or social disability. Successful interventions will both significantly improve the quality of life of carers, and reduce care costs. However, if these third party benefits are not included in cost effectiveness calculations then certain interventions will always be systematically undervalued. In seeking to be a universal health care measure QALY places older people and those with long standing mental illness at some disadvantage.

5.7 With regards to the guidance on public health the technology appraisals outlining specific treatments seem to be very effective. Amongst the issues regarding guidance for public health interventions is cost effectiveness in the longer term. Many public health improvement activities will not see a benefit in the short term and because of this may not be evaluated until much further down the line as a result there is often a shortage of evidence and research upon which to assess their effectiveness.

5.8 Whilst the RCN welcomes the integration of the public health into NICE's remit, there is concern amongst public health nurses that since NICE has integrated the Health Development Agency (HDA), there has been considerably less activity on public health guidance. The HDA was an active and well respected organisation that focused on improving health and health inequalities and produced a wide range of relevant information as well as acting as a resource and referral point for individuals and organisations. We acknowledge that the HDA's work continues under NICE but the public health work seems to have lost

some publications including very valuable case studies, with evidence based examples from across a spectrum of activity which could be obtained from the HDA website. It would be good to have these resources available on the integrated NICE website.

5.9 The RCN would welcome proposals for issues of diversity and inequality to become more influential and visible particularly for community based interventions in public health and health improvement

6. *The Speed of Publishing Guidance*

6.1 NICE are subject to a number of pressures to reduce the time taken for decisions to be made. For instance technology is changing quickly with some guidance requiring to be reviewed much earlier than previously ie the technology appraisal on insulin pumps, although up-to-date when published was quickly out of date as treatments changed and pumps became more common.

6.2 The RCN welcomes the fact that NICE has responded to public concerns on the length of time it takes to produce and publish guidance. NICE is currently consulting on the process for establishing the 'short clinical guideline' procedures. The RCN supports this principle but recognises that this should not jeopardise the development process, and the selection of the right advisory group participants which are a crucial element of ensuring a robust decision.

6.3 The RCN would also like NICE to reflect the current difficulties for clinicians getting permissions from their employers in order to fully contribute to advisory groups. Members have fed back that single day attendance to advisory groups is often more demanding than two day meetings. In the light of recent difficulties emerging from NHS deficits, the College would be supportive of NICE reviewing processes supporting the development of guidance.

6.4 In order to reduce the time taken to publish guidance NICE has, in the last 12 months, for small topics reduced by 50% the number of experts on the guideline development groups. Whilst the need to reduce the time taken to make decisions there is some concern that this could be at the cost of expertise and thereby the quality of the outcome for patients.

7. *The Appeal System*

7.1 NICE's objective is to have an open and transparent process in which stakeholders are accorded the opportunity to raise issues where necessary. The appeal process is part of this openness and this has been broadly welcomed by the RCN. Indeed the RCN has on two occasions appealed against NICE's decision and one appeal is taking place on 4th April 2007 on the use drugs for the treatment of rheumatoid arthritis.

7.2 Whilst not commenting specifically on the pending appeal, generally, the issues that have been raised are focused on inequitable access to effective treatments for patient. This is also concerned with full consideration of social and carer costs.

7.3 The RCN believes that if steps are taken to make the process more representative and more transparent appeals would be less frequent. The views of patient groups and representatives could be sought more vigorously.

8. *Comparison with the Work of the Scottish Intercollegiate Guidelines Network*

8.1 The main area in which SIGN and NICE differ regards the guideline development group. Unlike NICE clinicians are involved at the proposal stage, and clinicians and patients are involved with topic selection, and patients can propose topics for guidelines ie Hepatitis C was a proposal by a patient. The SIGN Guideline Development Groups also undertake the literature review and are supported through development of research and critical analysis skills to enable them to do the development themselves.

8.2 In terms of governance the SIGN Council choose guidelines to review and develop by voting following discussion and a prioritising process which again seeks to empower clinicians and patients and for them to take greater ownership over guidelines.

8.3 More work is now being done in the clinical areas on implementation and many of the Health Board in Scotland has SIGN Guideline Implementers. Technology Appraisals (TA) from NICE are processed by NHS Quality Improvement Scotland for relevance and accuracy then either approved or not approved by them for implementation in Scotland.

8.4 In the past SIGN has been very open and inclusive, asking for opinions from a wide number of health care professionals. However, there has been a shift towards clinical benefits being balanced against cost and shifting more towards the way NICE make decisions.

8.5 A continuing challenge for the College is that it serves members in all four countries of the United Kingdom. NICE is English/Welsh based and SIGN is Scottish based and the differences in what applies in

the different countries have been raised in some submissions. For instance, in the appeal against drugs for the use of mesothelioma (asbestos related lung cancer) the drug (pemetrexed disodium) is available to patients in Scotland, but not available to English and Welsh patients. This was seen as being inequitable access to patients who after all are UK citizens. Equally Wales and Scotland receive a block grant and can prioritise and fund different health priorities based on their health economies.

8.6 The RCN believes that SIGN that here could be more done to bring the UK agencies together to work in a more coherent way as they are all dealing with the same evidence base.

9. The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines (Which Guidance is Acted on, Which is Not and the Reasons for This)

9.1 To some extent, implementation of NICE guidance often depends on whether the clinicians want to use it and whether the patient groups know enough to insist. For instance, the NICE guideline re Type 1 diabetes has had varying degrees of effect ie it is common now for adolescents and many children to have a basal bolus type insulin regime. Most teams would now use this as a result of the guideline, although not many teams changed to home stabilisation as a result of the guideline. This has more effect directly on how the team actually works. With regards to the insulin pump a technology appraisal, when the guidance was first published, the guidance gave the teams ammunition to try to fund the pumps so was widely used. The Health Care Commission monitors how trusts implement NICE guidance, they now have to be NICE compliant or justify why not. The speed at which a guideline is fully adopted though depends on how much the clinical team want to use it.

9.2 The Department of Health and Primary Care Trusts will probably be more of a problem in this regard for the future, as the principles of devolved responsibility to local areas, according to local need, make this much more of a challenge in ensuring fair access to all.

9.3 RCN Members have helped in supporting implementation. NICE holds implementation planning meetings prior to the publication of the clinical guidelines. These meetings enable NICE have an understanding of relevant clinical issues and current policy topics that may impact on implementation. Nurses (and other healthcare professionals and patients representatives) with knowledge and understanding of the systems and structures in place, are invited to these planning meetings, to provide NICE with any information which could act as levers or barriers to implementation. The attendees are invited to give a national, high-level perspective on how these could be utilised or overcome.

9.4 RCN members who have attended these meetings have reported that they have found them very useful and that their contributions have informed the final guidance. The College invests member funding in implementation activity, and is fully supportive of the point that more investment needs to be made to encourage a fuller uptake of NICE guidance. The main element of difficulty is the apparent intransigence of some commissioners to respond positively to clinical guideline recommendations, as these do not have the same mandatory weight as technology appraisals.

10. RECOMMENDATIONS

10.1 The RCN believes that there needs to better communication and full involvement of clinicians throughout the process to reinforce the collaborative role of the Royal Colleges in being opinion leaders and supporters of NICE.

10.2 Develop involvement of patient groups in the process to ensure that the patient view is represented.

10.3 The RCN will welcome proactive processes to continue to increase the public's confidence in the role of NICE and its work including proposals to ensure that guideline development groups are inclusive of the appropriate and relevant healthcare professionals and patient representatives.

10.4 The RCN would welcome proposals for issues of diversity and inequality to become more influential and visible particularly for community based interventions in public health and health improvement.

10.5 The RCN recognises that NICE works hard to balance the needs of the patients and the demands on NHS resources. NICE is recognised internationally as having inclusive and high quality guidance development processes and this should be applauded. Its process is continually reviewed and it does change in the light of feedback.

Royal College of Nursing

March 2007

Evidence submitted by the Royal College of Physicians of Edinburgh (NICE 45)

The Royal College of Physicians of Edinburgh is pleased to respond to the House of Commons Health Committee on its Inquiry on the *National Institute for Health and Clinical Excellence (NICE)*.

Why NICE's decisions are increasingly being challenged

The College understands the perception that NICE's decisions are being challenged, but questions whether this is evidence based. Clearly, there has been considerable media attention to the decisions taken by NICE, and some recent concerns from patient support groups and the pharmaceutical industry eg drugs for Alzheimer's disease and multiple sclerosis. Such dissent may arise from concern about the fact that NICE generally takes an NHS perspective, and so is not able to take into account necessarily all the potential benefits that may come from an intervention, such as those to carers and associated with getting patients back to work.

Another concern, not now so often expressed, is that because NICE has its work programme defined by the Department of Health and the Welsh Assembly, it is influenced significantly by government. Health economists are core members of the NICE guideline development groups and cost effectiveness analysis is always undertaken, using the available economic data irrespective of quality. This may feed the view that NICE is there to ration healthcare rather than to evaluate the clinical effectiveness of healthcare interventions and comment on the resource implications.

NICE appraisals are carried out by methodologists, whose conclusions are reviewed or supported by healthcare professionals. This, coupled with concerns about the applicability of cost effectiveness data, may reinforce a perception that NICE decisions can be influenced unduly by government or special interest groups.

Over the years that NICE has been in operation, there has been a view that the organisation does not always interact constructively with the pharmaceutical industry, and certainly NICE keeps the industry very much at arm's length. This difficult relationship may have led to some of the criticism from industry. In addition, there has been concern from industry, and more recently by some well-informed patient support groups, that the Health Technology Appraisal (HTA) process, and the models used, are not completely transparent and are not open to external scrutiny.

Finally, high profile successful challenges, based on what may appear to be minimal additional evidence, will encourage more to follow the same path, as will a growing understanding of NICE methodologies.

Whether public confidence in the issue is waning and, if so, why?

It is not clear that public confidence is waning, although the high profile media response to certain decisions might sway opinion. It is clear that there are some concerns about the delay with which decisions are arrived at by NICE on important new drugs. One reason for the delay is that the Department of Health sets the agenda, and usually only does this some time after a new drug is licensed. In addition, the process at NICE for Health Technology Assessment takes over 12 months to complete, which means that decisions at NICE on new drugs often come in anywhere between 18 months and four to five years after decisions are made on similar medicines in Scotland by the Scottish Medicines Consortium (SMC). The media attention to such delays may have stimulated the recent creation of the rapid appraisal process at NICE called NICE Single Technology Assessment (STA).

Another concern about NICE is that its decisions, though intended to be binding in England and Wales, are not always well implemented and there are continuing allegations of a "postcode lottery" for some treatments. Whatever the extent to which these concerns are real, there is little doubt that they have been substantially amplified by the media.

NICE's evaluation process, and whether any particular groups are disadvantaged by the process

The process of NICE guidance is delivered from an NHS perspective, and primarily focuses on NHS costs. In this regard, there has no doubt been a concern that additional societal costs may not have been taken into account and, in particular, the costs associated with unemployment, the reduction in quality of life that may occur for other family members of someone with a severe illness, and the burden on carers or social services. Clearly, these issues are important in Alzheimer's disease and multiple sclerosis and have been a major focus of attention.

There has been a concern expressed that those who are older, where the ability to gain long-term QALYs is more difficult, may have been disadvantaged. However, this is denied by NICE and there is no clear evidence of age discrimination. Others have argued that those with substantially life-threatening conditions, such as cancer and heart failure, may gain a particular benefit from even short periods of additional life. An additional three months of life to somebody who is likely to live 10 or more years may be very different from an additional three months of life for somebody who has only three months to live. There is a concern that QALYs do not adequately capture the benefit of medicines that extend life under these circumstances.

The process itself can introduce an unintended but nonetheless systematic bias towards treatment in areas where there are existing funds available to demonstrate effectiveness (eg a new drug) at the expense of other areas for which there is little evidence. Similarly, conditions with a small number of patients may be disadvantaged as NICE gives priority to common diseases.

The speed of publishing guidance

As explained above, NICE MTA is a slow process that usually only begins after a drug is licensed and runs for a period of at least 12 months, even if there are no appeals against the decision. This delay, sometimes called “NICE blight”, is a well recognised problem in England and Wales that has been less of a problem in Scotland since the creation of the Scottish Medicines Consortium (SMC). The comparison between SMC and NICE has shown the latter in a bad light, and has attracted significant media attention. Indeed, the pressure has become so great on NICE in relation to cancer drugs that NICE has introduced a new process called NICE Single Technology Assessment (STA) to allow decisions to be made earlier. So far, this has only produced a relatively small number of outputs and it is not clear yet whether this new development, very much modelled on the SMC approach, will deliver the early decisions that are needed.

The quality of Health Technology Appraisal at NICE is unquestionable, and has been recognised in the recent OFT Market Report on the Pharmaceutical Price Regulation Scheme (PPRS), as has the quality of work by SMC. It is clear that the early appraisal process is an important model for the future. Later appraisal of multiple technologies for a single disease offers a complementary approach to reviewing the treatment of a disease area at a time that a substantially larger evidence base is available, some time after drug licensing when more clinical trials have been published, and both clinical and cost-effectiveness are likely to be clearer.

The appeal system

The appeal system is attractive for its transparency and inclusiveness, but extends the process substantially and therefore means that decisions are delayed. Also, and as stated above, it appears that decisions can be overturned on appeal with minimal additional evidence. It would seem that the appeal system may not be fit for purpose and could be telescoped in some way to the benefit of all parties.

Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)

It is interesting that the Health Committee draws particular comparison with SIGN, given that most public disquiet has been in comparison to the work of the Scottish Medicines Consortium (SMC) in relation to Health Technology Appraisal. This College (Royal College of Physicians of Edinburgh) created the SIGN network and continues to support its work following the transfer of the Executive staff to NHS Quality Improvement.

There are benefits to both systems. NICE clinical guidelines have been more willing to include assessment of both clinical effectiveness and cost effectiveness, and identify those treatments which provide good value for money. An example would be the NICE clinical guideline on hypertension, prepared with the British Hypertension Society, which gives a clear view on both clinical effectiveness and the cost effectiveness of different hypertension treatments and the order in which they should be introduced to achieve best value for money. However, the College understands that NICE Collaborating Centres work to their own rules and methodologies, which can be confusing for clinicians. Also, NICE does not have a robust method for ensuring all relevant stakeholders are engaged in guideline development and this may influence public and professional confidence.

SIGN focuses on clinical effectiveness and involves healthcare professionals fully in the development process, whether as members of the guideline development or participants in national meetings before the guidelines are completed. SIGN’s programme of work is selected according to clinical priorities and the availability of evidence and agreed with the Health Department. This builds professional and public confidence in the resulting guidelines and assists implementation.

NICE documents can be unwieldy and difficult to digest where SIGN documents are succinct and supported by quick reference guides for clinicians. However, there is significant overlap in the work of both and the College would be keen to see continuing collaboration over such issues as topic selection or sharing evidence

The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)

Health Technology Appraisals from NICE are mandatory within the NHS in England and Wales, whereas the clinical guidelines are not. On this basis, the clinical guidelines provide helpful advice whereas Health Technology Appraisal should dictate treatment. One would expect that NICE Health Technology Appraisal would be better implemented than the clinical guidelines, though both are generated with the intention of improving patient treatment. The College is unable to comment on the effectiveness of implementation of NICE appraisals and guidelines. An important next step would be an audit of

implementation of NICE guidance to provide the evidence on which to base any decision about how effective such guidance has been in moulding the behaviour of the NHS in England and Wales and their impact on clinical outcomes.

Guidelines perhaps provide a more significant implementation challenge, as they are designed to support clinical decision taking and there are often several competing (and sometimes conflicting) guidelines available to doctors and patients.

Royal College of Physicians of Edinburgh

March 2007

Evidence submitted by the Royal College of Paediatrics and Child Health (NICE 66)

Firstly, SIGN and NICE need to plan collaboratively what areas they will be developing guidelines for. They need to develop mutual respect for the roles they can each play and ensure that they work collaboratively without duplicating one another's work, in particular avoiding a situation where there are two "national guidelines" offering conflicting advice on the same clinical condition.

Secondly, the issue of implementation should be taken further than simply establishing whether the guidelines are being implemented. There should be a programme of national audits of the guidelines which encompass all practitioners in auditing both the process (ie whether the guideline is being implemented) and, arguably more importantly, whether the guideline is actually improving clinical care/standards.

On a wider issue, the DH need to consider their relationship with Map of Medicine, its use of the NICE guidelines, and how it is dealing with the "pathways" that Map are developing for areas where there are no NICE guidelines. The College is concerned that there is nothing on the map to indicate whether or not these particular pathways are objectively developed according to standardised guideline development programmes.

Royal College of Paediatrics and Child Health

March 2007

Evidence submitted by the Royal College of Psychiatrists (NICE 22)

The Faculty of Old Age Psychiatry of the Royal College of Psychiatrists (the Faculty) welcomes the Health Select Committees inquiry into aspects of the work of the National Institute for Health and Clinical Excellence (NICE) and for the opportunity to submit evidence to that inquiry.

Members of the Faculty have served as members of Guideline Development Groups, Expert Advisors to Health Technology Appraisals, on the Topic Selection Panel for Mental Health, as policy advisors to the Department of Health and have represented the Royal College of Psychiatrists at appeal against appraisals produced by NICE.

In submitting this evidence the Faculty recognizes the important role that NICE performs informing evidence based practice, in the quality control of clinical practice and the delivery of cost effective health care.

WHY ARE THE DECISIONS OF NICE INCREASINGLY BEING CHALLENGED?

1. We believe there are several reasons why this is the case. We have addressed most of these elsewhere in this response but summarise here, with specific reference to the Guidance on Alzheimer's disease, the Guideline for Dementia and the Guideline for Parkinson's disease. We believe these examples demonstrate why both the public and health professionals have good reason to be dissatisfied with decisions from NICE.

2. The clinical community and the public are concerned when a NICE judgement lacks a credible link with clinical practice or is irrational. We believe that both of these concerns apply to the NICE Guidance on the use of cognitive enhancing drugs for Alzheimer's disease (TA 111) which we discuss in more detail below. This may explain why this guidance attracted the largest number of responses to consultation of any NICE guidance and extensive criticism from national professional bodies, academic institutes and the public and may be the subject of Judicial Review.

3. In this example, the use of a simple scale is applied inappropriately in a rigid way to determine eligibility for treatment. This scale is not necessary in clinical practice and its intrinsic limitations mean that such rigid application is quite irrational and intellectually unsupportable. These points were made by experts during the Appeal against the Final Appraisal Determination but dismissed. The consequence is that people with early disease are ineligible for treatment (NICE confirming that these treatments are equally effective in the

early stage as later) which they can only receive once they have deteriorated to a more disabled state. This is irrational, the recommendations have no meaning in clinical practice and, consequently, lack credibility in the eyes of both the clinical community and the public.

4. Such an approach seems completely inconsistent with views expressed by Sir Michael Rawlins, the Chairman of NICE, in the *British Medical Journal* (2004) “Underlying all the decisions, however, is one fundamental social value judgment: that advice from NICE to the NHS should embody values that are generally held by the population that the NHS serves”. Further, we believe it is totally inconsistent with the Institute’s own position that, while it endorses the use of cost utility analysis in the economic evaluation of particular interventions, such information is a necessary, but not sufficient, basis for decision making. Social value judgements are also required. We believe that one of those generally held values is the early treatment of disease when effective treatment is available.

5. This failure of NICE to show consistency with regard to its basic principles must be challenged.

6. Furthermore, the Guideline for dementia (clinical guideline 42, also discussed below), published simultaneously, provides rather different guidance on the same matter. This is irrational.

7. There is great concern that NICE will totally disregard expert opinion. In the case of TA 111 respected experts, including advisors to NICE and the Department of Health, approached NICE to help resolve their irrational position while still achieve their intention to produce satisfactory guidance on cost effectiveness. These approaches were rejected.

8. In the case of Dementia of Parkinson’s disease (discussed in more detail below) not only did NICE disregard clinical opinion but also the scientific evidence when they over-ruled the guideline group. This was a serious betrayal not only of clinical opinion but also the fundamental principle of NICE that their recommendations always represent the evidence.

9. Discontent with NICE processes, particularly the composition of Health Technology Appraisal Committees and Appeals Panels, are shaking confidence in NICE. We address these below.

10. An example of the extent of this discontent was the decision by the Royal College of Psychiatrists Faculties of Old Age and Learning Disability Psychiatry with the British Geriatrics Society to issue a statement to its members reminding them of their professional duties as doctors which they believed were being compromised by the publication of TA111. This is a serious indictment by the major prescribers of the treatments that are the subject of that guidance.

WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING?

11. We believe this is the case. We believe it is also the case that clinician’s confidence in NICE is waning and this has very serious implications. We believe that clinicians are deeply concerned about some NICE procedures, particularly Health Technology Appraisals and the Appeals process, and the “editorial” influence exerted by NICE (see discussion on Dementia in Parkinson’s disease). We will expand on these issues with specific examples below.

12. Clearly this lack of confidence will influence the implementation of technology appraisals and clinical guidelines and if clinicians hold that opinion this will affect the confidence of the public. A lack of consistent implementation would seriously question the existence of NICE.

THE EVALUATION PROCESS AND WHETHER PARTICULAR GROUPS ARE DISADVANTAGED?

13. We wish to cite specific evidence that people with dementia and, by implication older people who are the main group affected by this condition, have been clearly and wrongly disadvantaged by the evaluation process. To demonstrate this belief we will specifically refer to the NICE recommendations on Alzheimer’s disease and Dementia in Parkinson’s disease as reflected in guidance and guidelines published in 2006.

14. The NICE technology appraisal on the clinical and cost effectiveness of cognitive enhancing drugs for the treatment of Alzheimers disease published as Guidance (TA111) in November 2006, has been seriously criticized by the academic and clinical community, and organizations representing patients and carers, may be subject of Judicial Review. The fact that this will be the first claim for Judicial Review against NICE is an indicator of the concerns raised by this appraisal and the increasing concern, or waning confidence, in NICE procedures.

15. We appreciate that a detailed criticism of this appraisal is not the purpose of this inquiry but would draw the Committees attention to the notes of the Appeal against this guidance where many of these issues were raised.

16. However, it is pertinent to this aspect of the Committees inquiry to note that the Appraisal Committee employed measurements, particularly those for the assessment of intellectual function and quality of life, inappropriately to serve the purpose of the appraisal and not to represent clinical practice. We believe that this is evidence of a flawed process that has disadvantaged older people and people with Alzheimer’s disease.

17. We believe that this poorly informed judgement is partly explained by the constitution of an appraisal committee which, purposefully, excludes people with expert knowledge of the subject to be appraised. Consequently, a fundamentally crucial understanding of the condition is absent from the appraisal process. In the case of the Alzheimer's disease appraisal no member of the committee had any special expertise or knowledge of the condition and no clinical competence in its treatment. While experts in the field are consulted, we are aware of many who gave evidence in the development of this HTA and the appeal who considered their views were summarily disregarded.

18. We believe that this exclusion is unfortunate and misguided. NICE justify this policy decision on the basis that the committee will have no vested interest in the outcome. We believe this is naïve as everyone working in the NHS and the public has a vested interest in the distribution of NHS resources, and therefore, the outcome of every health technology appraisal. Furthermore, if the assertion of NICE is true that its guidance and guidelines simply reflect the evidence then it should not matter how the committee is constituted other than to be sure that it has the capability to absorb, understand and interpret that evidence. We believe that a detailed knowledge of the condition or circumstance in question is a necessary prerequisite to establish that capability and a process that only seeks that capability by advice is flawed.

19. We believe that a committee that includes experts in the field in question is more likely to have that expertise and produce meaningful guidance. Furthermore, a committee that includes experts in the field will give far greater credibility to that guidance in the eyes of practitioners and the public and this has implications for confidence in the recommendations and subsequent implementation. Clinical guidelines, on the other hand, produced by a stakeholder guideline group involving informed professionals and the public, are received, in our experience, with far greater confidence as they are seen to have clinical validity.

20. We believe this point is made, in the case of drug treatments for Alzheimers disease, by contrasting the response to the controversial guidance (TA 111) and the guideline for dementia (NICE clinical guideline 42) that were published simultaneously in November 2006. The former remains highly controversial and may be the subject of Judicial Review while the latter has been received with considerable acclaim. That NICE decided to publish the two documents as one highlights this contrast while at the same time causing confusion with contradictory recommendations about the use of drug treatments sitting within a single document. This is irrational.

21. The NICE clinical guideline for the diagnosis and management of Parkinsons disease (PD) was published in June 2006. In the main it has been well received and seen to represent good practice. We wish to draw the Committees attention to the recommendations for the treatment of Dementia in Parkinsons disease (PDD) with cholinesterase inhibitor drugs (pages 121-124 of the full guideline). These are the same class of drugs that were the subject the Alzheimer disease appraisal (TA 111).

22. In this instance NICE over-ruled the guideline group, disregarded the evidence, imposed its own position and disadvantaged people with dementia. This is the only recommendation within the guideline where this occurred and, therefore, NICE chose to treat the case of dementia differently.

23. It is clear from the evidence that these drug treatments are effective and safe in the treatment of PDD. This is demonstrated by the evidence that was available to the guideline development group. This would normally be considered by NICE to represent a high level of evidence producing a recommendation for use and annotated to reflect that. In the draft version this was properly reflected in the recommendation that these drugs may be used with the appropriate annotation.

24. Despite the evidence, NICE refused to publish that recommendation in the guideline and over ruled the opinion of the guideline development group. Contrary to strong objections from the guideline development group the recommendation was changed by NICE. This is a direct contravention of the fundamental principle that NICE guidelines always reflect the evidence.

25. And so the published guideline recommendation reads:

“Although cholinesterase inhibitors have been used successfully in individual people with PD dementia, further research is recommended to identify those patients who will benefit from this treatment.”

26. The rating of the recommendation is that of a good practice point (annotated as D (GPP)), which indicates a low level of evidence and only the opinion of the guideline group. A recommendation based on the findings of a large randomized controlled trial, as in this case, will usually be identified by the NICE annotation A or B, indicating a high level of evidence. In the case of PDD the status of the evidence has been misrepresented by NICE.

27. The view of the guideline development group is still contained in the evidence to recommendation section that precedes the recommendation (page 123 of the full guideline) but is not reflected in the recommendation:

“There is evidence from randomized placebo controlled trials of the effectiveness and safety of cholinesterase inhibitors in the treatment of PDD. They are effective in treating both cognitive decline and psychosis in this context.

At the time of writing only one of the cholinesterase inhibitors has a product licence in the UK. The GDG considers that these are useful agents that are commonly used in clinical practice and that they should be available.”

28. Importantly, the full guideline is rarely consulted by most practitioners who will refer to the short guideline version to inform their practice and will not be aware of these statements that actually reflect the evidence based position.

29. We believe, in the case of PDD, that NICE has overruled expert opinion based on evidence and has failed to maintain its fundamental principle of presenting evidence based guidelines.

THE APPEAL SYSTEM?

30. We believe the NICE appeal system is unsatisfactory and perverse.

31. Members of the Faculty have first hand experience of appeal against NICE guidance and we will focus on the appeal against TA111, the guidance on cognitive enhancing drugs for the treatment of Alzheimer's disease held in July, 2006.

32. In this case, there were five appellants with the Royal College of Psychiatrists and British Geriatrics Society submitting a joint appeal. Two members of this joint appeal had acted as expert witnesses to the Health Technology Appraisal Committee. Despite this appraisal being highly controversial every point raised by the five appellants was dismissed by the Appeals Panel.

33. In this instance, the Appeals Panel consisted of five members appointed by NICE. Three of these were working for NICE. The Chair of the Panel was the Vice Chair of the Board of NICE itself.

34. Regardless of the integrity of individual members of the Appeals Panel this must raise concerns about impartiality and cast doubt on the objectivity and credibility of the Panel's judgement. There can be no doubt that this panel had an obvious conflict of interest. This will inevitably lead to a cynical and deeply suspicious response to the guidance that will, undoubtedly, affect implementation by clinicians and confidence in NICE.

35. We consider it unacceptable that a panel charged with the responsibility to hear an appeal against the processes of a NICE appraisal should be either appointed by NICE itself or include people working for NICE.

36. It is contradictory that NICE exclude experts from Health Technology Appraisal Committees on the basis that they have a vested interest in the outcome but do not apply the same reasoning to the constitution of an Appeals Panel.

37. We believe that an Appeals Panel should be entirely independent of NICE and that this would be in the best interests of NICE and the National Health Service.

COMPARISON WITH THE WORK OF THE SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK (SIGN)?

38. The SIGN Guideline on the Management of Patients with Dementia (SIGN 86) was enthusiastically received across Scotland. This was published before the NICE Guidance (TA111) and the NICE Guideline (clinical guideline 42). The development of the SIGN guideline is broadly similar to that of a NICE guideline.

39. In relation to dementia the SIGN Council specifically referred to a study (known as the AD2000 trial) which they felt was methodologically flawed and suspect and the SIGN Guideline Development Group expressed the view that this study was given too much weight in the production of the recommendations of TA111 by NICE. This was also a point of concern raised at the appeal against TA111 but dismissed by the Appeal Panel. Clearly the experts on the SIGN development group had similar concerns to experts in England about the process employed by NICE in producing this particular guidance and the decisions of an appraisal committee without knowledge of Alzheimer's disease.

40. SIGN is now absorbed into the remit of NHS Quality Improvement Scotland (QIS) but retains its independence and SIGN guidelines are respected by the Scottish Executive. In relation to dementia NHS QIS, required to endorse NICE guidance, recommends referring to the SIGN dementia guideline when interpreting TA111 guidance. We believe that this provides further evidence that the recommendations contained in TA111 lack the confidence of a large body of experts and our belief that NICE processes have disadvantaged people with dementia.

THE IMPLEMENTATION OF GUIDANCE, BOTH TECHNOLOGY APPRAISALS AND CLINICAL GUIDELINES (WHICH IS ACTED ON, WHICH IS NOT AND THE REASONS FOR THIS)?

41. In general, guidelines produced by an informed stakeholder group are less controversial than guidance produced by a health technology appraisal committee that purposefully excludes informed people. This is partly because the former has greater credibility with clinicians who recognize and respect recommendations that reflect good practice produced, as they are, by professionals and the public involved with these aspects of health care. Guideline groups understand the issues in question, understand the clinical context and are able to understand and interpret the evidence.

42. Technology appraisal committees on the other hand, as we have stated, lack all of these essential attributes. For psychiatrists to receive a mandatory direction on the treatment of, for example Alzheimer's disease, from cardiologists, anaesthetists, neo-natal paediatricians and others, or, for a neo-natal paediatrician to receive a direction from psychiatrists, orthopaedic surgeons and dermatologists, for example, is a process which is perverse and lacks credibility. This will be reflected in the way such guidance is received by clinicians and this will reflect the likelihood of implementation.

43. In answer to the question "which guidance is acted on" the answer would be guidance in which clinicians have confidence because they believe it arises from a reliable and informed source, and evidence base, and has a meaningful connection with clinical practice.

Dr David Anderson
Chair of the Faculty of Old Age Psychiatry
Royal College of Psychiatrists

March 2007

Evidence submitted by the Royal National Institute of the Blind (RNIB) (NICE 63)

BACKGROUND

1. RNIB is the leading UK charity helping blind and partially sighted people. One of our Royal Charter objectives is the prevention of blindness and in this context we are involved in NICE's appraisal of two new powerful drugs for treating wet Age-related Macular Degeneration (AMD), the main cause of registerable blindness in the UK. In addition, we are consultees for the development of guidance on the treatment and management of glaucoma and are members of the PiN (Patients in NICE) group.

2. We would like to limit our observations to a number of the questions set out by the Committee in its press notice of 2 February, which reflect our direct involvement with NICE.

EXECUTIVE SUMMARY

Why are NICE's decisions increasingly being challenged?

3. As a patient organisation RNIB has had to challenge NICE's decisions because of its failure to take adequate account of the impact of sight loss on patients who have conditions that can be treated.

4. In addition, we have challenged NICE's decisions because of the lack of consideration of costs of disease that are outside the NHS and Social Services remit.

NICE's evaluation process

5. We feel that the evaluation process is very thorough and reasonably open. However, it is likely that smaller charities representing orphan diseases will find it much more difficult, if not impossible to contribute to any appraisals.

The speed of publishing guidance

6. The speed of publishing guidance is a very serious issue because of the uncertainty created from the time when a new treatment is licensed for use in the UK until the time when NICE issues its guidance. Unfortunately, this has led to a post-code lottery with some PCTs providing funding and others not. In areas where funding is not available, having failed in their appeal, patients are then forced to opt for private treatment.

7. Against this background it is not surprising that many people are questioning the time it takes for NICE to come to a decision, particularly when the Scottish Medicines Consortium manages to issue guidance on new drugs within three months of their marketing authorisation.

Implementation of NICE guidance

8. In a report published in 2005 the National Audit Office found that only 26% of NHS bodies participating in their study regularly undertook horizon scanning to assess the financial impact of forthcoming guidance on their organisation.

9. At present neither NICE, nor the NHS are collecting relevant data on implementation. The only available data is that provided by the drug manufacturers. The systematic collection of data by the NHS would facilitate an assessment of gaps in the provision of treatment in different parts of the country.

OUR DETAILED COMMENTS

WHY ARE NICE'S DECISIONS INCREASINGLY BEING CHALLENGED?

10. In 2003 RNIB mounted a robust challenge to NICE over its decision to reject the use of photodynamic therapy for the treatment of wet Age-related Macular Degeneration on the NHS. The main reasons for this were:

- NICE's failure to take adequate account of the impact of sight loss through AMD on patients with the condition.
- Lack of consideration of costs of disease that are outside the NHS and Social Services remit.

NICE's failure to recognise the impact of sight loss on a person's quality of life

11. As a patient organisation RNIB aims to gauge patient views in discussions about the availability of treatments while at the same time using an evidence-based approach to establish our general policy. From a patient perspective, the need to make economic decisions about the availability of treatments is hard to accept. Patients affected by a condition that is treatable feel that they should not be forced to pay for private treatment. In the case of AMD these are often elderly patients who have paid taxes all their lives and expect treatment on the NHS.

12. While most people feel that they have right to treatment they also recognise that the NHS does not have unlimited resources and that some treatments need to be prioritised over others. What they do not accept is an assumption that sight loss is not a severe disability, that people can adapt to losing their sight and that therefore treatment is not a priority. We contend that the main tool used by NICE to assess cost effectiveness (QALY values) does not adequately reflect the severe impact sight loss has on a person's quality of life.

13. This view is supported by a number of studies. In the case of AMD a literature review commissioned by the AMD Alliance International strongly questions the use of QALY values to measure quality of life in AMD patients. The authors of the review contend that: "The QALY values obtained using time trade-off and standard gamble methods are not measuring quality of life and such measures give no impression of the ways in which AMD impacts on a person's life. There are many reasons why a person may not want to relinquish any years of life in spite of serious visual impairment but this does not imply that they are content with the present situation or that their quality of life would not be much better without their vision problems."¹²⁵ In addition the use of QALY values puts people with long-term conditions at a disadvantage over people with life-threatening conditions. Our concern is that drugs that extend life will always achieve higher values even if they do not guarantee a high quality of life.

14. The concerns outlined above compel us to call on NICE to review the tools it uses to assess quality of life gains as part of its technology assessments.

Lack of consideration of costs of disease that are outside the NHS and Social Services remit

15. NICE appraisals only take account of costs of non-treatment to the NHS and Social Services. In the case of sight loss this ignores a whole range of additional costs to the economy due to the provision of care to blind and partially sighted people. These include benefits, tax allowances, transport, education and training costs, employment services, informal care and productivity loss.¹²⁶ As the retirement age is being raised these costs will increase. Not taking them into account is a serious flaw in NICE's decision-making.

EVALUATION PROCESS

16. We feel that the evaluation process is very thorough and reasonably open. As a large charity we are fortunate to be able to put the required resources into participating in a consultation. However, it is likely that smaller charities representing orphan diseases will find it much more difficult, if not impossible to contribute to any appraisals. The drawn-out process and the level of technical knowledge required are likely to exclude some patient organisations.

THE SPEED OF PUBLISHING GUIDANCE

17. The speed of publishing guidance is a very serious issue because of the uncertainty created from the time when a new treatment is licensed for use in the UK until the time when NICE issues its guidance. The Department of Health has made it clear on numerous occasions that absence of NICE guidance is not a reason for PCTs to avoid taking decisions on the provision of funding for new treatments. PCTs should decide on the basis of available evidence whether individual patients should receive treatment on the NHS.

¹²⁵ Mitchell J, Bradley C: Quality of Life in AMD: A review of the literature. AMD Alliance International. September 2006.

¹²⁶ Winyard, S: The cost of sight loss in the UK. RNIB campaign report 23 August 2004.

18. Unfortunately, this has led to a post-code lottery with some PCTs providing funding and others not. PCTs are careful not to use the absence of NICE guidance as the sole excuse for not providing treatment. However, more often than not, exceptionality rules applied in case-by-case appraisals represent a de facto ban and appeals are usually unsuccessful since they need to prove that there have been procedural errors or that new evidence supports treatment.

19. Having failed in their appeal patients are then forced to opt for private treatment. In fact, in the case of AMD, they have to take that decision even before a PCT has looked at their case because the “window of opportunity” for treatment is very narrow and they risk losing their sight by the time they have gone through the appeals process.

20. Against this background it is not surprising that many people are questioning the time it takes for NICE to come to a decision, particularly when the Scottish Medicines Consortium manages to issue guidance on new drugs within three months of their marketing authorisation.

IMPLEMENTATION OF NICE GUIDANCE

21. Implementation of NICE guidance and the introduction of the new treatments, if they are recommended by NICE, is not part of the work of the NICE appraisal committee. However, assisting with introduction and monitoring is within the overall remit of NICE as shown on the NICE web site: “NICE has set up a programme to help support implementation of NICE guidance. The implementation team does not get involved in developing the guideline recommendations but works alongside the guideline developers, the communications team and field based teams to:

- Ensure intelligent dissemination to the appropriate target audiences.
- Actively engage with the NHS, local government and the wider community.
- Work nationally to encourage a supportive environment.
- Provide tools to support putting NICE guidance into practice.
- Demonstrate significant cost impacts—either costs or savings at local and national levels.
- Evaluate uptake of NICE guidance.
- Share learning.
- Develop educational material to raise awareness of NICE guidance and encourage people to input into its development”.

22. When NICE finally approved the use of photodynamic therapy for choroidal neovascularisation (wet AMD), having had it under review for two and a half years, a further nine months delay was imposed by the Department of Health because no groundwork had been done on how to introduce the treatment. Although we do not have data on other drugs, we can assume that this is not a unique occurrence. In a report published in 2005 the National Audit Office found that only 26% of NHS bodies participating in their study regularly undertook horizon scanning to assess the financial impact of forthcoming guidance on their organisation.

23. Work is currently ongoing to assess the implications for service configuration and delivery if, as expected, NICE approves the new treatments for wet AMD for use on the NHS. However, we are not confident that this will be sufficient to ensure that all eligible patients presenting for treatment will receive funding during the coming financial year.

24. Finally, we strongly welcome NICE’s aspiration of evaluating the up-take of its guidance and feel that this should be an ongoing process. The problem is that there does not seem to be any independent way of assessing the level of up-take. At present neither NICE, nor the NHS are collecting relevant data. The only available data is that provided by the drug manufacturers. The systematic collection of data by the NHS would facilitate an assessment of gaps in the provision of treatment in different parts of the country.

CONCLUSION

25. As a major patient organisation our responsibility is to ensure that people with sight threatening conditions receive the best possible treatment to prevent avoidable sight loss. We recognise that NICE has an important role to play in assessing the safety and efficacy as well as the cost-effectiveness of new treatments to help end the post-code lottery that has bedevilled the provision of treatments in England and Wales. Unfortunately, NICE is playing this role at a time when the ability of the NHS to meet patients’ expectations is increasingly being questioned. With or without NICE guidance PCTs have to make difficult choices partly based on evidence but also increasingly determined by the level of pressure they experience from the media and/or patient organisations.

26. Increasingly, the ability to lobby for treatments is becoming a deciding factor. This is not where most people would have imagined the NHS ending up and it raises questions about the way prioritisation in the NHS is being handled. There may therefore be a case for additional Government intervention, or perhaps the abolition of £2 billion worth of unnecessary procedures that the Government has identified in efforts to reduce financial pressures.

27. However, outside this wider debate NICE needs to continue its role in a more streamlined manner, with shorter consultation periods, redefining quality of life and cost issues and focusing more strongly on implementation.

Barbara McLaughlan
Campaigns Manager, Eye Health and Social Care
RNIB

March 2007

Evidence submitted by Sanofi-aventis (NICE 57)

EXECUTIVE SUMMARY

Sanofi-aventis endorses the aims of NICE, which is to provide national guidance for more equitable access to modern treatments in England and Wales, on the basis of cost effectiveness rather than affordability. NICE is a relatively “youthful” organisation which has undergone a constant process of review since its inception, including the Health Select Committee (HSC) Inquiry of 2002. The recent introduction of the new Single Technology Appraisal (STA) process is to be particularly welcomed. However, as with any new process, there are some issues and inconsistencies that need to be addressed.

Implementation of NICE guidance remains subject to regional variations, and a mechanism should be found to ensure that NICE guidance is fully implemented across England and Wales.

Full engagement in all elements of NICE’s work, and that of other UK HTA agencies, is extremely resource intensive for all stakeholders. Serious consideration should be given for a review on the suitability of the current arrangements for HTA in the UK. This includes whether three independent review bodies add value or whether a single UK body might be more appropriate. An expanded NICE, with a national remit to assess all products at or prior to launch, must only be considered in close collaboration with other stakeholders.

INTRODUCTION TO SANOFI-AVENTIS

1. Sanofi-aventis is Europe’s largest pharmaceutical company, and ranked number three in the UK. Backed by a world-class R&D organization, Sanofi-aventis is developing leading positions in seven major therapeutic areas: cardiovascular medicine, thrombosis, oncology, internal medicine, metabolic disorders, diseases of the central nervous system, and vaccines.

2. Our portfolio of medicines mirrors the priorities of the National Health Service which are to: reduce mortality from heart disease; reduce mortality from cancer; reduce mortality from suicide; reduce adult smoking rates and tackle obesity and support people with long term conditions. We also have an equally exciting pipeline of new medicines and are well placed to help meet the present and future needs of patients and healthcare professionals alike.

3. Sanofi-aventis is committed to the UK, as shown by our investment in six sites in the UK, which reflect the full range of product life cycle activities—from pre-clinical development of new molecules through to manufacture and distribution, marketing, regulatory compliance, product education and professional support.

4. Sanofi-aventis (as both legacy companies and as Sanofi-aventis) has extensive experience of NICE. We have undergone twenty-two NICE appraisals, and Sanofi-aventis contributes as a stakeholder to the development of several other appraisals and guidelines.

NICE’S EVALUATION PROCESS

5. The last HSC inquiry into NICE (2002) made several recommendations which resulted in various refinements to NICE’s evaluation process. These improvements are welcome but we still have concerns about some key phases of the appraisal processes:

Topic Selection Process

6. Sanofi-aventis welcomes the recently revised topic selection process. However, we have concerns that this new process is not sufficiently transparent and needs further refinement. Having introduced new topic consideration panels, the Institute now publishes the notes of their meetings on its website. However, in their present form the notes are insufficiently detailed and too vague, in respect to pharmaceutical technologies, to understand why the decisions were made in the first place. Furthermore, the role and quality assurance of the National Horizon Scanning Centre in Birmingham in the new process is not clear.

7. There is extensive consultation between NICE and the manufacturer about the draft remit and scope of a particular technology appraisal, before the topic selection process is completed, and the Minister decides, which technologies are selected for inclusion in the next wave of appraisals. The consultation on “minded” referrals is a very useful exercise but, overall, the current process can take many months before final referrals are made. This can therefore result in increased delay to the assessment of new technologies and is inefficient for the Institute.

8. Following the scoping exercise, NICE and the Department of Health, collate the feedback and prepare a recommendation to Ministers on which technologies should be included in the next wave. The recommendations are not released to stakeholders meaning there can be no transparency as to the rationale and criteria behind the recommendations. Ultimately, when a wave is announced, it is often unclear why certain technologies have been selected for appraisal, and why certain assessment processes—multiple, or single technology appraisal process or guidelines—are considered most appropriate for the technologies in question.

9. We believe that attention should be given to further reducing the time taken to make final referrals to the Institute. Furthermore, greater transparency regarding the methodology, rationale and criteria for the topic selection process, including publication of the conclusions and recommendations put to Ministers, should be introduced.

10. There should be more transparency regarding the methodology, rationale and criteria for the topic selection process, including publication of the conclusions and recommendations that are put to Ministers.

11. Time taken in the topic selection process should be reduced by having the Department of Health and Ministers take final decisions on topic selection within one month of publication or each wave.

Single Technology Assessments (STAs)

12. We welcome the new STA process. It is hoped that the newly introduced STA process will speed up evaluations by the Institute, and result in the more speedy and efficient publication of guidance to the NHS and healthcare professionals when it is both appropriate and evidence permits. However, producing this guidance should not be at the cost of full, thorough and open consultation. The Expert Review Group (ERG) report, which is an assessment of the manufacturer’s submission and forms the basis of the Consultation panel’s deliberations, is not made available to manufacturers before it goes for consideration by the assessment panel. Industry should be given the opportunity to make representations about the ERG’s report to the Consultation Panel. Currently the only way to raise any issues is at the ACD or appeal stage. A more collaborative approach, earlier in the process, would be beneficial to all parties and would lead to more efficient decision making.

13. A more collaborative approach should be sought for STAs, to enable industry to make representations about the ERG report, prior to a decision being made.

14. As a relatively new process, we appreciate that many elements of the STA methodology are yet to be fully tested in practice. A key example is the actual process to define the “decision problem”. This element of the process requires further clarity to set out how it works in practice. Particularly when the decision problem submitted by a manufacturer is not accepted by the Institute in itself, which has an impact on further negotiations on the timelines for appraisal

15. Greater clarity is required around the process of establishing the “decision problem” in the STA process.

SPEED OF PUBLISHING GUIDANCE

16. Sanofi-aventis recognises that as NICE’s work programme increases, it will need to work hard to provide the NHS with holistic guidance that updates, cross references and reflects the interdependent nature of NICE’s different work programmes. Therefore, the speed of publication of guidance may vary significantly, and may be subject to delay when the Institute is developing related technology appraisals and clinical guidelines in parallel.

17. Given the continual expansion of the Institute’s work programmes, further transparency is required to clarify how related streams of work interact and influence one another. For instance, how a guideline development group and an appraisal committee should work together in developing their recommendations. Clearly, the two groups should work in close collaboration where remits overlap, but there is no explicit process as to how this should take place. For example, at which stages in the production of the guidance/guidelines do the two groups collaborate? How should any disagreements or conflicts be resolved? What contingencies are in place if the two groups are unable to reach agreement?

18. Greater clarification is required to define how the appraisal development groups and the guideline developing group should work together.

APPEAL SYSTEM

19. Despite changes implemented as a result of the recommendations in the last HSC inquiry, Sanofi-aventis continues to question the transparency of the appeal process. The appeal panel continues to be chaired by the Chairman of NICE and is predominantly staffed by non executive directors of the Institute. Limited public places are now available for the actual appeal hearing (which is a step in the right direction), but the panel's deliberations are still held in private. This end-stage of the appraisal process is therefore neither compatible nor consistent with the Institute's stated aims of transparency.

20. Additionally, it is at the discretion of the Appeal Panel Chair as to how an appeal is heard. Sanofi-aventis has noted that this occasionally results in inconsistency between appeals which is a disadvantage to NICE stakeholders.

21. The Appeal panel's evidence and deliberations should be fully transparent and made public within a reasonable and consistent time frame.

NICE COMPARISON WITH SCOTTISH MEDICINES CONSORTIUM (SMC) AND ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

22. NICE's remit covers England, Wales and Northern Ireland. In parallel, the AWMSG plans to prepare its own guidance for all cardiovascular and oncology technologies at launch, as well as for other existing high cost, low volume technologies. The SMC is responsible for producing guidance for Scotland, although NHSScotland will recognise MTA guidance, but currently not STA recommendations. This situation is confusing and potentially perpetuates the so called "post code lottery". HTA stakeholders in the UK are required to deal with three separate bodies, each with different purpose, requirements and methodologies. This is time consuming, resource intensive and results in duplication of effort. Sanofi-aventis recommends that a review be undertaken to consider the suitability of the current arrangement and assess whether three independent review bodies add value or whether moving towards a single UK body might be more appropriate.

23. A review should be undertaken to consider the suitability of the current arrangement and assess whether three independent review bodies adds value.

IMPLEMENTATION OF NICE GUIDANCE

24. Whilst we welcome the establishment of NICE's Implementation Directorate and the increased prioritisation of support for implementation, we remain concerned that implementation of NICE guidance can vary widely across the country. We hope that the Health Select Committee will propose solutions for NICE guidance to be fully implemented, in a fair and equitable fashion, across the country and the NHS.

25. NICE has put significant resource into establishing its own in-house implementation team to provide support to PCTs on the practical and financial considerations of implementation. This is admirable given that NICE has no formal jurisdiction to ensure implementation of its guidance. However, it is difficult to assess how effective the in-house NICE Guidance Implementation Team has been to date. This is because variation in the implementation of NICE guidance across the country remains striking.

26. A thorough review should be undertaken to assess the impact of the NICE implementation team, and the value to the NHS of its outputs.

27. NICE has recently initiated a new work programme to review ineffective practice in the NHS. Whilst supporting the programme's overall objectives, Sanofi-aventis questions whether it is appropriate to label products as "ineffective" before they have been fully assessed. Furthermore, it is unclear why a separate work programme is required to assess these products and why guidance could not be achieved using the multiple technology appraisal process which is already in place and well established.

28. Finally, Sanofi-aventis request that the Institute clarifies its process for selecting ineffective practice review topics. The current topics in progress were selected in-house by the Institute which is inconsistent with its topic selection process for all other work programmes.

29. There should be a review of the ineffective practices programme to consider whether its aims could be achieved under the existing technology appraisal processes.

SUMMARY OF RECOMMENDATIONS FOR ACTION

- There should be more transparency regarding the methodology, rationale and criteria for the topic selection process, including publication of the conclusions and recommendations that are put to Ministers.
- The topic selection process should be reduced and Ministers required to make final decisions regarding topic selection within one month of publication of each wave.
- A more collaborative approach should be sought for STAs, to enable industry to make representations about the ERG report, prior to a decision being made.

- Greater clarity is required around the process of establishing the “decision problem” in the STA process.
- Greater clarification is required to define how the appraisal development groups and the guideline developing groups should work together.
- The Appeal Panel’s deliberations should be transparent and made public within a reasonable and consistent time frame.
- A review should be undertaken to consider the suitability of the current arrangement and assess whether three independent review bodies (SMC, AMWMSG and NICE) adds value.
- A thorough review should be undertaken to assess the impact of the NICE implementation team, and the relative effective change it is bringing to the NHS.
- There should be a review of the ineffective practices programme to consider whether its aims could be achieved under the existing technology appraisal processes.
- There should be greater transparency and clarity around the review of the ineffective practices programme.

Sanofi-aventis

March 2007

Evidence submitted by Schering Health Care Limited (NICE 56)

INTRODUCTION

1. We welcome the Health Committee Inquiry into aspects of the work of the National Institute for Health and Clinical Excellence.
2. We fully support all the points made in the submission by the Association of the British Pharmaceutical Industry, and wish to take this opportunity to highlight a number of additional issues based on our experience within the process.
3. As a specialist pharmaceutical company, we lead in our four fields of business:
 - gynaecology & andrology—global market leader in female contraception;
 - diagnostic imaging—expert in MRI contrast media;
 - oncology—leading position in haematological oncology; and
 - specialised therapeutics—pioneer in treatment of multiple sclerosis.
4. The evidence provided below is drawn from our experience of both the Multiple and Single Technology Appraisal (MTA and STA) processes and our participation as Consultee and Commentator on a number of occasions.

SCOPING OF NICE APPRAISALS

5. The duration of NICE appraisals is of particular significance and impact in the area of oncology. Advances in cancer treatment are often fast when effective products become available. A typical pattern is that of effective single agents being combined with other agents to even further improve their efficacy. This research evolves more rapidly than either a pharmaceutical company can match in terms of licensing or NICE can review. Despite this, if a certain combination proves effective, it becomes clinical practice regardless of licence. However, NICE does not scope its appraisals in terms of current clinical practice, rather the scope is crafted within the narrow confines of a product licence, even though it is clear (eg from randomised controlled trials) that patients would be better served with the newer combination treatment than any pre-existing treatment available on the NHS. In these situations it wastes government and public money pronouncing on monotherapies that nobody uses and preventing effective combination therapies being made available to patients.

APPRAISAL PROCESS FOR TREATMENT OF LONG-TERM CONDITIONS

6. Chronic diseases by their very nature are not curable and, in many cases, patients health and quality of life deteriorates slowly over many years. Treatments for such diseases are often given early in the course of the disease, in order to delay the disease progression. In these instances many major benefits (in terms of cost effectiveness) are not realised until many years after the treatment is initiated.

7. For example in multiple sclerosis patients become increasingly disabled. The median time to reach irreversible disability are 8 years regarding limitation of ambulation, 20 years for walking with a stick, and 30 years for wheelchair dependency.¹²⁷ Interferon-beta, given early in the course of the disease, slows the

¹²⁷ The Natural History of Multiple Sclerosis, Confavreux C, Vukusik S, *Rev Prat* 2006 Jun 30;56(12):1313-20

rate of disability progression. However whilst the major costs (ie drug treatment costs) occur early in the disease the major cost and quality of life savings occur much later when the treated patient has not progressed, has not become wheelchair bound and is still able to look after their children and work.

8. Whilst it is possible to model the cost and quality of life benefits of delaying disability progression it is not possible to assess these in randomised clinical trials. The results of models using longer term time horizons are therefore, by necessity, much less certain than those for acute diseases. When reaching its recommendations NICE assess levels of uncertainty around model outputs but makes no allowance for the fact that levels of uncertainty are necessarily higher when using long-term time horizons which are entirely appropriate for chronic conditions. Long-term conditions are therefore disadvantaged compared to acute therapies.

9. The current appraisal methodology does not take into account other factors that may be equally as important to either the patients with a chronic disease, where even small benefits of treatment make significant differences to their lives and abilities to support themselves, or the state systems supporting patients with chronic diseases. The major costs and benefits with chronic disease are often seen 15-20 years from diagnosis. Hence it would be more appropriate to include societal costs in the decision-making. Again, using the example of MS, this could be particularly significant when you consider that MS is more frequently diagnosed in people during their most productive years, typically between 20 and 40 years of age.

10. In order to adapt the appraisal process so that it is as fair for long-term conditions as it is for acute therapies, societal benefits should more obviously be taken into consideration and a larger range of uncertainty should be accepted when treatment benefits require modelling over a longer period of time. This would help correct the current inequality for patients requiring treatment for chronic diseases.

COMPARISON WITH WORKING WITH THE SCOTTISH MEDICINES CONSORTIUM (SMC)

11. Our overall view when comparing our interactions with NICE versus working with the SMC is that there are areas where the lack of dialogue and transparency with NICE make the process adversarial and inefficient.

12. It is easier to have open, constructive communication with the SMC. Whilst NICE have scheduled scoping meetings, we have found it difficult to have constructive dialogue regarding submission content. In discussions with NICE about whether modelling using assumption x or assumption y would be preferable, the response is often that we should do whatever we feel is appropriate. We have, typically, found the SMC to much less process driven and more willing to discuss submission content ensuring that their new drugs committee receives the information it needs to reach its decisions.

13. We would therefore welcome more open dialogue and debate at an earlier stage within a NICE review on matters such as the most appropriate methods of modelling or data collection, and agreement of the assumptions to be used within cost effectiveness models.

Schering Health Care Limited

March 2007

Evidence submitted by ScotME (NICE 91)

1. EXECUTIVE SUMMARY

1.1 This submission is relevant to three issues identified by the Health Select Committee. These are:

- why NICE's decisions are increasingly being challenged;
- whether public confidence in the Institute is waning, and if so why;
- NICE's evaluation process, and whether any particular groups are disadvantaged by the process.

1.2 These are addressed considering the Institute's evaluation process as it operated in the development of the recent draft guideline on diagnosis and management of "CFS/ME",¹²⁸ to illustrate how the guideline development process can produce unacceptable results.

1.3 Myalgic encephalomyelitis (ME) charities and voluntary groups have comprehensively condemned this document, seriously challenging the suitability of the Institute's draft guideline. These concerns give rise to a lack of confidence in the Institute. The main issues are:

¹²⁸ "Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children" draft for consultation, National Collaborating Centre for Primary Care, September 2006.

1.4 *Diagnostic guidance*—The Institute’s guidance conflates ME—a neurological illness with a unique and distinctive clinical presentation—with chronic fatigue due to mental health problems. These conditions are classified separately by the World Health Organisation. Furthermore, management approaches which may help the latter group of patients are contra-indicated in respect of those with ME. This basic flaw renders the guidelines unsuitable for their purpose.

1.5 *Composition of Guideline Development Group (GDG)*—It is notable that few, if any, of the GDG had direct clinical experience of the illness they were advising upon. Authoritative medical professionals and researchers with in-depth experience and understanding of the neurological disorder ME were absent from the GDG, while representatives with a belief in a “biopsychosocial” theory (which does not stand up to critical scrutiny) were many.

1.6 *Eligibility and assessment of evidence*—Difficulties arise from the narrow view taken as to what constitutes admissible evidence, with the consequent potential for a broad range of relevant information being disregarded. This can lead, as with proposed document on “CFS/ME”, to false conclusions and inappropriate and dangerous guidance.

1.7 *Evaluation: disadvantaged groups*—Certain aspects of the consultation process were unsuitable for stakeholders suffering from a debilitating illness.

1.8 *Comparison with other processes of evaluation*—Elsewhere, superior results have been achieved by following a quite different process of guideline development.

2. SCOTME

2.1 ScotME represents a small but highly committed group of ME patients and carers who seek detailed, authoritative information on ME and related issues. Our aim is to share this with patients, decision makers, and other interested parties, striving to ensure that decisions affecting the lives of ME sufferers—such as the development of clinical guidance through the Institute—are based on the best quality information and understanding, taking due cognisance of patients’ experience.

2.2 ScotME includes members who have a background in social policy and research. A qualified nurse with specialist knowledge and experience in delivering cognitive behavioural therapy is also represented. All have direct experience of living with ME, either as a sufferer or as the carer of one or more close relatives with this illness.

3. NICE’S EVALUATION PROCESS

3.1 In the case of the draft clinical guideline on “CFS/ME”, the Institute’s development process has produced a document that many believe will significantly harm rather than help people with myalgic encephalomyelitis (ME).

Diagnostic Criteria

3.2 The heterogeneous nature of the label “CFS/ME” as currently applied in the UK is widely recognised. For example, A Report of the CFS/ME Working Group: Report to the Chief Medical Officer of an Independent Working Group¹²⁹ clearly acknowledges this. Disappointingly, the Institute has made no attempt to acknowledge concerns about, far less resolve the issue of, the unsuitability and considerable dangers of attempting to construct a definitive guideline for patients suffering with a broad spectrum of disorders unscientifically subsumed under the category “CFS/ME”.

3.3 The “CFS/ME” draft guideline conflates ME, the neurological illness with a unique and distinctive clinical presentation, with chronic fatigue (ie fatigue due to mental health problems). This has led to patients with different disorders being viewed and treated similarly, to the serious disadvantage of ME patients. The overlap of the common symptoms of both disorders is being exaggerated whilst the vital differences are being ignored, resulting in the present draft guideline being fundamentally flawed.

3.4 It is essential that the Health Select Committee is aware of the significance of the relevant World Health Organisation (WHO) classifications. In 1969 the WHO determined that the neurological disorder ME was a distinct disorder from chronic fatigue/neurasthenia.

3.5 Accordingly, the WHO classified ME at G93.3 under Diseases of the Nervous System in the International Classification of Diseases [ICD], with chronic fatigue/neurasthenia remaining in the mental health chapter at F48.0. These classifications remain in place to this day, with the current version [ICD 10] indexing the chronic fatigue syndrome (CFS) directly to ME at G93.3, since ME is now often referred to in this way.

3.6 It is also noteworthy that the WHO stipulates that no illness or condition may appear in more than one category. In accordance with the WHO ICD10, ME(CFS) is an exemption to chronic fatigue.

3.7 The UK Dept of Health formally accepts, and therefore must adhere, to all ICD classifications.

¹²⁹ London, Department of Health, 2002. The relevant extract is enclosed as supplementary material [Enclosure 1].

3.8 This is a crucial point in relation to our submission to the Select Health Committee Inquiry, as this fundamental problem renders the draft guideline fatally flawed and unfit for purpose with regard to the clinical care of ME patients.

3.9 The unsatisfactory composition of the Guideline Development Group (GDG) is relevant here. This failed to represent the views of clinicians and researchers who understand the complex physical nature of ME/CFS [ICD10 G93.3]. At the same time, those with a belief in a “biopsychosocial” explanation for this condition—a model which consideration of the full range of relevant evidence does not support—were well represented. Few, if any, of the GDG had direct clinical experience of the illness they were advising upon, and the three patient representatives were outnumbered and their views effectively ignored.

Eligibility of evidence and assessment of evidence

3.10 Difficulties arise from the narrow view taken as to what constitutes admissible evidence, with the consequent potential for relevant information to be disregarded. This can lead, as with proposed document on “CFS/ME”, to false conclusions and inappropriate and dangerous guidance.

3.11 Evidence from controlled trials is given enormous weight. On the face of it this may seem reasonable, since such trials are generally considered to represent the “gold standard” of research evidence. However, the controlled trials which indicate positive outcomes for the management approaches recommended in the draft guideline—ie graded exercise and cognitive behavioural therapy (CBT)—selected participants using broad fatigue criteria and as such are unsuitable as a basis for management guidance on strictly defined ME/CFS.

3.12 In this and other respects interpretation is crucial. In this instance patient’ groups and well informed academic and clinical commentators have questioned the conclusions drawn. Unfortunately, “Papers, commentaries and editorials that interpret the results of a published paper” are not deemed admissible in evidence.¹³⁰

3.13 The beneficial effects recorded in respect of behavioural interventions have undoubtedly become exaggerated in translation, with the clear implication that these can result in a return to normal pre-morbid levels of activity.¹³¹ A close reading of the original source material¹³² fails to bear this out.

3.14 Stringent conditions are in place concerning the forms of evidence that are acceptable. These specifically exclude results from clinical practice and patients’ own accounts of outcomes “unless assessed as part of a well-designed study or a survey”.¹³³ It is neither appropriate nor safe to disregard or play down the significance of such evidence.

3.15 Government directives to develop patient led services and treatments have not been fulfilled in this instance. Material submitted by stakeholders regarding the findings of patient’ surveys was set aside and overridden by other forms of evidence, specifically controlled trials on chronic fatigue, the findings of which are quite the opposite to ME patients’ experience in respect of the behavioural management regimens concerned.

3.16 By way of contrast, the Chief Medical Officer’s Working Group, presented with survey findings indicating a high incidence of adverse responses to graded exercise and CBT, astutely observed that these “clearly indicate that . . . [the results of the research review] do not reflect the full spectrum of patients’ experience.”¹³⁴

3.17 The Institute has alleged irrelevance of management and treatment options where controlled trials have not yet been conducted, rather than accepting that it is not yet possible to evaluate such approaches by this type of evidence-base. The absence of evidence is not evidence of lack of efficacy unless a reasonable effort has been made to establish such evidence in the first place.

3.18 The Institute’s method, in particular the reliance on research trials, may fail to discriminate between different reactions occurring even within well defined patient groups if the methods used are insufficiently sensitive. Thus, on the basis of average findings, those who respond well to a certain treatment may be denied it, while patients who do not may be subjected to inappropriate intervention.

3.19 A final and fundamental problem regarding the evidence base on which the “CFS/ME” guideline has been drafted is the failure to take due cognisance of the biomedical evidence regarding aetiology and pathogenesis. In line with the GDG’s terms of reference, the literature review conducted is confined to

¹³⁰ “*The guideline development process: an overview for stakeholders, the public, and the NHS*” National Institute for Health and Clinical Excellence, 2nd edition September 2006. See “Stakeholder material not eligible for consideration by the GDG” page 23, box 7.

¹³¹ See, for example, page 21 of the draft guideline: “When the adult or child’s main goal is to return to normal activities then the therapies of first choice should be CBT or GET because there is good evidence of benefit . . .” Reference: as per note 1.

¹³² As referenced in the literature review which forms Appendix 1 of the draft “CFS/ME” guideline. See note 8 for full review reference.

¹³³ Reference: as per note 3.

¹³⁴ This statement is contained in an unpublished section of the report—“*Annex 3: Patient evidence*”, page 3. Unpublished annexes are available to download from the Department of Health website (<http://www.dh.gov.uk>).

papers on diagnosis, treatment, and management.¹³⁵ The draft guideline fails to properly address the significance of biomedical evidence, both in discussing aetiology and in attempting to formulate information requirements for professionals and the patients in their care. Instead, the views of “a few individuals”¹³⁶ on the GDG who assert a biopsychosocial perspective are overtly stated, and indeed underpin the draft guideline document.

3.20 Nonetheless, a wealth of biomedical evidence does exist: this evidence fundamentally challenges the relevance and appropriateness of the Institute’s proposed management guidance for strictly defined ME (CFS) patients.

Comparison with existing published guidelines

3.21 In North America, superior results have been achieved by following a quite different process of guideline development. The resulting publication—Carruthers B et al Myalgic Encephalomyelitis/Chronic fatigue syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols¹³⁷—sets out evidence-based clinical guidelines developed from the best available research evidence provided by a panel of world experts.

3.22 In this instance an expert subcommittee of Health Canada established terms of reference and selected an expert medical consensus panel of world leaders in research and clinical management.

3.23 Based on the panel’s collective clinical experience diagnosing and/or treating more than 20,000 ME/CFS patients a clinical case definition encompassing the pattern of positive signs and symptoms of ME/CFS was developed to encourage a diagnosis based on characteristic patterns of symptom clusters reflecting specific areas of pathogenesis. A short overview of both biomedical as well as management and treatment research is given.

3.24 The consensus panel present a reasoned and incisive critique of the putative relevance of behavioural management strategies to patients with ME/strictly defined CFS.¹³⁸

3.25 In the light of the prior publication of this authoritative diagnostic and treatment protocol it is astonishing that the Institute’s GDG “reviewed the current diagnostic criteria, but did not find any one of them particularly helpful in managing the condition or in making a definitive diagnosis”.¹³⁹

The Consultation Process

3.26 A serious lack of consideration was given to patients wishing to participate. The process included an unreasonably large and heavy questionnaire (488 pages) that was unsuitable for people who are sick and disabled with ME to complete. In addition, the allotted completion time was too short.

3.27 The development process includes an eight week stakeholder consultation period, but once a draft guideline has been released and faces fierce and trenchant criticism—as in the case of the “CFS/ME” draft guideline—there is no method in place to allow stakeholders an opportunity to comment further on the document with the proposed changes in place. This contrasts unfavourably with the Institute’s former procedure ie two consultation periods of four weeks each, the second for responses to the amended draft. This retrograde change was introduced in March 2006.

4. WHY NICE’S DECISIONS ARE INCREASINGLY BEING CHALLENGED

4.1 This submission focuses on the reasons why the Institute’s decisions in relation to ME (CFS-ICD10) are being challenged.

4.2 The Institute’s website asserts that:

“Patients and members of the public, whether as individuals or members of organisations, have the opportunity to help ensure that the guidance that NICE produces is actually used by the correct people, in the most appropriate way, for the right groups of people.”

¹³⁵ *The diagnosis, treatment and management of chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) in adults and children: work to support the NICE guidelines* A Bagnall et al, Centre for Reviews and Dissemination, University of York, October 2005.

¹³⁶ See page 133. Reference: as per note 1. The guideline then devotes two pages to “A conceptual framework for patients and health professionals when making a diagnosis of Chronic Fatigue Syndrome”, which explicitly sets out a biopsychosocial model, and is followed by what can only be described as an exceedingly partial list of references.

¹³⁷ *Journal of Chronic fatigue syndrome*, Vol 11 [1] 2003, pages 7–115. The description which follows is taken from this guideline and the accompanying editorial: De Meirleir, K & McGregor, N *Editorial: Chronic Fatigue Syndrome Guidelines* *The Journal of Chronic Fatigue Syndrome*, Vol 11 (1) 2003, pp 1–6.

¹³⁸ In view of the central importance of this issue, a relevant extract from the paper is enclosed as supplementary material with this submission [enclosure 1].

¹³⁹ See page 124. Reference: as per note 1.

4.3 The recent draft guideline on “CFS/ME” cannot be deemed to target “the right people.” Any attempt to do this in respect of the mixed collection of patients commonly referred to as “CFS/ME” sufferers would have required sub-grouping of patients with a view to developing individualised guidelines to suit any and all homogeneous groups of patients discovered within the unscientific label “CFS/ME”.

4.4 Thus in the guideline in question the Institution has flouted its own recommendation that “Patients about whom a Guideline is intended must be specifically described”. It has instead produced a “one size fits all” guideline for a non-specific, artificially created diagnostic label ie “CFS/ME”.

4.5 It is of deep concern that the draft guideline recommends what many consider to be unsafe management regimens for ME patients, approaches which wrongly assume that such patients are physiologically de-conditioned and can return to normal functioning by gradually increasing activity levels.

4.6 Such approaches have been tested on “fatigued” patients rather than on strictly defined ME (CFS ICD-10) patients. ScotME profoundly disagree with the Institute’s assessment regarding graded exercise ie that “the overall research evidence is that the benefits outweigh any harmful effects”.¹⁴⁰ There is, on the contrary, reason to believe that graded exercise is harmful to patients with strictly defined ME/CFS.

4.7 This disturbing situation reflects an underlying failure to root the guideline in a basic understanding of the clinical presentation of ME, a disregard for the findings of patient’ surveys, and a failure to engage with the wealth of published research evidence regarding the biomedical basis of this illness. Biomedical research evidence supports the inappropriateness, and at worst harmfulness, of graded exercise to people with ME.¹⁴¹

5. WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING AND IF SO WHY

5.1 There is no surer way of establishing and strengthening a lack of confidence in an organisation than a personal negative experience.

5.2 Many ME patients now lack confidence in the Institute because they are aware of the implications of the draft guideline. Simply put, there is immense concern among ME patients because they know, from their own experience of their illness, that the management regimens recommended in the draft guidelines exacerbate their symptoms making them more ill. Many have tried carefully paced increases in exercise and have suffered serious and lasting deterioration. An abundance of research exists to support what these patients are saying—but did the Institute give either biomedical evidence or patient’ survey findings due consideration?

5.3 As noted above, the fundamental flaw underlying the guideline is the endorsement of the unsatisfactory non-specific label of “CFS/ME”. The development of a one size fits all guideline for what is widely recognised to be a heterogeneous cohort of patients was destined to lead to unsatisfactory results.

5.4 The unsatisfactory make up of the Guideline Development Group, as discussed above (see para 3.9), underlies this problem and in itself gives rise to a lack of confidence in the Institute.

ScotME

March 2007

Evidence submitted by Servier Laboratories (NICE 41)

EXECUTIVE SUMMARY

Servier believes that NICE has an important role to play in encouraging clinical excellence and effective resource utilisation within the NHS.

As a result of our experience as a stakeholder in the ongoing NICE technology appraisals on postmenopausal osteoporosis, we have identified several areas for improvement, as presented in this submission. In particular:

Lack of transparency in economic model

There is a lack of transparency in the economic modelling used by NICE. The economic model used to determine cost-effectiveness of technologies has not been shared with all relevant stakeholders in the consultation process.

¹⁴⁰ Page 204: see note 1 for reference.

¹⁴¹ See *Is Graded Exercise Safe for People with ME?*, enclosed as supplementary material [Enclosure 3]. This ScotME document cites many examples from scientific research indicating that exercise is contra-indicated. It was submitted to the Parliamentary Inquiry into progress in the scientific research of ME chaired by Dr Ian Gibson MP.

Limited role for clinical judgement in allocation decisions

Technology appraisals make allocation decisions based on a hierarchy of cost effectiveness ratios. These cost-effectiveness ratios overlap. We believe it would be more appropriate for a group of cost-effective treatments to be recommended where there is this level of uncertainty. Clinical judgement would then take into account factors not captured by the economic modelling in order to determine which treatment is most suitable for a particular patient.

Failing to appropriately consider important clinical data

NICE have not adequately taken into account clinical evidence brought to the attention of the Appraisal Committee during the consultation process and especially evidence that has implications for the appropriate use of medicines.

Unfairly restricting access to treatment

Current draft guidance unfairly restricts access to effective treatments for women under the age of 70, regardless of risk factors.

Lengthy technology appraisal process

The review is now entering an unprecedented fifth year with guidance still in draft format. This raises questions about whether NICE would be able to cope with a further increase in workload as suggested by the OFT in its recent report into the PPRS.

Servier Laboratories Limited is the UK subsidiary of The Servier Research Group, a leading French research-based organisation, specialising in ethical pharmaceuticals. Servier UK offers a range of products in a number of medical areas: cardiovascular disease, especially hypertension and cardiac disease, diabetes and, more recently, osteoporosis. Servier develops truly innovative drugs and we invest in therapeutic areas where there is an unmet patient need.

INTRODUCTION

1. Servier welcomes this inquiry into NICE. NICE has an important role to play in encouraging clinical excellence and effective resource utilisation. Indeed, as a pharmaceutical company committed to the development of innovative medicines aimed at addressing the unmet needs of patients and prescribers, Servier supports the role of NICE in driving uptake of new treatments based on clinical and cost-effectiveness leading to better use of NHS resources, and in supporting the use of innovative new treatments.

2. However, we have concerns about the way that NICE currently undertakes technology appraisals and we believe there are lessons to be learnt from a technology appraisal in which we are currently involved, which we have detailed below. Servier manufacture Protelos (Strontium Ranelate), one of the technologies currently being evaluated as part of the ongoing NICE appraisal on primary and secondary prevention of osteoporotic fragility fractures in postmenopausal women.¹⁴²

BACKGROUND TO NICE TECHNOLOGY APPRAISALS ON POSTMENOPAUSAL OSTEOPOROSIS

3. The World Health Organisation define osteoporosis as a progressive skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequential increase in bone fragility and susceptibility to fracture. There is increased risk of fracture particularly of spine, hip, pelvis and forearm. It is pre-dominantly a disease of post-menopausal women and risk of fracture increases with age. Fractures caused by osteoporosis affect one in two women and one in five men over the age of 50.¹⁴³ The most serious complication is hip fracture, which has a mortality rate of up to 20% at one year.¹⁴⁴ The combined cost of social and hospital care for patients with a hip fracture amounts to more than £1.8 billion per year in the UK and is likely to increase to £2.1 billion by 2020.¹⁴⁵

4. NICE is currently developing guidance on osteoporosis in the form of technology appraisals on the primary and secondary prevention of fractures in osteoporosis. Primary prevention refers to the prevention of fragility fractures in post-menopausal women who have osteoporosis but who have not sustained a fracture, whereas secondary prevention refers to the prevention of fragility fractures in women who have osteoporosis and have previously sustained a clinically apparent fracture.

¹⁴² Osteoporosis—primary prevention: Appraisal consultation document; <http://guidance.nice.org.uk/page.aspx?o=411354>; Osteoporosis—secondary prevention: Appraisal consultation document; <http://guidance.nice.org.uk/page.aspx?o=411941>

¹⁴³ Van Staa T P, Dennison E M, Leufkens H G *et al*, Epidemiology of fractures in England and Wales, Bone 2001; 29(6): 517–522.

¹⁴⁴ Cooper C, Atkinson E J, Jacobsen S J *et al* Am J Epidemiology 1993; 137: 1001–1005.

¹⁴⁵ National Osteoporosis Society. A proposal to improve health outcomes for people at risk of osteoporotic fractures through the Quality and Outcomes Framework. NOS Working Party on the GMS Contract. May 2005.

5. The NICE evaluation of osteoporosis initially started in 2001 with a review of osteoporosis and its management. NICE carried out a technology appraisal of the osteoporosis treatments to assess how they should be used and in what patient groups to reduce the number of fractures in osteoporosis. NICE then evaluated treatment of osteoporosis in the setting of secondary prevention, which resulted in published guidance in January 2005.

6. A further set of guidance is currently being developed with separate technology appraisals for both primary and secondary prevention in osteoporosis. Several draft appraisal consultation documents (ACDs) have been released for consultation with 26 March 2007 the closing date for the current consultation phase.

LESSONS FROM SERVIER'S EXPERIENCE OF THE NICE TECHNOLOGY APPRAISAL PROCESS IN OSTEOPOROSIS

Lack of transparency in economic model

7. The economic model used by NICE to determine cost-effectiveness of technologies and patient access has not been shared with all relevant stakeholders in the consultation process. This lack of transparency limits the ability of consultees to understand and comment on conclusions derived from the model, and thus on the proposed guidance. For example, prior to publication of the previous ACDs the cost of one of the principal treatments, alendronate, decreased by almost half and this input to the model was adjusted accordingly. Decreasing the cost input for alendronate in the model should improve the cost effectiveness for this treatment. However, the resultant guidance was even more restrictive as NICE also altered other input parameters to the model without explanation or justification.

Limited role for clinical judgement in allocation decisions

8. The current NICE appraisal process makes allocation decisions according to a hierarchy of average cost-effectiveness ratios. However, the cost-effectiveness ratios of the various treatments overlap and so it is impossible to say with certainty that one treatment is categorically more cost effective than another. Where there is this level of uncertainty we believe it would be more appropriate for a group of cost-effective treatments to be recommended. Clinical judgement would then determine which of these treatments is most suitable for a particular patient, resulting in more personalised patient care. This clinical judgement would take account of factors such as the risk of side effects and the likelihood of compliance combined with baseline risk to define which patients are appropriate for a particular treatment. The economic analysis alone cannot fully account for this inter-patient variability.

Failing to appropriately consider important clinical data

9. NICE has not adequately taken into account independent evidence that Servier have submitted to the Appraisal Committee during the consultation process, which we believe has important implications for the appropriate use of medicines in women with postmenopausal osteoporosis:

- There is emerging evidence of increased risk of fracture associated with proton pump inhibitor (PPI) use, with three independent data sources that demonstrate statistically significant increases in the risk of fracture including hip.¹⁴⁶ Significantly, patients prescribed bisphosphonates are more likely to be prescribed a PPI to counteract the adverse effects of the bisphosphonate. Indeed, NICE have undertaken a systematic review of bisphosphonate use that demonstrates that new bisphosphonate users are up to three times more likely to require prescribed acid suppressant agents such as PPIs.¹⁴⁷ Such prescribing patterns may therefore be putting vulnerable patients at increased risk of fracture. However, NICE appear to have ignored these data, despite Servier's request for an urgent review of the clinical studies of bisphosphonates to determine if this evidence from clinical practice is also demonstrated in the clinical studies.
- Strontium ranelate is the only medication with proof of efficacy in both vertebral and non-vertebral fractures in patients with post-menopausal osteoporosis who are 80 years or older.¹⁴⁸ In contrast, current evidence suggests that bisphosphonates do not protect against non-vertebral fracture in the very elderly.¹⁴⁹ This distinction is important as non-vertebral fractures may be considered to be more serious consequences of osteoporosis than vertebral fractures in terms of

¹⁴⁶ Yu E W C Shinoff, T Blackwell, K Ensrud, T Hillier, D C Bauer, Use of Acid-Suppressive Medications and Risk of Bone Loss and Fracture in Postmenopausal Women; Vestergaard, P, L Rejnmark, L Mosekilde. 2006, Proton Pump Inhibitors, Histamine H2 Receptor Antagonists, and Other Antacid Medications and the Risk of Fracture *Calcified Tissue International* Vol 79:76–83; Yang Y-X, J D Lewis, S Epstein, D C Metz. 2006, Long-term proton pump inhibitor therapy and risk of hip fracture, *JAMA*, 296:2947–2953.

¹⁴⁷ Myfanwy Lloyd Jones, Anna Wilkinson. 2006. Adverse Effects and Persistence with Therapy in Patients Taking Oral Alendronate, Etidronate or Risedronate: Systematic Reviews.

¹⁴⁸ Seeman E, *et al.* 2006. Strontium ranelate reduces the risk of vertebral and non-vertebral fractures in women 80 years of age and older. *JBMR* Vol 21:7:1113–1120.

¹⁴⁹ Boonen S *et al* 2004. Safety and efficacy of risedronate in reducing fracture risk in osteoporotic women aged 80 and older: Implications for the use of anti-resorptive agents in the old and oldest old. *JAGS* Vol 52:1832–1839.

morbidity, mortality and cost.¹⁵⁰ Despite this unique evidence supporting use of strontium ranelate first line for patients aged 80 years and over, the current draft guidance recommends the bisphosphonate alendronate as the only treatment for initiation, including in the very elderly.

Unfairly restricting access to treatment

10. Current recommendations unfairly restrict patient access to treatment. Draft guidance on primary prevention excludes women under the age of 70 years, regardless of risk factors, from primary prevention treatment. Indeed, such an approach would effectively discriminate against younger patients even if their absolute risk of fracture were identical to or higher than that of an older patient meeting the eligibility criteria as set out in the draft guidance.

Lengthy technology appraisal process

11. The NICE review of osteoporosis is now entering an unprecedented fifth year with guidance still in draft format. Some Primary Care Trusts are currently restricting access to osteoporosis treatments by recommending to doctors that they do not prescribe strontium ranelate until NICE publishes its guidance.¹⁵¹ In addition to escalating costs that will have to be met by the taxpayer we have got evidence that patients are being denied treatment, and therefore exposed to increased risk of fracture, while doctors wait for finalised guidance. If final guidance is produced based on the current recommendations, the result of over four years of work will simply make the recommendation that only generic alendronate (the cheapest treatment) should be used for treatment initiation in patients with postmenopausal osteoporosis. This raises questions about whether NICE would be able to cope with a further increase in workload if, as recommended by the recently published OFT report into Pharmaceutical Price Regulation Scheme (PPRS), it would have the additional responsibility of appraising all new medications as they come to market.¹⁵²

CONCLUSION

12. As we have stated above, Servier supports the work of NICE in encouraging clinical excellence and effective resource allocation. However, our experience of engaging with NICE through its review of osteoporosis has highlighted some areas of concern which we believe need to be addressed, particularly if any expansion in its reach is taken forward in the future. We hope this submission will provide the Health Select Committee with some practical examples of areas of NICE's work which could be improved and lessons which can be learnt going forward. We would be happy to provide any additional information to the Committee in both written or verbal form to support this submission.

Servier Laboratories

March 2007

Evidence submitted by Sirtex Medical (NICE 54)

1. EXECUTIVE SUMMARY

1.1 Sirtex Medical was formed in 1997 to research and develop effective treatments for liver cancer using novel small particle technology.

1.2 Selective Internal Radiation Therapy (SIRT) is a relatively new medical technique for the treatment of advanced primary and secondary (metastatic) liver cancer that cannot be removed by surgery. The safety and tolerability of SIRT is well established, with over 4,500 patients treated worldwide. The procedure normally requires an overnight stay in hospital with patients typically experiencing relatively minor side effects such as pain or nausea that resolve in a matter of days.

1.3 At the time of the Interventional Procedure appraisal by NICE, Sirtex were the only manufacturer in Europe with an approved SIRT product—yttrium-90 labelled SIR-Spheres[®] microspheres—licensed for the treatment of unresectable primary and secondary liver cancer.

1.4 At the time of the NICE appraisal of SIRT, the results of only one pivotal randomized clinical trial were available. This trial was halted prematurely after the FDA advised Sirtex that they would accept response rate and time to disease progression as endpoints for regulatory approval. The study demonstrated that adding SIR-Spheres microspheres to hepatic arterial chemotherapy (HAC) significantly increased the

¹⁵⁰ Center J R, Nguyen T V, Schneider D, Sambrook P N, Eiman J A 1999. Mortality after all types of osteoporotic fracture in men and women: an observational study. *Lancet* 353:878–882.

¹⁵¹ Primary Care Trust, 2006, Traffic Lights List 2006–07.

¹⁵² The Pharmaceutical Price Regulation Scheme; An OFT Market Study. February 2007. http://www.of.gov.uk/shared_of/reports/comp_policy/oft885.pdf.

tumour response rate and significantly lengthened the time to disease progression. There was a trend towards prolonged survival, even though the study was not adequately powered to demonstrate a survival benefit and had been halted early. There was no major adverse impact on patients' quality of life.

1.5 The results of a second pivotal randomized clinical trial were not in the public domain at the time of the NICE appraisal. Sirtex warned NICE that the timing of the appraisal was premature, but this was ignored. Sirtex offered to provide the results, in confidence, but NICE advised that the Interventional Procedures Programme did not accept "in-confidence" material. This is in direct contrast to NICE Technology Appraisals, where companies and clinicians can submit material "in-confidence". Once the appraisal process had started, updated clinical data from the second pivotal trial became available that demonstrated significant benefits, but NICE refused to accept this information.

1.6 The guidance issued by NICE accepted SIRT as a therapeutic option for colorectal liver metastases in September 2004 (IPG 93), and advised that clinicians should audit and review clinical outcomes of the treatment, and ensure that patients are fully informed. However, the guidance noted that there was a lack of evidence of symptom relief or increased survival. Subsequent clinical trial data that was not reviewed by NICE showed a substantial and significant survival advantage—16 months extra survival—for patients receiving SIRT in addition to systemic chemotherapy.

1.7 This second pivotal randomized trial compared the addition of SIR-Spheres microspheres to systemic 5FU/LV chemotherapy, demonstrating significantly longer survival for the combination compared to 5-FU/LV alone (29.4 months vs 12.8 months), plus significantly longer time to disease progression and higher response rates without any compromise to patients' quality of life.

1.8 Subsequent clinical trials established the safety of SIR-Spheres microspheres in combination with the current standard of care first- and second-line chemotherapy regimens recommended by NICE, and demonstrated impressive efficacy. These studies reported that in some patients, tumours were decreased in size sufficiently to enable the remaining disease to be removed by surgery, which provides the best prospect of a long-term cure for colorectal cancer. A retrospective study of over 200 patients failing chemotherapy demonstrated a 6-month survival benefit for SIRT.

1.9 The pathways for the NICE interventional procedures appraisal have proved to be extremely difficult, with NICE consistently adopting an adversarial approach and repeatedly deviating from their published procedures.

1.10 Despite the proven effectiveness of SIRT, and the substantial potential benefits for patients in terms of survival, the process of adoption by the NHS in the UK has been difficult and tortuous. The majority of the 60+ patients treated in the UK have been funded by private medical insurance, self paid, or have had the SIR-Spheres microspheres donated by Sirtex, while only a handful have been approved by NHS fundholders. That the number of NHS patients treated has started to rise is a testament to the perseverance of NHS physicians in seeking the best treatment options for their patients.

1.11 There is no mandatory funding for NICE interventional procedures guidance. Therefore PCT fundholders can easily deny funding of a treatment that a multi-disciplinary team has decided is the best option for the patient.

1.12 In our experience, NICE appraisal of SIRT has done little, if anything, to enable patient choice for those under NHS care.

2. INTRODUCTION TO SIRT

2.1 SIRT (also known as radioembolisation) is a new medical technique for the treatment of primary and secondary (metastatic) liver tumours that cannot surgically resected.

2.2 SIRT utilises SIR-Spheres microspheres—biocompatible resin microspheres labelled with radioactive yttrium-90 that emits high-energy pure beta radiation. SIR-Spheres microspheres are administered by an Interventional Radiologist by infusion through a catheter placed in the hepatic artery. Liver tumours derive ~90% of their blood supply from the hepatic artery, whereas normal liver tissue derives ~90% of its blood supply from the portal vein. SIRT uses this trait against the tumour to selectively target radiotherapy at the liver tumours.

2.3 The SIR-Spheres microspheres become trapped in the small blood vessels of tumours, delivering high doses of beta radiation to the tumours while maintaining a tolerable radiation dose to the normal liver. The half-life of yttrium-90 is 64.2 hours. By two weeks, 97% of the radioactive dose has been delivered to the tumours.

2.4 SIR-Spheres microspheres gained CE Mark approval in October, 2002, and are fully approved in Europe for the treatment of unresectable liver tumours.

2.5 SIR-Spheres microspheres is also approved by the US FDA for treating colorectal liver metastases and is fully reimbursed by the Center for Medicare and Medicaid Services (CMS).

2.6 The safety and tolerability of SIRT is well established, with over 4,500 patients treated worldwide using SIR-Spheres microspheres since its approval. The procedure is currently used in over 100 centres worldwide. The procedure normally requires an overnight stay in hospital with patients typically experiencing relatively minor side effects such as pain or nausea that resolve in a matter of days.

2.7 At the time of appraisal by NICE's Interventional Procedure Advisory Committee (IPAC), Sirtex were the only manufacturer in Europe with an approved SIRT product licensed for the treatment of unresectable primary and secondary liver tumours.

2.8 At the time of the NICE appraisal, only the results of one pivotal randomized clinical trial were available. This trial had been halted prematurely after the FDA advised that they would accept response rate and time to progression as endpoints for regulatory approval. The study investigated adding SIR-Spheres microspheres to HAC using FUDR, demonstrating:

- 2.8.1 a statistically significant increase in the tumour response rate (44% vs. 17%), and in median time to disease progression (15.9 months vs 9.7 months) compared to FUDR HAC alone;
- 2.8.2 a trend towards prolonged overall survival, although the study was not powered to show survival and had been halted early; and
- 2.8.3 these positive results were achieved without deterioration in quality of life of patients, with patients in both groups demonstrating an improvement in QoL.

2.9 The results of an additional pivotal randomized clinical trial were not in the public domain at the time of the NICE appraisal. Sirtex offered to provide the results, in confidence, since public disclosure would jeopardise publication in a peer-review scientific journal, but NICE advised that the Interventional Procedures Programme did not accept in-confidence material. Sirtex believe that this was incorrect and that NICE are bound to accept in-confidence material for both Technology Appraisals and Interventional Procedures. Sirtex warned NICE that the timing of its appraisal was premature, but this was ignored.

2.10 This second study compared the addition of SIR-Spheres microspheres to systemic chemotherapy with 5FU/LV, demonstrating:

- 2.10.1 significantly longer median overall survival for the combination of SIR-Spheres microspheres plus 5-FU/LV compared to 5-FU/LV alone (29.4 months vs 12.8 months);
- 2.10.2 significantly longer median time to disease progression for those receiving SIR-Spheres microspheres (18.6 months vs. 3.6 months);
- 2.10.3 significantly higher response rate for patients receiving SIR-Spheres microspheres (73% vs 0%); and
- 2.10.4 quality of life of patients was not compromised by adding SIR-Spheres microspheres.

2.11 Subsequent clinical trials have established the safety of SIR-Spheres microspheres in combination with current standard of care first- and second-line chemotherapy regimens recommended by NICE, and have demonstrated impressive efficacy. Investigators reported that in some patients, the tumours were decreased in size sufficiently to enable the remaining disease to be removed by surgery, which provides the best prospect of a long-term cure for colorectal cancer.

2.12 A retrospective study of SIRT as salvage treatment in over 200 patients who had failed chemotherapy demonstrated a significant survival benefit for patients treated with SIR-Spheres microspheres (10.5 months in responders vs 4.5 months in non-responders or historical controls).

2.13 Unlike the guidance issued by NICE, the clinical benefits from SIRT for patients with liver tumours are not restricted to colorectal cancer. Clinical studies have demonstrated benefits following SIRT using SIR-Spheres microspheres for patients with hepatocellular carcinoma (primary liver cancer), and liver metastases from neuroendocrine tumours, breast cancer, pancreatic cancer, lung cancer and various other cancers.

3. TERM OF REFERENCE: NICE'S EVALUATION PROCESS

3.1 When it commenced the Interventional Procedures appraisal, NICE failed to confirm formally to Sirtex that our technology was to be appraised. As the only manufacturer in the world with a SIRT product approved for colorectal cancer, Sirtex was disappointed and concerned that NICE failed to advise us that the procedure was being assessed.

3.2 It was clear from the speed with which NICE began the investigation that the main stakeholders were not consulted adequately, if at all.

3.3 The refusal of NICE to accept the results of clinical trials, in confidence, in order to avoid jeopardising publication in a peer-review scientific journal or disclosure of commercially sensitive information is in direct contradiction of the policies NICE adopts for its appraisals, where companies and clinicians can submit material in-confidence to NICE.

3.4 NICE initially refused to delay the timescale of the Interventional Procedures Advisory Committee in order to allow them to consider interim data from the second pivotal randomised trial. Following the eventual acceptance of our data, once the appraisal process commenced, NICE refused to accept more mature, updated data from Sirtex despite the significant clinical benefits that were demonstrated.

3.5 Sirtex's warnings to NICE that the timing of the Interventional Procedure appraisal on SIRT was premature were ignored by NICE. As forewarned by Sirtex, data from the second pivotal randomized clinical trial—demonstrating a 16-month survival benefit by adding SIR-Spheres microspheres to systemic chemotherapy—should have made a substantial difference to the guidance issued by NICE.

3.6 NICE appear to be under the illusion, in oncology at least, that use in a clinical trial of a product in isolation is desirable since this makes interpretation of the results easier. NICE noted in its guidance on SIRT that “combination with other treatments makes interpretation of the published literature difficult.” Where there is a clear benefit from combining different treatments, it would be unethical to conduct a clinical trial one element in isolation. The clinical reality is that there are synergies from combining different treatment modalities ie radiotherapy plus chemotherapy, that provide greater clinical benefits for patients due to the radiosensitising effects of some chemotherapy agents that translate into improved survival and quality of life benefits for patients. In its Assessment Report for the Technology Appraisal on the management of advanced colorectal cancer using 5FU, FA (or LV), irinotecan and/or oxaliplatin, NICE noted that interpretation of results from trials is complicated by the fact that the disease is often managed with sequences of either mono- or combination therapy, with frequent use of unplanned second- or third-line salvage chemotherapy. This understanding of oncology needs to be shared more broadly within NICE.

3.7 The NICE Interventional Procedures appraisal process has proven to be extremely difficult for Sirtex to negotiate, and we repeatedly had to remind NICE of its own published procedures to ensure that these were followed.

3.8 Throughout, we were confused by NICE's use of terminology and its inconsistency. We were informed that NICE was assessing SIRT as “a procedure” under the Interventional Procedures Programme. However, SIR-Spheres microspheres is licensed as a “medical device” and not as a “procedure”.

3.9 In this context, the NICE appraisal of SIRT therefore appeared to us to amount to a review of the product (or medical device), something that is explicitly excluded from NICE's own terms of reference (“The programme looks at procedures and not the devices (or drugs) used during the performance of the procedure” About Interventional Procedures, NICE Website).

3.10 Alternatively, if the Advisory Committee intended to focus on the benefits and risks of SIRT as an interventional radiological procedure for treating hepatic tumours by introduction of anticancer agents through the hepatic artery, then this principle is already well established, both in medical practice and the scientific literature. It is the same procedure used in Trans-Arterial Chemo Embolisation (TACE), which is not a novel treatment strategy but standard practice in most countries, including the UK. NICE has announced that they will not perform any appraisal on TACE.

3.11 Since the procedure itself is well established, Sirtex was left with the distinct impression that NICE appeared to be undertaking an assessment of the device itself rather than the procedure of treating hepatic tumours via agents introduced through the hepatic artery.

3.12 To our knowledge, none of the growing number of UK Interventional Radiologists or Medical Oncologists experienced in the use of SIRT or cancer organisations with direct knowledge of SIRT were contacted by NICE or by the IPACmembers. In addition, no charities or patient organisations in the UK that we were in contact with were approached by NICE.

3.13 This suggested to us that “adequate consultation” as defined by NICE had not taken place.

4. TERM OF REFERENCE: THE IMPLEMENTATION OF NICE GUIDANCE

4.1 NICE issued Interventional Procedures Guidance on SIRT for colorectal metastases in the liver in September 2004. Since this time, Sirtex has noted much ignorance about the existence of NICE guidance on SIRT. NICE has a regulatory duty to inform all stakeholders of its own decisions and it appears that this responsibility is discharged by simply posting the decision on the website and emailing Trust CEOs etc.

4.2 Despite their apparent antipathy towards industry, it would appear that NICE abdicates its responsibility of ensuring wide understanding of its guidance amongst the appropriate medical specialists who would conduct an interventional procedure, and instead leaves industry to perform this task. We note that it can be very difficult and expensive for a small company to effectively inform all UK stakeholders. Over two years after NICE Guidance was issued, there is still considerable lack of knowledge among healthcare professionals, Trust personnel and the general public on the existence and nature of the Guidance. Effectively, the Guidance is only implemented when Sirtex actively pursues the issue with Trusts.

5. TERM OF REFERENCE: WHETHER PUBLIC CONFIDENCE IN NICE IS WANING, AND IF SO WHY?

5.1 There is no mandatory funding for NICE interventional procedures guidance. If a MDT determines that SIRT is the best treatment for a patient, an already overworked consultant is forced to apply on a case-by-case basis to PCT fundholders to get approved funding for treatment. This can easily be denied by fundholders, and delays to the process can result in patients missing the opportunity to receive a treatment that could extend their lives and improve their quality of life.

5.2 Despite NICE guidance on the use of SIRT for the treatment of colorectal cancer liver metastases, NHS patients are still dying prematurely in the UK because their physicians are unable to secure funding from PCT fundholders. How can patient choice be a cornerstone of NHS policy when the majority of patients with liver-dominant cancer are not offered a treatment option that could provide the possibility of downstaging the tumour to permit surgical resection or extending overall survival as well as time to the progression of their disease?

6. RECOMMENDATIONS

6.1 Sirtex experienced great difficulties negotiating with NICE. We recommend that NICE ensures that they proactively identify all key stakeholders before undertaking an assessment and include the manufacturers in that exercise.

6.2 NICE should adopt a less adversarial negotiating position and should stop treating manufacturers and clinicians with suspicion and mistrust.

6.3 NICE should listen to advice from manufacturers and clinicians when they advise the Institute that they may be reviewing a technology prematurely.

6.4 NICE should ensure that adequate procedures are in place to monitor their own published procedures and that NICE keeps to those procedures during the appraisals process.

6.5 The NICE Interventional Procedures Programme should be more transparent and stakeholders should be able to enter into dialogue with NICE at the start of the process to discuss the assessment.

6.6 The NICE process should be flexible enough to allow the Advisory Committees to accept relevant published data as the assessment progresses.

6.7 The dissemination of NICE Guidance needs to be more structured and owned by NICE. It needs to consist of more than publication of its guidance on the NICE website.

6.8 The Select Committee should give strong consideration to recommending to Government that funding for interventional procedures that have been appraised by NICE be made mandatory where a multidisciplinary team of specialists has determined that the recommended treatment is in the best interests of the patient, and particularly where the treatment is for cancer.

Nigel Large, Chief Executive, and *David Turner*, Director of UK Operations
Sirtex Medical Europe

March 2007

Evidence submitted by the South Asian Health Foundation (NICE 12)

BACKGROUND

This submission was prepared by Dr Kiran C R Patel¹⁵³ on behalf of the South Asian Health Foundation (SAHF). The SAHF aims to promote improvements in the quality of, and access to, healthcare and health promotion in South Asians. The organisation achieves this by three main mechanisms:

- Promotion of high quality scholarship and research.
- Health promotion and education at a grassroots level to communities.
- Health advocacy via interaction and advisory input into organisations and processes such as those at NICE.

Further information about the organisation may be obtained via the website www.sahf.org.uk and annual reports submitted to the charities commission.

¹⁵³ Consultant Cardiologist and Honorary Senior Lecturer, Sandwell & West Birmingham NHS Trust and University of Birmingham. Dr Patel is a member of two NICE guideline and programme development groups and has accepted honoraria from the pharmaceutical industry. SAHF has received unrestricted funding from the Department of Health and the pharmaceutical industry. The views expressed in this submission are those collated following the interactions of SAHF with NICE and do not represent the views of NICE or the pharmaceutical industry.

EXECUTIVE SUMMARY

- A minority of NICE's decisions are challenged and even fewer are upheld after appeal.
- There is an understandable incentive for pharmaceutical companies to appeal NICE's decisions and the relative lack of constraints in embarking on an appeal make this a feasible strategy within the current appraisal structure.
- Allowing NICE to define the maximum acceptable price for a technology would allow implementation of the Office of Fair Trading Report recommendations and might resolve the issue of exploitation of its appeals process.
- Independent reports indicate that NICE functions successfully within the field of Health Technology Appraisal.
- Broader support and recognition of NICE's valuable role within the NHS would counter some adverse negative publicity that NICE receives.
- NICE has played a valuable role in recognising the needs of south Asian patients in the UK.

Why NICE's decisions are increasingly being challenged

"What this shows is not that NICE is in trouble but that it is doing its job. It was set up to ensure that treatments available on the NHS provide value for money. Decisions to restrict drug treatments are hugely emotive to patients and clinicians. Controversy is inevitable."

Fiona Godlee, Editor, *British Medical Journal*, 2006

"It has become lamentably commonplace for decisions made by the UK's National Institute for Health and Clinical Excellence (NICE) to be greeted with public outrage. But this reaction says less about NICE's decision-making processes—which are commendably rigorous—than about the gulf between patient expectations of the UK's tax-funded health system, and understanding about the necessity for rational spending."

"If the Government really wants to extend choice within the NHS, as it has pledged, it should launch a debate about the health-financing framework necessary to support this philosophy. But its first obligation should be to show vocal support for NICE as the best mechanism to ensure equity in the UK's current health system."

Richard Horton, Editor, *The Lancet*, 2006

NICE's Decisions: How Many Are Taken to Appeal and How Many Are Actually Upheld?

1. The fact that NICE is engaged with ensuring justifiable expenditure within the NHS on drugs and therapeutic interventions inevitably attracts criticism. NICE's 117 recommendations in the period 2000–05 have been evenly distributed across the four possible outcome decisions: "No" (19%), "yes" (23%), "yes with major restrictions" (32%) and "yes with minor restrictions" (26%). Of the negative recommendations, almost two thirds were on the grounds of insufficient evidence, the remainder due to unacceptable cost-effectiveness.

2. NICE's 86 guidances between 2000 and 2005 have been subject to 25 appeals (29%). Fifteen were dismissed. Of the 10 appeals that were upheld, five resulted in relatively minor changes in the wording of the guidance. Only five decisions were referred back to the appraisal committee for further appraisal—approximately 6%.

3. Given the relatively high proportion of decisions referred (29%) but the low proportion upheld and re-evaluated (6%), the following factors are relevant to understanding why NICE's decisions are challenged without substantial basis in the majority of cases:

- the current role of NICE;
- the structure of NICE's processes;
- the role of health care professionals and their representative organisations;
- the role of patient interest groups;
- the role of the pharmaceutical industry; and
- the role of the media.

(a) The Current Role of NICE

4. If NICE's decisions did not attract criticism the Health Select Committee would be justified in asking why NICE was ineffective and whether it represented a justifiable appropriation of public funds. By virtue of the roles and responsibilities NICE undertakes, it is both appropriate and anticipated that the decisions it delivers as well as the processes by which it arrives at these decisions are open to criticism. The defined remit of the organisation, to address challenging issues and justify often difficult and emotionally fuelling decisions, represents a justifiable appropriation of public funds.

5. Resource allocation is inherently controversial—all needs cannot be met and the public expectation is that healthcare should be universally and comprehensively available to all. The UK population is ageing, healthcare costs are rising and expenditure on drugs represents the largest component of this increase in costs (2). Consequently, bodies such as NICE will increasingly find themselves in the invidious position of regulating the availability of healthcare technologies while the relative availability of resources decreases.

6. In conclusion: The long-term trend for allocative decision making will be perceived and recognised as increasingly restrictive in nature but necessary to allow the functioning of a viable NHS.

(b) The Structure of NICE's Processes

7. Through its numerous interactions with NICE, SAHF would make the following observations regarding NICE's processes:

- Equity of voice accorded to stakeholders (“open-ness”).
- A high standard of transparency.
- Consequent accountability resulting from the above.
- An appeals system that may be freely used by third parties to further self-interest over the public good.

8. Objective analysis from the World Health Organisation has evaluated NICE's methods and processes and declared them to be sound while a recent independent report from the Office of Fair Trading similarly reported positively and proceeded to further recommend an extension of its powers to undertake drug pricing.

9. Allowing NICE this mandate to define the maximum acceptable price for a technology would allow implementation of the Office of Fair Trading Report recommendations whilst being appropriately mindful of R&D considerations for industry.

10. We believe that NICE's current process is subject to overuse as a result of four issues:

- (1) the lack of adequate safeguards to prevent exploitation of the appeals process;
- (2) the requirement for an appeal process;
- (3) the requirement of fiscal constraints within the NHS; and
- (4) the high costs of R&D for medical therapies and interventions.

11. There is no service user cost to pharmaceutical companies when challenging NICE despite significant potential commercial gains in potential market share for drugs that might offer little extra value for money to the health service. It is not unexpected that pharmaceutical companies have acquired increasing confidence in NICE's process and their apprehension in routinely employing the appeals procedure may have diminished. It is natural that organisations and lobby groups are likely to appeal decisions they do not like.

12. Conclusion: Objective reports give reason for confidence in NICE's processes. The NICE appeals process is highly vulnerable to overuse by parties with commercial or vested interests. Safeguards to protect NICE and henceforth the health economy should be introduced.

(c) The Role of Health Care Professionals and their Representative Organisations

13. NICE consults widely when making its decisions and it employs multidisciplinary panels that include patients and specialists to ensure a balanced view. To understand how healthcare professional groups may perceive NICE one must consider the situation before the inception of NICE. Pre-NICE, clinical care was guided by professional groups, who were often poorly integrated into the mainstream NHS and took little account of the overall fiscal consequences of their recommendations beyond a single specialty focus. Industry supports many of these professional groups they are potentially susceptible to bias and if not, perceived to be susceptible to bias.

14. It is difficult to reconcile these historical approaches with that of a body such as NICE, which must operate transparently, equitably and consider the needs of the NHS as a whole. This situation reflects a challenge for professional groups to create transparency with respect to their interactions with the pharmaceutical industry. A previous Health Select Committee, which examined the relationship between healthcare professionals and the pharmaceutical industry, recommended that a register of interests be instituted—there has been no move to implement this recommendation to date.

15. Conclusion: The establishment of NICE has resulted in an increasingly democratic, patient centred and quality focussed system, with attention to health economics which is vital to the NHS today. Ongoing deficiencies in the transparent declarations of interaction of professional groups with pharmaceutical companies results in unrepresentative engagement from some stakeholders.

(d) The Role of Patient Interest Groups

16. As an organisation that represents the interests of south Asian patients in the UK, SAHF have a vested interest in this particular area of healthcare provision to ethnic groups and reduction of health inequalities. Organisations and charities with other specific interests will naturally have a similar bias to toward their own interests.

17. As a frequent stakeholder within NICE guidance and guidelines SAHF has recognised that that our work in promoting the healthcare issues faced by south Asian patients should not disadvantage other groups and/or be perceived as detrimental to the welfare of people in general.

18. SAHF has sought to provide assurance that our structure and function are not contaminated by financial ties that might be seen to compromise its decision-making or policies. SAHF functions at a level of transparency akin to NICE. Single-issue groups are not remitted to balance their demands with the needs of the population as a whole. This lobbying and stakeholder representation is both expected and appropriate for special interest groups. NICE is highly commendable for providing this voice, even to minority stakeholders.

19. The experience of SAHF is that NICE has provided an equitable, transparent framework to address issues pertinent to south Asian health in the UK. Previous guidelines from professional groups have frequently neglected south Asian health and we are definitely of the view that that NICE's existence has allowed a "voice" for marginalised groups that would not previously be heard over the demands of much more powerful voices that represent high profile disease areas. SAHF has never challenged a decision of NICE.

20. Conclusion: SAHF acknowledges that NICE has provided a valuable conduit to address issues surrounding south Asian health, a conduit that before the inception of NICE never existed.

(e) The Role of the Pharmaceutical Industry

21. The "industry" naturally has a clear purpose with respect to NICE (1) to ensure its products receive recommendation for NHS use and that such approval allows as widespread a dissemination as possible. To expect otherwise would be unhealthy for the economic aspects of industry. These interests must be balanced with the moral responsibility of ensuring appropriate and safe treatments reach patients.

22. With drug development costs of approximately £800 million and the cost of challenging NICE's decision within an appeal being comparatively small, it is inevitable that a reasonable and appropriate strategy for the pharmaceutical industry is to challenge unfavourable decisions from NICE. The commercial factors that can motivate the promotion of some drugs beyond their optimum use have been described in the recent Office of Fair Trading Review of the PPRS Scheme. The appeals launched against NICE's decisions represent another facet of a structural design limitation that understandably requires companies to seek maximum competitive advantage within a marketplace.

23. Conclusion: The current weakness in NICE's appeals process means that it is structurally vulnerable to excessive exploitation.

(e) The Role of the Media

24. The Health Select Committee will undoubtedly be aware of the role played by the media in denigrating public service organisations. NICE has relatively little resources allocated to marketing and promotion. It has an invidious role yet valuable function in maintaining the viability of the health service.

25. Medical trade publications, particularly those that are "free" but largely funded by industry advertising frequently attempt to confront NICE and report divisive headlines.

26. Subscription press coverage has been increasingly favourable to NICE. The BMJ and also the Lancet have recently acknowledged the valuable role that NICE now plays in the UK health economy. Both of these publications are recognised as internationally respected publications yet also have significant industry based revenue from advertising.

27. The lay press eg newspapers focus almost entirely on highlighting NICE's restrictive recommendations despite the fact that the majority of NICE's recommendations result in some form of approval. Consequently, NICE is losing public support due to inadequate representation to the public whom it serves NICE's perception should not judged solely according to the popularity it enjoys as a result of the number of positive recommendations it makes, but the appropriateness of its decisions in relation to its remit (value for money) should also be a benchmark.

28. Conclusion: NICE should receive an appropriate budget for disseminating its recommendations within the wider health economy and public.

Whether public confidence in the Institute is waning, and if so why

29. There are no objective measures that indicate the level of public confidence in NICE. All submissions to this point are likely to represent opinion.

30. Public confidence is the view of the integrity with which NICE makes decisions regardless of whether a particular party finds them agreeable or not should be separated from public perception.

31. Public perception is influenced by media coverage that is also influenced by emotive patient vignettes and professional groups that may seek to distort the priorities of the NHS. Many people will probably be unaware of the intricacies of the health service and organisations such as NICE. For some people who are aware of NICE it may be when unfavourable press coverage is relayed to them, often presenting a distorted view of NICE's objectives.

32. Conclusion: NICE may be experiencing adverse publicity which requires its aims and objectives to be better represented and supported by the health service.

NICE's evaluation process, and whether any particular groups are disadvantaged by the process

33. As an organisation that represents the health needs of the UK south Asian population we feel that NICE has an exhaustive stakeholder process that the "voice" of ethnic minority representation to be heard. Conversely, some expert groups may feel their influence has been moderated.

34. Conclusion: We believe that NICE has "levelled the playing field" no longer is decision making and resource allocation a case of "he who shouts loudest" but based upon evidence.

The speed of publishing guidance

35. We believe that speed at which NICE produces its guidance is a favourable reflection of the demand it is subject to and its capacity to deliver guidance. However speed of decision making could improve, as we also understand the frustration that a decision making process which may take months if not years, can cause. Such lengthy processes sometimes mean guidance is out dated as soon as it is published and therefore the NHS may not be practising at the frontiers of medical advance and delivering such guidance may be cost ineffective per se.

36. Conclusion: We believe that the speed at which guidance is produced is usually appropriate but sometimes frustrating for service users. This statement is tempered by the realisation that there was no guidance at all before NICE's introduction. The recommendations of the previous Health Select Committee that NICE receive additional funding have yet to be implemented. Only further investment and periodic secondment of panel members to NICE can expedite the guideline development process.

The appeal system

37. We refer to the comments we have previously made regarding NICE's appeal system under the related section "why NICE's decisions are increasingly being challenged".

38. Conclusion: The current weakness in NICE's appeals process means that it may be excessively subject to exploitation and potentially to abuse.

Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)

39. NICE presides over England, Northern Ireland and Wales, a population of approximately 55 million. SIGN, presides over Scotland only which has a population of five million people. This ten-fold difference precludes equivalence between the two organisations.

40. The most important difference between NICE and the SIGN is that NICE undertakes technology appraisals and incorporates health economic analyses which are not undertaken by SIGN (although SIGN is increasingly referencing health economics in its deliberations). Without health economic analysis we believe that NICE's decisions would be unacceptable to the pharmaceutical industry in view of the size of the UK pharmaceutical market and potential criticisms that NICE did not promote the true value of drugs because it was not integrating cost-effectiveness analyses. Such criticisms have arisen in the United States toward evidence review bodies which fail to incorporate formal health economic analysis.

41. Conclusion: Given the size of the market for therapeutic interventions in England and Wales, along with the wide range of stakeholders who must be consulted we believe that NICE's processes are commensurate with its function. Indeed, we believe that NICE's decisions would be subject to challenge considerably more frequently if an objective health economic framework did not underpin them.

The implementation of NICE guidance, both technology appraisals and clinical guidelines

42. Technology Appraisals: We believe that NICE should be further supported in the implementation of its technology appraisals by appropriate mandating of its recommendations within the reporting structure of the health service. There is no formally monitored scheme for monitoring the adherence of hospitals or PCT's with NICE Technology Guidance that has an appropriate priority. Many groups, including the ABPI amongst others have called for guidance to be made mandatory—we would agree. A study in 2004 suggested that implementation of NICE guidance was variable and more likely to be adopted when there is strong professional support, a stable and convincing evidence base, and no increased or unfunded costs. Further and more detailed research from 2005 covering 28 appraisals suggests the situation is improving: 12 appraisals were implemented fully, 12 were incompletely implemented, and four over-implemented).

43. Guidelines: Within the current budget, NICE appears to have insufficient resources to promote its guidelines at local health service level. One solution, might be to introduce requirements for PCT's to provide or commission local NICE implementation Units at a regional level. An enquiry by the Audit Commission supports the need for improvements at local health economy level, in particular, ascribing lack of implementation to poor financial management at local NHS trust level.

44. Conclusion: NICE is inadequately resourced to ensure the implementation of its output and structural health service reform that targets often poor financial planning and organisation within local acute and primary care trusts. A more robustly defined interaction with industry is essential to serve the interests of patients and the health economy.

Dr Kiran Patel
Chairman of Trustees
South Asian Health Foundation

March 2007

Evidence submitted by the Specialised Healthcare Alliance (NICE 80)

The Specialised Healthcare Alliance is a broad coalition of 41 patient groups supported by eight corporate members.¹⁵⁴ It has been set up to campaign on behalf of people with conditions which require specialised medical care. These conditions tend to be rarer and both complex and expensive to treat. Examples are numerous but include certain cancers, cystic fibrosis, haemophilia, HIV and neurological conditions. Accidents or complications of more common conditions such as diabetes can also trigger the need for specialised services. Cumulatively, the number of patients affected by such conditions number many tens of thousands.

We welcome this opportunity to submit evidence to the Health Select Committee's inquiry into aspects of the work of the National Institute for Health and Clinical Excellence.

1. Executive Summary

1.1 The Specialised Healthcare Alliance considers NICE to have a critical role in ensuring that treatment delivered by the NHS is equitable, cost effective and to a uniformly high standard.

1.2 The existence in NICE of an independent national forum where decisions about cost effectiveness and prioritisation can be made in a consistent and fair manner is particularly important for patients with specialised medical conditions.

1.3 The Alliance believes the Institute's evaluation system should be more transparent. Reform of the process may allow for a fairer consideration of some treatments. In the case of orphan or ultra-orphan treatments social value judgments are likely to be necessary which should rest with parliament.

1.4 The Specialised Healthcare Alliance welcomes the recent moves by NICE to ensure lifesaving drugs can be assessed more quickly and supports this process being extended to other technologies.

1.5 Unless greater consideration is given to how and when tariffs reflect NICE guidance, patients could face greater delays in accessing recommended treatments.

1.6 The Alliance believes that much greater priority should be attached to ensuring the implementation of NICE guidance. If NICE were to assume responsibility for this it would need additional resources.

¹⁵⁴ A full list of members is available on our website at www.shca.info

2. *Public Confidence in the Institute*

2.1 The Specialised Healthcare Alliance believes that NICE has an important role to play in ensuring that patients receive equitable and fair treatment and that decisions about whether medicines are cost effective are made in a robust manner free from political influence.

2.2 The existence of a body such as NICE is particularly important for patients who have specialised medical conditions which may be expensive to treat. Devolution within the NHS means that local priorities increasingly drive allocation of resources. Whilst this development has many benefits it can unfairly disadvantage patients with specialised conditions who will inevitably be smaller in number and may therefore have less of a voice locally. NICE provides an important national forum where decisions about which drugs are cost effective can be considered with input from a range of stakeholders.

2.3 The members of the Specialised Healthcare Alliance and the patients they represent do not consider that public confidence in NICE has suffered substantially. In some respects current concern about the role of NICE appear to have arisen as a result of the Institute's success. NICE guidance is for the most part highly respected and significantly influences clinical and purchasing behaviour within the NHS.

2.4 However, the Alliance does believe that a number of factors would support public confidence in the Institute. In particular, promoting greater understanding of the role of NICE, greater transparency in terms of topic selection,¹⁵⁵ changes to the evaluation process and above all a greater focus within the NHS on the implementation of guidance would benefit the Institute's public standing (see sections 3 and 5).

3. *NICE's Evaluation Process, and Whether any Particular Groups are Disadvantaged by the Process*

3.1 The Specialised Healthcare Alliance recognises that NICE's evaluation process is rigorous and has gained international respect. However, the Alliance is concerned that the current process may disadvantage certain groups.

3.2 The Alliance understands that NICE does not publicly admit to any formal cost-effectiveness threshold, but many observers believe it is around £30,000 per quality of life-year (QUALY) gained. Whether or not this is the case, a number of orphan or ultra-orphan drugs are unlikely to receive NICE approval if the same cost effectiveness threshold applies as for other treatments. This could mean that patients suffering from rare and in some cases extremely serious health conditions are denied treatment on the NHS. It might also deter innovation which ultimately benefits the wider population eg as new indications are discovered and developed.

3.3 The Specialised Healthcare Alliance is aware the NICE has considered this issue in some detail and welcomed the contribution that a Citizen's Council made to the debate in a report issued in November 2004. However, we believe that such social value judgements eventually rest with those who are democratically accountable and that the government, informed by NICE and initiatives such as the Citizen's Council. The Alliance strongly believes that the standard and availability of such treatments is fundamental to a properly functioning National Health Service.

3.4 In addition, the Alliance believes consideration should be given to reforming the evaluation process to allow for consideration of broader economic costs when assessing the cost-effectiveness of particular treatments. The SHCA is concerned that in the current financial climate, with a tendency to silo budgeting, decisions about whether to fund treatment are often made without weighing the wider cost implications, such as palliative care, social service costs and lost productivity. NICE is well placed to broaden understanding of costs and benefits and these considerations should be reflected in its evaluation process.

3.5 Above all, the Alliance considers that NICE should be more transparent about the appraisal process. Lack of clarity and openness about how decisions are taken about clinical effectiveness and cost-effectiveness and the weight that the Institute gives to different kinds of evidence may erode the credibility and authority of NICE.

4. *The Speed of Publishing Guidance*

4.1 The Specialised Healthcare Alliance is aware that striking a balance between maintaining the integrity of the NICE process and the speed with which it can complete appraisals is difficult. The new "single technology appraisal" process has been developed as a means of more rapid assessment of treatments.

4.2 It was initially to be applied to lifesaving drugs that have already been licensed and to new lifesaving medicines close to the time that they first become available. The Specialised Healthcare Alliance considers that this process should be open to all technologies where patients and other stakeholders believe a more rapid appraisal process would be beneficial.

4.3 This is particularly important given the development of payment by results which may add a further delay exacerbating the process commonly known as "NICE blight" where PCTs refuse to fund new technologies until a NICE assessment is completed. It is not known how often tariffs will be reviewed in the

¹⁵⁵ The SHCA responded to the DH consultation on NICE topic selection and believes the changes instituted as a result of this process should be evaluated in due course. A copy of the SHCA submission is available upon request.

future, but even if revisions occur annually there is likely to be a considerable delay between NICE guidance and the reflection of the cost of the technology in the tariff price. Under payment by results a “pass through payment” can be negotiated between a Trust and PCT to cover the cost of new treatments, but these are subject to local negotiation and are unlikely to be applied fairly or consistently.

4.4 The Alliance believes that the resources open to NICE should be substantially increased to enable it to assess more technologies and to produce guidance more quickly where there is a need. Furthermore the Alliance would like to see greater collaboration between NICE and the PBR team to ensure that tariff prices reflect NICE guidance as soon as possible.

4.5 In the medium term, it would seem likely and desirable that the single technology appraisal should become the standard approach. Care will need to be taken to ensure that assessment of existing classes of therapy, which may provide the most cost-effective treatment options, does not get left in a slow lane.

5. The Implementation of NICE Guidance, both Technology Appraisals and Clinical Guidelines (Which Guidance is Acted on, Which is Not and the Reasons for This)

5.1 The Specialised Healthcare Alliance is greatly concerned by the continuing problems regarding the implementation of NICE guidance. The SHCA recognises that the NHS necessarily operates within cash limits and that difficult decisions regarding priorities need to be made by commissioners and other staff on a daily basis. However, NICE was established in part with the aim of ensuring the process of prioritisation was consistent, well-founded and fair. We therefore believe that much greater emphasis should be given to ensuring NICE guidance is implemented.

5.2 The Alliance is aware the NICE has no formal powers or remit with regard to implementation of its guidance. Despite this, it has recently developed new commissioning tools and databases to aid implementation in addition to establishing local representatives to explain guidance. These initiatives are welcome as is the growing emphasis on withdrawing investment from outmoded, cost ineffective technologies.

5.3 Implementation of NICE guidance forms part of the Healthcare Commission’s assessment process. However, this process is largely based on self-assessment and is constrained by the fact that it only formally assesses PCTs and other Trusts. This presently means that Specialised Commissioning Groups, which will be responsible from 1 April 2007 for commissioning of many of the areas covered by NICE guidance, may not be assessed. The Alliance is greatly disappointed by this and urging the Commission to assess Specialised Commissioning Groups as a function of its assessment of their constituent PCTs.

5.4 Meanwhile, the Alliance considers that NICE’s remit should be extended to include responsibility for promoting and monitoring implementation of its guidance. If this is to be successful it will be necessary to allocate sufficient additional resources to NICE for it to carry out its role successfully.

The Specialised Healthcare Alliance

March 2007

Evidence submitted by Wyeth Pharmaceutical (NICE 88)

Wyeth is a global pharmaceutical company dedicated to the discovery, development, manufacture and sale of human and animal pharmaceutical products. Wyeth is the 7th largest pharmaceutical company based on sales in the UK.¹⁵⁶ Four of Wyeth’s products are the subject of nine multiple health technology appraisals (MTAs).

As a member of the Association of the British Pharmaceutical Industry (ABPI), Wyeth supports and endorses the submission to the Health Select Committee made by the Association. In addition, Wyeth welcomes the opportunity to submit evidence of its experience to inform the committee’s inquiry into aspects of the work of the National Institute of Health and Clinical Excellence (NICE).

1. Executive Summary

In this submission Wyeth identifies a number of factors relating to; the challenge of NICE’s decisions, NICE’s evaluation process, the speed of publishing guidance, the appeal system and the implementation of guidance. To address the issues raised, Wyeth recommends:

- A greater consideration of factors other than cost per QALY in decision making; eg acceptability, appropriateness, preference and innovativeness of the technology, degree of clinical need, consideration of national clinical priorities and a broader (societal) view of the costs and benefits associated with the technology.

¹⁵⁶ Source: IMS Health, HPAI/BPI Database, January 2007.

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- Enabling NICE to commission work directly with the academic assessment groups thus giving them greater control over the quality of work carried out.
 - Reciprocal access to economic models between the Assessment Group and contributing Stakeholders.
 - Manufacturers should have the same opportunity to attend Appraisal Committee meetings as nominated members from other stakeholders.
 - Access to the ERG report should be given to stakeholders prior to the Appraisal Committee meeting.
 - There should be consultation over the Costing Templates and Costing Report.
 - In the event of little or no change to the FAD post appeal, the Guidance Executive should make the necessary changes and publish the guidance in accordance with section 4.6.9 of the NICE Guide to the Technology Appraisal Process.
 - An independent Appeal Committee, without NICE board members, hears appeals.
 - The opportunity, at appeal, for stakeholders to challenge the clinical rationale and the quality of the evidence upon which the recommendations are made.
 - Appropriate audit/measure of the implementation of NICE guidance and guidelines.
 - Incentives for the implementation of guidance and guidelines.
 - That subsequent guidance is placed in context with existing guidance.
 - Mandatory funding for clinical guidelines.

2. *Why NICE's Decisions Are Increasingly Being Challenged*

2.1 NICE's decisions are becoming increasingly reliant on the estimated cost effectiveness, expressed as cost per quality adjusted life year (QALY) gained, as the sole determinant of whether or not to recommend a therapy for use within the NHS. The cost per QALY gained frequently does not accord with both patients' and health care professionals' experience of the value of the therapy being appraised. For example the cost per QALY fails to account for the impact of disease and its treatment on carers and the immediate family of the patient.

2.2 Cost per QALY also fails to account for the broader societal benefits derived from treatment such as ability to continue/return to work; with associated reduction in unemployment and/or disability benefits and increase in tax revenue from the individual maintaining or restarting work. This disparity in value is greatest in early onset, chronic, degenerative conditions such as Ankylosing Spondylitis (AS). Despite acknowledging that up to 30% of sufferers are unable to work, the recent Appraisal Consultation Document (ACD) for the use of TNF inhibitors in the treatment of AS, seeks to restrict the long-term use of these agents to the 6% of patients whom NICE consider achieve a cost per QALY of less than £20,000.

2.3 There is variability in the quality and consistency of the Assessment Reports, commissioned on NICE's behalf from various academic centres within the UK and upon which the Appraisal Committee's base their recommendations. Our concerns relate to the adequacy with which the resultant Assessment Reports address the scope of the appraisals, the appropriateness of the structure and inputs to the economic models, the extent to which comments from stakeholders are addressed by the assessment groups and the handling of uncertainty with respect to the cost effectiveness analyses. Failure to address these issues during the appraisal process increases the likelihood of the final decision being challenged.

2.4 The above concerns may be exacerbated in part by the system under which Assessment Groups are contracted to produce the reports that inform NICE decision-making. There are no direct agreements between NICE and individual Assessment Groups (with the exception of the Decision Support Unit). The Department of Health contracts with the umbrella organisation, the National Collaborating Centre for Health Technology Assessment, which is responsible for managing the contracts with individual Assessment Groups. The Institute thus has no direct contractual relationship with the Assessment Groups, although it is their ultimate customer. As such, NICE has limited ability to require and ensure that the reports produced by the Assessment Groups are fit for purpose.

2.5 Wyeth are appealing the recent Final Appraisal Determination (FAD) for use of TNF inhibitors in the treatment of Rheumatoid Arthritis (RA). One of the aspects of this appeal relates to the Assessment Report failing to evaluate the earlier use of these agents despite the scope indicating that the appraisal should attempt to identify the stage in the pathway of care where these agents should be used. Another aspect of Wyeth's appeal relates to the failure of the assessment group to carry out the analysis of uncertainty defined in NICE's Guide to the Methods of Technology Appraisal.

2.6 It is often difficult to determine why estimates of cost effectiveness derived by the assessment groups differ from those generated by the manufacturers and other stakeholders. Whilst the assessment groups have full access to the economic models produced by the manufacturers the assessment groups maintain their models in confidence in order to protect the intellectual property rights to their work. In the event that NICE

negotiates release of the assessment groups' models they are "locked" to prevent stakeholders from re-running them, which thwarts stakeholders attempts to understand how they work. Given stakeholders concerns over the quality of the assessment groups' work, failure to fully disclose how their estimates of cost-effectiveness are derived further increases the likelihood of the final decision being challenged.

2.7 Thus far despite concerns raised by both manufacturers and healthcare professionals over the construct of the assessment group's model for the appraisal of TNF inhibitors in the treatment of AS, neither the assessment group or NICE have attempted to address these issues.

2.8 In conclusion, differences in the perceived value derived from the technologies being appraised and a lack of transparency regarding how decisions are reached results in an increasing number of challenges from patient, healthcare professional and manufacturer stakeholders.

2.9 Wyeth recommend:

- a greater consideration of factors other than cost per QALY in decision making; eg acceptability, appropriateness, preference and innovativeness of the technology, degree of clinical need, consideration of national clinical priorities and a broader (societal) view of the costs and benefits associated with the technology;
- enabling NICE to commission work directly with the academic assessment groups thus giving them greater control over the quality of work carried out; and
- reciprocal access to economic models between the Assessment Group and contributing Stakeholders.

3. *Whether Public Confidence in the Institute Is Waning, and If So Why*

3.1 The public's perception of NICE is informed to a large extent by the media coverage of its activities which focus on the frequent challenges to its decisions by patients, healthcare professionals and manufacturers. The media coverage is associated with the failure of the decisions taken by NICE to promote the faster uptake of innovative medicines and a failure to prevent postcode prescribing.

4. *NICE's Evaluation Process, and Whether Any Particular Groups Are Disadvantaged By the Process*

4.1 Manufacturers, having developed and licensed the technologies, provide much of the evidence being appraised and yet they are excluded from the initial Appraisal Committee meeting when the evidence base is first discussed prior to the committee drafting its initial recommendations. This denies the Appraisal Committee the opportunity to have addressed any outstanding questions that can only be answered by those directly involved in generating the data. Enabling the manufacturer to hear the discussions would also increase the transparency of the subsequent decision-making and likely lead to a reduction in appeals brought about due to a failure to understand how decisions have been reached. Manufacturers are singularly disadvantaged as patients and healthcare professional organisations are asked to nominate experts who are invited to submit a personal view of the technology and to attend the first Appraisal Committee meeting.

4.2 Within the newer Single Technology Appraisal (STA) process it is the critique of the manufacturers submission, performed by an academic Evidence Review Group (ERG) that is provided to the Appraisal Committee to inform their decision-making. As the report is not made available prior to the Appraisal Committee meeting and the manufacturer is not invited to attend the meeting, despite generating the original submission, the manufacturer remains unaware of the content of the final report until after the ACD or FAD has been issued. The lack of opportunity to correct any factual errors contained within the ERG's report clearly disadvantages the manufacturer and may lead to subsequent delays as these errors are addressed later in the process.

4.3 The "Implications for the NHS" section of draft guidance has been replaced by reference to implementation tools, in particular a "Costing Template and Costing Report", which are not made available until after final guidance is issued. NICE invite stakeholders to comment on whether they consider that the preliminary views on the resource impact and implications for the NHS are appropriate. However the failure to release draft copies of these tools along with the ACD prevent stakeholders from commenting on this important aspect of the draft guidance. NICE have announced the intention to consult with stakeholders over the Costing Template and Report, however these tools have not been released with either the ACD or FAD for the previously mentioned AS and RA appraisals respectively.

4.4 The variability of the quality of Assessment Reports has resulted in the need to issue addenda to correct errors in estimates of effectiveness, costs, utilities and additional benefits gained. In the event that the Appraisal Committee is not happy to make a recommendation on the strength of the evidence contained within the Assessment Report NICE have undertaken, or commissioned the Decision Support Unit (DSU) to undertake further analysis to address deficiencies. This results in delays in publication of Guidance and, as a consequence, delays in patient access to the appraised medicines. NICE have recently announced with regret that they have asked the DSU to undertake further analysis to inform the aforementioned AS appraisal. As yet NICE have not been in a position to provide stakeholders with a revised timeline for publication of guidance.

4.5 Clinical specialists and patient experts whilst invited to attend the first Appraisal Committee meeting, often have, insufficient understanding of health economic methodology and NICE's processes and methods to effectively and fully engage in the HTA process. In addition, the groups that they represent often have limited resources, which further reduce their ability to make effective representations.

4.6 Wyeth recommend:

- manufacturers should have the same opportunity to attend Appraisal Committee meetings as nominated members of other stakeholders;
- access to the ERG report should be given to stakeholders prior to the Appraisal Committee meeting; and
- there should be consultation over the Costing Templates and Costing Report.

5. *The Speed of Publishing Guidance*

5.1 Capacity to undertake appraisals, requirements for additional analyses and appeals to FADs all serve to reduce the speed with which guidance is published. As an example, despite advanced notification to the Department of Health of the anticipated license of etanercept for the treatment of AS in January 2004, the HTA for this technology is still ongoing. In October 2003, based on the extent of the burden of illness of AS, the likely budget impact and the anticipated funding issues, Wyeth requested that etanercept, along with infliximab, be included in the 8th wave of products referred to the Institute for appraisal. The topic was subsequently referred in the 9th wave with guidance anticipated in February 2006. NICE delayed the appraisal by 10 months to include the third TNF inhibitor adalimumab. There was a three-week delay in release of the Assessment Report, which was finally issued in June 2006 and a four-month delay in release of the draft guidance (ACD), which was finally released in December 2006. The delay in generation of the draft guidance was due to a request from the Appraisal Committee to the Assessment group for additional sub-group analysis. At this stage final guidance was anticipated in June 2007. However due to the repeated concerns expressed by all stakeholders as to the structure and inputs to the Assessment Group's model, NICE have asked the Decision Support Unit to conduct further analysis to inform generation of the FAD. At the time of this submission the extent of this further delay is not known.

5.2 Until such time as NICE publish its final recommendation on the use of TNF (inhibitors for the treatment of AS, funding is restricted to the few individuals for whom treatment can be negotiated on a case by case basis. In a recent survey of its consultant membership, the British Society of Rheumatology (BSR) identified that one third of respondents have no access to TNF inhibitors to treat patients with AS.¹⁵⁷ Only 25% of respondents reported the ability to prescribe in accordance with BSR guidelines. Clearly the delay in publication of NICE guidance is having a significant negative impact on patient access to these innovative treatments.

5.3 Despite the vast majority of the appeal points being dismissed, and those upheld resulting in no substantiate change to the recommendations, the FADs for the Psoriasis and Psoriatic Arthritis appraisals were returned to the Appraisal Committee to be amended and reissued. This resulted in a lapsed time of 5–6 months from the appeal hearing to final publication of the guidance.

5.4 Wyeth recommend:

- in the event of little or no change to the FAD post appeal the Guidance Executive make the necessary changes and publish the guidance in accordance with section 4.6.9 of the NICE Guide to the Technology Appraisal Process.

6. *The Appeal System*

6.1 Wyeth share the concerns raised by the ABPI regarding the deficiencies in the current appeal procedure. In particular, the role of the Chairman of the Appeals Committee in the initial scrutiny of appeals and the constitution of the Appeal Panel result in the lack of an independent review of the conduct of and decisions reached by the Appraisal Committee. The initial scrutiny of lodged appeals is intended to ensure that the appellant has a valid and arguable case. In practice, however, this review frequently addresses the merits of the appeal also. Given that the Chairman of the Appeals Committee subsequently sits on the Appeal Panel such initial scrutiny could prejudice the appeal. Two or three of the five members of the Appeal Panel, including the Chairman of the Panel, are members of NICE's own board. Such board members could be expected to have an inherent interest in defending the decision reached by the Appraisal Committee, which again one could argue would be prejudicial to the fair hearing of the appeal.

6.2 As indicated throughout this submission, many of the concerns surrounding the NICE appraisal process relate to the quality of the evidence base upon which decisions are reached and the scientific merits of those decisions. However current interpretation of the very restrictive grounds for appeal prevent either of these aspects being challenged at appeal.

¹⁵⁷ Rheumatology 2006; 45: 1376–1379.

6.3 The criteria for the successful appeal, made under the ground that the Institute has prepared a FAD that is perverse in the light of the evidence submitted, is so unrealistically high as to prevent any substantive review of the recommendations made.

6.4 Wyeth recommend:

- an independent Appeal Committee, without NICE board members, hears appeals; and
- the opportunity, at appeal, for stakeholders to challenge the clinical rationale and the quality of the evidence upon which the recommendations are made.

7. *The Implementation of NICE Guidance, Both Technology Appraisals and Clinical Guidelines*

7.1 The extent of implementation of both HTA guidance and clinical guidelines is difficult to determine as they are not systematically assessed. Whilst the Healthcare Commission is responsible for assessing the performance of NHS organisations to ensure they conform to NICE technology appraisals, this currently consists of the self-assessment of whether an organisation has a procedure in place to ensure conformity, rather than a measure of the effectiveness of the procedure.

7.2 From the various assessments of the implementation of individual health technology appraisals it is clear that the uptake of recommended therapies can be both slow and inconsistent across England and Wales. The BSR's survey of its membership identified that despite a positive NICE recommendation for the use of TNF inhibitors to treat RA patients published in 2002, 42% of respondents indicated that, four years on, they still had some form of restriction on the prescribing of these agents in line with NICE guidance. 70% cited some form of cap on funding whilst 21% and 9% cited lack of staff or facilities, respectively.

7.3 With the advent of the STA process, there will be increasingly an MTA and a number of STAs covering the same patient population, as will be the case in the near future with TNF inhibitors for the treatment of psoriasis. If MTAs and STAs do not inter-relate it will be difficult for clinicians to identify which piece of guidance to follow.

7.4 Wyeth are concerned that the replacement of HTA guidance, and associated mandatory funding, with clinical guidelines, for which funding is not mandated, may lead to restrictions in patient access to these medicines as NHS organisations prioritise the funding of guidance.

7.5 Wyeth recommend:

- appropriate audit/measure of the implementation of NICE guidance and guidelines;
- incentives for the implementation of guidance and guidelines;
- that subsequent guidance is placed in context with existing guidance; and
- mandatory funding for clinical guidelines.

Wyeth Pharmaceuticals

March 2007

Evidence submitted by Dr Daphine Austin (NICE 20)

EXECUTIVE SUMMARY

- The increasing number of challenges to NICE's decision making should be seen and understood in a wider context.
- Challenge should not always be seen as a bad thing. Nor should legal action if the case is testing an important principle. The courts are there to define the parameters within which public bodies can act.
- No organisation, including NICE, should have the power to commit resources without also having the budgetary responsibility. The mandatory nature of the technology guidance should be removed at the very least.
- As currently constructed NICE's decision making and the mandatory requirement for PCTs to implement its guidance on individual technologies (mainly drugs) creates an ethical dilemma that needs to be resolved. It also creates a distortion of clinical and service priorities.
- NICE does and can do useful work on behalf of the NHS. Although there are problems, most see a role for NICE.
- Although NICE's decision-making may come under criticism caution must be exercised in making recommendations which create a situation that even further undermines priority setting.

GENERAL COMMENTS

1. This response is confined to NICE's technology appraisal programme, the implementation of which is mandatory for primary care trusts.

THE COMMITTEE'S AREA OF INTEREST

Why are NICE's decisions increasingly being challenged?

I believe there are three main reasons for this.

Misperceptions About the Role of NICE

2. The need to consider "value for money" in the NHS is accepted but this is not always linked with "rationing".

3. When NICE was established, it was "sold" to the public as an organisation which would "end postcode rationing". In my working day I regularly come across the view of NICE as "defender" of patient access.

4. The public has a poor understanding of the "effectiveness" of treatments and the concept of "cost-effectiveness". This is true also of many people working in the NHS, including healthcare professionals. In addition we have not yet reached the tipping point at which the need for priority setting is not only fully accepted but also faced openly and squarely.

5. Confusion exists over the role of licensing and how this relates to the role of NICE. For many licensing is seen as the stamp of approval for a drug (although few policy makers feel that licensing provides adequate information on which to properly judge the value of a drug).

6. Given this, many individuals find it perplexing that doctors have the freedom to prescribe a drug but that the NHS does not have to pay for it.

Given the above, it is not surprising that a "no" decision from NICE comes as a shock to patients and the public.

Challenges are an expression of general social trends

7. NICE and primary care trusts (PCTs) are the organisations tasked with making explicit decisions about the availability of services in the NHS. This task, by definition, is going to create controversy and invite challenge. Anger is a common emotion associated with loss. Those who have had a long term involvement with priority setting understand that having to deal with fear, anger, denial and bargaining is a part of their role.

8. With respect to legal challenge, NICE is not unique in experiencing threats of legal challenges and at an increasing rate. This is part of a trend in readiness to use the courts. During most of my time as a consultant in public health (about 15 years) there were about 5 significant court cases related to funding issues. In contrast, in the last year there have been at least 5 cases that I am aware of.

9. The recent high number has, in part, been encouraged by the very unusual precedent one judge has set by requiring the PCT to fund treatment before the case was heard.

10. As a result most commissioners expect an ongoing rise in the number of legal challenges. It is not surprising that NICE finds itself defending its decisions in court. Most of us working in this area are only surprised that it has taken this long.

11. Legal challenge should not be seen as a bad thing or a result of bad decision making. True, for an organisation to lose a case because of poor process is neither good for the organisation nor for the NHS. This is to be avoided. However, it is important sometimes to use the courts to test principle and define more clearly the parameters within which public bodies operate. Unlike local authorities, the NHS and the Department of Health has always been extremely court adverse. This is frequently counter-productive.

12. A greater readiness to challenge (even when there is no real threat of actual legal action) also stems from a belief that the courts supports patients' right to treatment, which it does not. Health is often talked about as a basic human right. One can understand the sentiment but clearly this cannot be the case. When need is greater than the resource available which individual has a health need has "right to be met" and which does not?

13. The perception that it is wrong to deny treatment is fuelled by the fact that PCTs frequently step down when there is a real threat of legal action. This is interpreted as an acknowledgement of the PCT being "in the wrong". This is often not the case. PCTs are most likely to step down for one of four reasons (or a combination of them):

- Fear of the court process and hostile publicity.
- PCT manpower is stretched at the best of times and judicial review is very labour intensive. Some see defending a court case as creating a major diversion of their organisation's main purpose.

- A reluctance to put the PCT at financial risk or concern over the fact that court costs have to come out of the same fund which is used for patient services.
- PCTs are frequently subjected to covert political pressure to overturn their first decision not to fund.

14. Finally, there are a number of wider social changes and forces that increase the likelihood of challenge:

- There is a well-described changing dynamic between both the public and public authorities and also patients and the NHS. This change is being promoted by the “patient as consumer” model of healthcare and increased access to information.
- The Pharmaceutical Industry are becoming ever more sophisticated in the ways they can fuel demand for drugs.
- The media plays a major role in creating demand and indeed dissatisfaction with public services—some of it justified and some of it not.
- Politicians themselves also play a role. For example, the message that is frequently conveyed is that if a treatment is effective it will be either be freely available on the NHS. This is constantly reinforced yet clearly this cannot be the case when demand and need are greater than the resources available.

15. Public policy makers also need to be mindful of the information that is available to patients. The World Wide Web has completely transformed the information available to the individual and this has great potential for democratising Society. However it must be appreciated that there is a great deal of poor information and misinformation on the web. For example—a drug which “extends life by 4 weeks” is often described as one which “increases survival”. Clearly these are two very different things. On more than one occasion I have talked to a patient or a carer following a decision not to fund some treatment, only for them to learn that the treatment will neither cure nor provide a remission. Not only to I find it appalling that in these instances patients have been so ill-informed but worse, that they should learn of a more realistic prognosis from a stranger, in such a stressful circumstance.

16. We cannot perhaps be surprised at the lack of good information available to the public and the patient. Interpreting the complexities of trial data is often beyond even individuals such as myself, and most certainly many practising clinicians. Presenting research data in a way that is accurate and meaningful to the lay person is a real challenge that we have not yet fully resolved.

NICE's basis for decision making make it particularly susceptible to challenge

17. Although most people are supportive of the need to take cost-effectiveness into consideration when committing resources, very few PCTs would support it as the ONLY basis for making a decision. For many involved in priority setting a treatment has to be cost-effective in order for it to be considered for funding. Its priority must then be determined by comparing its value with that of other competing needs.

18. Decision making basis only on cost-effectiveness creates problems on a number of fronts, some of which are dealt with in section 3 below. This method of allocating resources drives the decision maker to agree to fund a treatment when it lies below the threshold and decline funding when it is above. In this case the threshold is the QALY threshold set currently at an indicative figure of £30,000.

19. This basis for decision making sets up the environment for hot debate about whether the QALY is £29,999 or £30,001 (I know that NICE are not that rigid but this is for illustrative purposes only). If other factors and principles are used in decision making then the precise figure is less important—a rough figure is often good enough.

20. The situation is made worse of course, because in deriving a cost-effectiveness figure for a QALY assumptions have to be made. This is true of whether NICE is developing the costing model or whether the Pharmaceutical Industry is. Needless to say because assumptions are, just that, assumptions such decision making is likely to make it vulnerable to challenge and an endless debate about whether this figure is correct or that. Never mind that the Pharmaceutical Industry are considered by experts to frequently use overly optimistic assumptions, and therefore inflate the benefits—controversy has been created and a seed of doubt has been placed in the public's mind. Other problems with this type of decision making leads us to the next section.

The Committee's area of interest 3: Does NICE's evaluation process disadvantages particular patient groups by the process?

21. In short the answer is yes. This is related to both the fact that NICE's uses largely cost-effectiveness to determine funding and how NICE is used to commit the resources of PCTs.

22. Because NICE uses only a limited range of factors when coming to a decision—its decisions are often at complete odds with those of PCTs. The automatic assumption that this is because they come to better conclusions can be brought into question and from the PCTs perspective NICE does not say “no” often enough.

23. Most importantly this situation presents a real ethical problem, because the NHS now has two decision makers, committing a single budget, but making decisions in very different ways and using very different values. This is illustrated below. NICE's high threshold for saying no is also unsustainable.

24. NICE is in the position of not needing to worry about the NHS budget, it is not required to look at affordability nor the real opportunity costs that might result from its decisions. It does not need to consider the priority of the treatment vis-à-vis other competing needs. Its decision making is also incompatible with programme budgeting which those most knowledgeable about priority setting see as a key way forward in priority setting.

25. Fairness, in allocating resource, at the very least demands that everything gets a *chance* to be considered along side everything else. The mandatory nature of the technology guidance means certain drugs are treated preferentially—regardless of whether they are the most important and valued service to fund at any point in time. Indeed, it is often the controversial treatments that are referred to NICE. It is wrong to allow drugs and other individual interventions to queue jump priority setting processes.

26. The fact that NICE guidance is mandatory, however well intentioned this move was, has resulted in a serious distortion of health service priorities. To illustrate this, when I was working in Worcestershire I tried for over 5 years to establish a number of palliative care units in the County. At that time the County only had 5 beds for a population of 500,000. Year after year funding earmarked for beds was diverted to fund mandatory guidance by NICE. In some instances these drugs extended life by a matter of only a few weeks. When the treatment had done its work patients still then needed palliative care. It is completely perverse to have a situation where it is mandatory to fund a drug of marginal benefit (and no PCT would invest in treatment extending life by only 1-2 months by choice) yet a service as basic as palliative care beds are not. If the NHS is to consider mandatory services, which eradicating postcode variation, then it needs to look to the basics—not the latest “wonder drug” which very rarely fulfils this description. Yet we NEVER have had a discussion about what provision must not vary across country.

27. One might of course ask why would NICE support treatment that extends life by only a few weeks? The answer is related to point 18 above. It has to be understood that the QALY needs interpretation, which under the current system, NICE would find difficult to do. When it is estimated that a drug has a cost effectiveness £20,000 per QALY for example—it would be difficult for NICE to refuse to support its use. However this figure does not distinguish between whether one patient gets one year of quality adjusted life or whether 365 patients get one day each.

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

28. The increasing number of challenges to NICE's decision making should be seen and understood in a wider context.

29. Challenge should not always be seen as a bad thing. Nor should legal action if the case is testing an important principle. The courts are there to define the parameters within which public bodies can act.

30. No organisation, including NICE, should have the power to commit resources without also having the budgetary responsibility. The mandatory nature of the technology guidance should be removed at the very least.

31. As currently constructed NICE's decision making and the mandatory requirement for PCTs to implement its guidance on individual technologies (mainly drugs) creates an ethical dilemma that needs to be resolved. There are a number of options for resolving this ethical problem: remove the mandatory requirement, harmonise its decisions in line with PCTs decisions (which would significantly drive down the threshold) or give it a cash limited budget within which it has to prioritise the treatments it considers.

32. We should not throw the baby out with the bath water. NICE does and can do useful work on behalf of the NHS. Although there are problems, most see a role for NICE—not the least of which is assessing evidence. Many PCTs would like to see this role retained and for NICE to rely less on Industry modelling (which has been the most recent requirement placed on NICE). Indeed NICE should have the freedom to demand information from Industry, to consider all sources of evidence and look at unlicensed protocols and unlicensed drugs. It should also have the freedom to demand better evidence including requiring treatment to be provided in the context.

33. On the other hand, if it must have a policy making role then its decisions need to come into line with those of PCTs who have a better grasp of the total needs of populations and services. NICE's horizons, in reality, are very limited.

34. Although NICE's decision-making may come under criticism caution must be exercised in making recommendations in order to avoid creating a situation that even further undermines priority setting. To react to the uncomfortable truth that Society cannot afford everything it wishes by pushing it underground merely adds injustice by placing the burden of rationing onto those with the least voice and those without big Industry interest. Making priority setting invisible is the worst of all scenarios.

35. Finally—I would make a plea to politicians, on behalf of those making difficult decisions on Societies behalf (both NICE and PCTs), to find ways to support those undertake the difficult task of priority setting. Providing leadership to create a debate about priority setting could most usefully do this. Until we can accept that not all needs can be met we will continue to have a distortion in health service priorities and, ironically, fail to get value for money overall.

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March 2007

Evidence submitted by Professor Michael Barkham and others (NICE 83)¹⁵⁸

EXECUTIVE SUMMARY

1. Psychological therapies are a crucial part of the delivery of health care within the NHS and NICE guidelines now exist to support these being commissioned across a range of mental health conditions. Government is also responding to public concern about lack of access and serious health inequities in the provision of psychological therapies, as recommended by NICE, through Department of Health pilot initiatives such as Improving Access to Psychological Therapies. However, there are a range of problems with implementing NICE's guidelines in mental health. Moreover, the systematic failure of implementation results in a reduction in public and professional confidence in NICE as well as a failure to deliver evidence-based health care, at an estimated cost of £64 billion in long-term incapacity and ill-health.¹⁵⁹ The mental health guidelines have questionable utility.

2. The main focus for NICE is on new developments in drugs. The conventional gold standard methods of randomised controlled trials (RCTs) in which patients can be “blind” to the competing medication is an appropriate method for scientific evaluation as to whether new drugs are cost-effective but is more problematic when applied to the area of psychological interventions. This creates a gap between treatment recommendations in mental health guidelines which are not being systematically tested in routine practice settings. This results in unrealistic assumptions, therefore, in terms of service redesign, and which ignore the capacity of NHS clinicians and service managers to deliver these new treatment approaches.

3. Without a scientific methodology which properly evaluates the evidence base for psychological therapies as they occur in NHS settings, the resulting recommendations based mainly on RCTs and small patient samples can identify a treatment approach which is most effective but misidentify or fail to identify the treatment which is most cost-effective. The risk is that when investment is available to implement NICE guidance, this will not lead to improved mental health outcomes.

4. There are a range of concerns, therefore, about gaps in the kind of evidence, which NICE's existing guidelines for mental health mainly rely on. These are:

4.1 A restricted model of science means that NICE guidance might be potentially misleading when generalized to patient populations in routine clinical practice [see 6 to 6.6]

4.2 Reliance on treatments tested only by RCTs threatens to restrict patient choice for important interventions, or individualized combinations of interventions, and over-resource standard treatments that are not panaceas and will not suit all patients [see 7 to 7.7]

4.3 The undue weighting given to evidence of treatment efficacy, which assumes it is the treatment model which matters, fails to account for evidence that what often matters more to a patient is the quality and experience of the practitioner, which then leads guidelines towards promoting best technologies over best practitioners [see 8 to 8.3]

4.4 Our limited evidence base for comparing different psychological therapies with each other in trials can be extrapolated for use in cost-benefit analyses, but probably only cautiously, to add value to existing services. There is concern that NICE guidelines might be misused as a basis for new commissioning strategies or for redesigning existing NHS psychological therapies when the evidence underlying their recommendations does not support this. No national audit has been undertaken for NICE's mental health guidelines, so the beneficial impacts of NICE guidelines on cost-effectiveness, if any, are not yet known [see 9 to 9.3]

¹⁵⁸ Signatories: Michael Barkham, Professor of Clinical & Counselling Psychology, Director, Psychological Therapies Research Centre, University of Leeds; Jeremy Clarke; Research & Development Lead, Association for Psychoanalytic Psychotherapy in the NHS; Tirril Harris; Research Fellow, Institute of Psychiatry, Kings College London; Psychoanalytical psychotherapist in private practice; R Peter Hobson; Tavistock Professor of Developmental Psychopathology, University of London; Phil Richardson; Professor of Clinical Psychology; Tavistock & Portman NHS Trust & University of Essex.

¹⁵⁹ We need to talk: The case for psychological therapy on the NHS (2006). A report from Mental Health Foundation, MIND, rethink, The Sainsbury Centre for Mental Health, Young Minds.

 AREA OF EXPERTISE

5. The signatories of this submission collectively represent an expert panel in the areas of research and delivery of psychological therapies in NHS service settings. We represent a wide range of approaches to the psychological therapies as well as a thorough knowledge base of the research evidence and methodologies associated with them.

WHY NICE'S DECISIONS ARE INCREASINGLY BEING CHALLENGED AND CONFIDENCE WANING

6. Because current NICE policy adopts a single/restricted model of science. Much of the evidence gathered from randomised controlled trials (RCTs) is derived from studies that do not correspond with routine NHS practice in the area of the psychological therapies. This is important in that it means that much of the evidence used in NICE guidelines does not bear directly on the indications for, or effectiveness of, NHS psychological therapies.

6.1 Patients are selected in trials according to very restricted clinical criteria that do not accord with the presenting problems of patients in the NHS. By contrast, most patients present in the NHS with wide-ranging difficulties. Although the former provides a good basis for controlled science, it is too restricting when it comes to “applied science” which is what is required in NHS settings.

6.2 Randomised allocation of patients to different treatment groups is not what happens in routine clinical practice where patients are treated as individuals with particular needs and in many cases clear preferences for their type of therapy. Further, NHS service delivery is very much a function of costs and resources, both of which are not considered sufficiently within RCTs.

6.3 The result from any RCT is, in effect, only a single observation. The logic of RCTs requires multiple (not just one or two) replications in order to build a robust knowledge base. Building an evidence-base on a single RCT is unsafe. However, some current NICE guidelines (eg, for depression) cite the highest level of evidence (termed level “A”) to include a single RCT. This is a relatively low level of evidence as compared with meta-analytic studies (ie, the study of multiple findings from multiple RCTs) which are also graded as level “A” evidence.

6.4 There is a widely recognised effect within research termed “researcher allegiance”.¹⁶⁰ In effect, this states that researchers research the type of psychological therapy to which they have some form of allegiance. Not surprisingly, most of the findings from RCTs involving psychological therapies arrive at findings which support the therapeutic approach to which the researcher has an allegiance. This is probably one of the most pervasive and powerful effects across all RCTs in the psychological therapies and derives from unwitting biases taking place in some of the 100s of decisions made in the course of a single study. The evidence which needs to be sifted out from the existing studies relates to those RCTs which are (a) led by people without a stated preference for one of the therapies, and/or (b) have a clear proponent/expert of each of the approaches being evaluated in a study, and/or (c) yield evidence contrary to the researcher's therapeutic allegiance.

6.5 It will likely be impossible to test out all psychological treatment approaches using adequately constructed RCTs because studies of the required size are too costly (> £1 million) and securing the results takes too long (may be four years). Much of the evidence from RCTs in the psychological therapies derives from studies with only 20 patients in the condition being evaluated. It is generally accepted that such studies do not have sufficient numbers of patients to make the claims they do because the small N makes them more vulnerable to biases (ie, an unwitting bias will have a greater impact amongst a smaller sample of patients). Often the effects achieved are because the target measure is so specific.

6.6 One recent Cochrane Review found that the average number of clients in RCTs as a whole (as opposed to treatment conditions) of Generalised Anxiety Disorder was only 53 and concluded that “it seems highly unlikely, therefore, that any of these studies were adequately powered”—meaning that the number of clients was too small.¹⁶¹ By contrast, studies using patients from routine NHS settings and totalling multiples of 100s are not considered as legitimate evidence by NICE because they do not use an RCT design.¹⁶² There is a need for both types to evidence.

7. Because it restricts patient choice. Current government initiatives have placed considerable emphasis on “patient choice”. However, there is an increasing focus on a single model of psychological therapy—cognitive-behavioural therapy (CBT)—in which this model is repeatedly identified in HTA and other government-funded trials as the form of intervention to be researched such that this model yields a disproportionate amount of evidence which could restrict patient choice.

¹⁶⁰ Jacobson NS (1999) The role of the allegiance effect in psychotherapy research: Controlling and accounting for it. *Clinical Psychology: Science and Practice*, 6, 116–119.

¹⁶¹ Hunot V, Churchill R, Silva de Lima M, Teixeira V. (2007). Psychological therapies for generalised anxiety disorder. *Cochrane Database of Systematic Reviews, Issue 1*. Art No. CD001848; DOI: 10.1002/14651858. CD001848.pub4.

¹⁶² Stiles WB, Barkham M, Twigg E, Mellor-Clark J, Cooper M. (2006). Effectiveness of cognitive-behavioural, person-centred, and psychodynamic therapies as practiced in UK National Health Service settings. *Psychological Medicine*, 36, 555–566.

7.1 When other forms of psychological intervention have been compared with CBT in government funded RCTs, findings have shown broad equivalence of outcomes, for example, in depression and anxiety in primary care.¹⁶³ However, such therapies have not been adopted within the NICE guidelines.

7.2 The over-emphasis on CBT has led to the identification of a shortage of CBT practitioners which would then require additional funding to correct. This approach has generated artificial problems regarding resources (ie, practitioners) to deliver psychological therapies.

7.3 There are other effective psychological therapies which are being viewed as “second class” because they often do not have RCT evidence associated with them: this is a funding issue and not an effectiveness issue. Absence of evidence of effectiveness is not the same as evidence of ineffectiveness. One example of this mismatch is the fact that the model of therapy most often espoused by practitioners is that of “integrative” therapy and yet this has never been evaluated in an RCT and probably couldn’t because it is not manualised and each practitioner is delivering their own form of integrative therapy honed over years of experience.

7.4 A model of evidence which cannot evaluate the most commonly delivered form of therapy at the scientific level which it deems to be highest (ie, RCTs) exemplifies the gap between the perceived relevance of NICE and routine NHS practice.

7.5 Such a strategy also restricts professional practice. An electronic petition submitted to 10 Downing Street (closing date 3 March 2007) objecting to the over-emphasis on CBT was signed by 10,025 (presumably) professionals:¹⁶⁴ “We the undersigned petition the Prime Minister to consider other psychotherapy approaches, not only cbt, in the proposed expansion of psychotherapeutic services within the NHS, instead of restricting choice for members of the public to one only model of therapy.”

7.6 An approach which would make far more useful clinical guidelines, starts with what the patient (or service user) needs, and with what practitioners are then able to offer them as an effective treatment, which is supported empirically by evidence from routine practice, thus promoting actual improvements in services.

8. Because NICE guidance focuses overly on technologies at the expense of practitioners and common factors. The content of guidelines—and invariably the research—focuses on specific treatment approaches (eg, CBT, problem-solving) when this is only one component within the service delivery framework. Most crucially, psychological therapy approaches are delivered by practitioners (ie, people) and while NICE guidance promotes evidence-based therapies, there is little—if any—attention to evidence-based practitioners. Given that practitioners are the most valuable resource, it would appear sensible to place equal focus on practitioners as is currently placed on technologies.

8.1 There is a growing debate within the area of the psychological therapies as the contribution (ie effectiveness) of practitioners versus specific therapies. There has been research arguing for both sides of the case.¹⁶⁵ The most logical response to this situation is that the government should invest not only in the “technology” of interventions but also in practitioners themselves when it is becoming clear that the effectiveness of practitioners may be of at least equal importance.¹⁶⁶

8.2 Because of the focus in RCTs on technologies in which practitioners are all assumed to be “equal”, such studies have not investigated practitioner effects. The contribution and variability of practitioners is an important component which is currently being determined from analyses of large data sets collected from routine NHS mental health settings. But, as above, because this data has not been collected within an RCT, it is not being considered by NICE. Such a strategy places NICE at a distance from everyday practitioners and does not facilitate practitioners adopting and implementing NICE guidance.

8.3 In addition, current NICE policy over-emphasizes techniques rather than factors which are common across interventions. In RCTs, treatment is administered according to closely monitored protocols, whereas much NHS treatment is not so restricted and is more flexible. NHS psychotherapy for given individuals often draws upon different treatment approaches. In addition, practitioners differ in style and effectiveness, and the critical, evidence-based influence of establishing a “therapeutic alliance” between patient and therapist—a matter at the heart of psychotherapy—is sidelined.

9. Because NICE guidelines are being misused in relation to the actual body of evidence. There are several problems in using NICE guidelines to introduce health efficiency savings in mental health, and some evidence to suggest this is not being achieved. Two examples are (a) the primary impact of the guidelines for anxiety and depression on encouraging continued soaring costs for anti-depressants, and (b) the resources on computerised CBT, subsequent to NICE’s technology assessment, when there are equally effective alternatives which are free to access.¹⁶⁷ Such outcomes could lead to commissioners seeking to de-invest in psychological therapies. There is a risk that patient care then suffers.

¹⁶³ King M, Sibbald B, Ward E, Bower P, Lloyd M, Gabbay M, Byford S (2000). Randomised controlled trial of non-directive counselling, cognitive-behavioural therapy and usual general practitioner care in the management of depression as well as mixed anxiety and depression in primary care. *Health Technology Assessment*, 4(19).

¹⁶⁴ e-petition: <http://petitions.pm.gov.uk/Therapy/>

¹⁶⁵ Special issue on therapist effects in *Psychotherapy Research*, 2006, 16, 143–187.

¹⁶⁶ Lutz W, Leon SC, Martinovitch Z, Lyons JS, Stiles WB (2007). Therapist effects in outpatient psychotherapy: A three-level growth curve approach. *Journal of Counseling Psychology*, 54, 32–39.

¹⁶⁷ MoodGym: <http://moodgym.anu.edu.au/>

9.1 It is also questionable as to whether clinical guidelines in and of themselves are an effective way to change professional behaviour, for example, amongst doctors. The development and dissemination of NICE's guidelines represents a huge investment, but there has been very little evaluation of what the impacts of the guidelines on costs and benefits are, and no national audit of whether NICE's mental health guidelines represent value for money.¹⁶⁸

9.2 NICE have undertaken an appraisal of the impact and implementation of their guideline for schizophrenia in terms of the cost savings to the health service through less in-patient stays. They have not undertaken similar appraisals of their other mental health guidelines however, for example, whether the guidelines for depression and anxiety are being implemented, and with what impacts on health and other related costs?

9.3 Much of the evidence derives from the US which has a different funding system to the UK so that findings on cost effectiveness do not translate well. Thus, NICE's guidelines have had little to say about who should deliver interventions, or where, despite the evidence that this has a large bearing on cost-effectiveness. Also, because the guidelines are condition-specific, patients with multiple problems, who can be a heavy burden on services, tend to get overlooked. Moreover, as noted above, there are very few studies where cost-effectiveness has been designed into the trial, which show one treatment approach consistently outperforms another.

CONCLUSION

10. Public confidence is waning in NICE guidance because its policies do not reflect NHS practice. Although for some purposes, it is appropriate to classify psychiatric problems in terms of diagnosed "conditions" according to standard medical practice, sometimes this does not map onto practitioners' experiences dealing with people who have mental conflict and distress. By their very nature, RCTs tend to select very specific foci for study. The results lead to an over-simplification which the practitioner in the NHS finds hard to equate with the complexity of problems with which patients present in routine NHS settings.

10.1 This is especially important when considering the diagnosis and treatment of "personality disorder", because it is widely recognised that with respect to personality disorder, psychiatric diagnoses are conflicting and confusing. Moreover, much "depression" and "anxiety" occurs in the context of patients' wider personality difficulties, and chronically embedded social and relationship problems. Correspondingly, many patients need help in developing through, rather than being "treated for", their difficulties.

RECOMMENDATIONS

11. We consider the instigation of NICE and the notion of "guiding principles" to have been a major step forward in building an evidence base for the psychological therapies within the NHS. However, by the very nature of the diversity of human beings, we need to ensure that patient choice is a reality by funding research into psychological approaches other than CBT and by placing an equal emphasis on evidence collected from routine settings to that currently derived from randomised controlled trials. We offer the following recommendations.

11.1 The Government should set up a review of the evidence hierarchy which NICE relies on for its mental health guidelines, led by CSIP, to investigate the impact of current criteria for evaluating research into psychological therapies and consequent clinical guidelines on patient choice, innovative services, and patient care.

11.2 Future guideline development groups set up by NICE for mental health guidelines should have a broader balance and cross-section of professional stake holders and peer reviewers to try to ensure researcher-allegiance bias does not distort the guideline development process. These appointments should be transparent and decided by elected representatives from the stake holder organisations.

11.3 NICE should publish the estimated costs of implementing mental health guidelines in terms of treating unmet need, delivering new psychological treatments, workforce and training implications and service redesign. These monies should be ring-fenced as additional investment provided via Strategic Health Authorities before clinical guidelines are issued.

11.4 Prior to NICE's review of its Depression and Anxiety guidelines in 2008, an evaluation of what impact they have had, and whether they are being implemented, should be undertaken by the Audit Commission. Where implementation is patchy or slow, a commissioning strategy should be included as part of the review process for clinical guidelines.

11.5 The Department of Health should work with NICE and the professional bodies in psychological therapies and the mental health charities to agree a national research programme, which identifies the gaps in the evidence (across all the mental health guidelines), and priorities for research, and provide funding for these to be undertaken as an important part of the implementation programme for NICE guidelines.

¹⁶⁸ Gilbody S, Whitty P, Grimshaw J (2003). Educational and organisational interventions to improve the management of depression in primary care. *Journal American Medical Association*, 289, 3145-3151.

11.6 NICE and the Department of Health should work with the professional and research departments for psychological therapies and mental health research charities to establish an evaluation and audit infrastructure within NHS services which will enable ongoing improvements in practice, and better monitoring of whether clinical guidelines are having beneficial impacts on patient care.

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March 2007

Evidence Submitted by Dr Imogen Evans, Mrs Hazel Thornton and Sir Iain Chalmers (NICE 21)

We welcome the opportunity to submit comments to the Committee's Inquiry into NICE.¹⁶⁹ Our expertise encompasses medical journalism/ethics (IE), independent patient advocacy (HT), and research and research evidence appraisal (IC). In 2006 we wrote a book for the general public—*Testing Treatments: better research for better healthcare*—in which we emphasised the need for unbiased research to assess the effects of treatments, and we highlighted the key role of NICE (Evans *et al.* 2006). We therefore hope that this submission will be helpful to the Committee. In particular, we wish to address the following interlinked issues: NICE's evaluation process; public confidence in NICE; and recent challenges to NICE decisions.

NICE'S EVALUATION PROCESS

1. The cost of healthcare weighs heavily on all national economies, and the need to set priorities is inescapable. NICE was established to provide independent guidance on the clinical and cost-effectiveness of health technologies for use in the NHS, partly because the drug licensing system is unable to provide this information. The NICE approach to evaluation has been commended by an external review conducted by the World Health Organisation, has found favour among other European countries, and has even aroused serious interest in the USA.

2. In its investigation of NICE in 2002, the Health Committee stressed the importance of transparency as a precondition for credibility of the Institute's appraisals and guidance. Paragraph 40 of the Committee's report read as follows:

“... much of the information on which NICE appraisals are based is unpublished, as it is supplied to NICE by manufacturers in confidence. Sir Iain argued that “while this state of affairs persists NICE cannot be expected to achieve the credibility that is essential for it to earn the trust of the public.” We recommend that all information which NICE uses in its decision making process is made available for public scrutiny. If industry or others have previously unpublished data which they want to use to support their case then this should no longer be presented to NICE subject to confidentiality.”

3. The Health Committee reiterated the need for greater transparency two years later in the recommendations in its report on the Influence of the Pharmaceutical Industry. Despite this, NICE's transparency was further eroded last year when the Institute switched from independent assessments of scientific evidence to sponsor-produced evaluations of effectiveness and cost-effectiveness. We urge the Committee to continue to press for greater transparency, which we continue to believe is a precondition for public confidence in NICE.

PUBLIC CONFIDENCE IN NICE

4. From the outset, the rationale for NICE has been undersold to the public, and NICE's decisions have been undermined by political interference. A passage we wrote in *Testing Treatments* illustrates the immense difficulties that NICE faces:

“Because the annual cost of treating each [multiple sclerosis, relapsing and remitting type] patient with an interferon was over £10,000, NICE... concluded that using these drugs... would not be a responsible use of limited resources. Many patients with this debilitating disease, and especially the organisations lobbying on their behalf, were outraged. They were angry that the NHS could deny patients drugs that appeared to hold out some hope. Yet did they fully realise the extent to which the available evidence was far from convincing? It was based on partial release of the relevant research results, outcome measures of dubious relevance, and follow-up over only two or

¹⁶⁹ From Dr Imogen Evans (IE), Mrs Hazel Thornton (HT) and Sir Iain Chalmers (IC), co-authors *Testing Treatments: better research for better healthcare*, British Library 2006.

IC has been a member of NICE's Research and Development Advisory Committee since its inception; addressed NICE's Citizens Council on 26 January 2007 on 'Uncertainty and the 'Only in Research' Option'; and has contributed a witness statement in connection with the judicial review of NICE's guidance on the use of anti-cholinergic drugs for people with dementia.

HT was invited to attend a meeting of the NICE Citizens Council 26 January 2007 as a Question Time Panel Member on day 2 of their deliberations on “Uncertainty and the 'Only in Research' Option”.

three years in a disease that usually lasts at least two decades. The government caved in under pressure. . . . But this effectively ended the possibility of learning whether [interferons] are helpful to patients.”

5. It is highly unlikely that the scheme agreed between the Medicines Division at the Department of Health and the companies making interferons to make interferons available to patients will yield reliable information about the impact of these very expensive drugs on important issues such as whether they delay dependence on mobility aids, or the moment when people with multiple sclerosis become bed bound. Provision of interferons in this way means that unbiased assessment of their effectiveness becomes virtually impossible. Moreover, for ostensibly inexplicable reasons, the contract for analysing the data has been moved from the University of Sheffield to Parexel (the contract research organisation associated with the TGN1412 disaster); this does little to promote confidence in the government’s reasons for overruling NICE’s guidance.

6. Uncertainties about the value of the interferons in multiple sclerosis have been handled in a much more responsible way in Italy. The Italians have begun a randomised comparison of interferon with azathioprine, a dramatically cheaper drug, which existing evidence suggests may be just as effective as interferon beta (Sudlow and Counsell 2003). It is worth noting that the costs of the Italian trial are being met from a fund of 35 million Euros derived from a 5% tax on the marketing budgets of pharmaceutical companies to support independent drug research (Chalmers In Press).

7. Many vested interests contribute to the public’s belief that expensive new treatments are better than existing, less expensive treatments. The truth is that new treatments (assessed in randomised trials) are as likely to be inferior as they are to be superior to existing, standard treatments (Kumar *et al.* 2005).

8. Although selling the rationale for and principles of NICE to the public was never going to be easy, this essential public relations challenge appears to have been entirely overlooked by the government when NICE was set up. It is sorely needed now, not least to explain why the criteria for licensing a drug are far less stringent than the criteria for establishing the clinical and cost-effectiveness of the self-same compound.

RECENT CHALLENGES TO NICE DECISIONS

9. Pressures from the pharmaceutical industry, and from patient lobby groups often funded by industry challenge a National Health Service such as ours, which is based on the principle of shared risk and equitable distribution of limited resources. Because of the lack of public appreciation and ministerial support for NICE’s decisions, it is unsurprising that the Institute’s decisions have been contested, and that the public has come to see it as a spiteful rationing organisation. Almost all the media coverage of NICE is negative, and this impression is made even worse when, as with interferons for multiple sclerosis and more recently herceptin for early stage breast cancer, ministers leap in and overturn or pre-empt NICE’s recommendations. Most recently, NICE’s guidelines on the use of anti-cholinergic drugs for people with dementia have been challenged by a manufacturer of these drugs, and the Institute is currently the subject of a judicial review.

10. The current situation with anti-cholinergic drugs for dementia would probably have been avoided had the Institute been making greater use of its option to recommend that a treatment be used only within the context of evaluative research. When there is uncertainty about the effects of a treatment, this is the proper way forward—as an ethicist once commented, in these circumstances “the trial is the treatment”. Yet again, the importance of public backing is crucial. And this will only come about when the public is engaged widely in the clinical research process, and when there is general appreciation that patient participation in research is a risk-limiting strategy and not a risky endeavour.

11. NICE has used this ‘only-in-research’ approach in only 15 out of its 400 appraisals between 1999 and 2006. When used, however, it has made an important contribution to generating the additional evidence needed, and has led to supportive recommendations when the original guidance was reviewed. The benefit of the “only-in-research” approach is faster accumulation of evidence to inform practice and make shared decisions. It also exposes to the public the need to reduce uncertainties concerning interventions in common use, as well as uncertainties about the effects of new treatments. Importantly, the “only-in-research” approach can reduce the risk of having to reverse previous decisions, as has happened with the anti-cholinergic drugs for dementia.

12. We suggest that promoting public partnership in the “only-in-research” approach should become a key role for NICE’s Citizens’ Council, and that the expertise of Council members be used to promote NICE more widely.

CONCLUSION

13. As a 2006 Guardian leader commented, NICE embodies “the least bad way of tackling an impossible job”. The Institute should be strengthened, freed from ministerial whims, encouraged to engage more with the general public, and allowed to do its work for the benefit of all who seek treatment in the NHS.

Imogen Evans, Hazel Thornton and Iain Chalmers

March 2007

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Evidence submitted by Professor Malcolm Hooper (NICE 07)

INTRODUCTION

1. This memorandum relates to the work of NICE in one specific area, namely its Guideline on the management of adults and children with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis ("CFS/ME") currently in preparation, a draft of which was issued on 29 September 2006.
2. It is submitted by Malcolm Hooper, Professor Emeritus of Medicinal Chemistry at the University of Sunderland, in conjunction with Eileen Marshall and Margaret Williams—an established team whose aim is to expose and prevent the injustice perpetrated on patients with ME/CFS in the UK by those whose job is to help, not abuse, such patients. Both Eileen Marshall and Margaret Williams formerly held senior clinical posts in the NHS.

IMPORTANT BACKGROUND INFORMATION

3. Terminology is confusing but important: the term "ME/CFS" reflects the two interchangeable terms (myalgic encephalomyelitis and chronic fatigue syndrome) that are listed in the World Health Organisation's International Classification of Diseases where, since 1969, ME has been classified as a neurological (ie an "organic") disorder. However, certain UK psychiatrists and the Government bodies they advise use the term "CFS/ME"; on their own admission, they do so merely to placate patients by retaining the term "ME". Their recorded intention is to eradicate "ME" and to re-classify "CFS" as neurasthenia (a mental disorder). This has serious ramifications for patients, since mental disorders receive lower rates of State sickness benefits and are excluded from medical insurance cover.
4. The incidence of ME/CFS is rising alarmingly. In order of insurance costs, one of the major medical insurance companies (UNUM Provident) reported in 1993 that ME/CFS came second in the list of the five most expensive chronic conditions, being three places above AIDS. In August 2004 the same company issued a Press Release reporting a 4,000% (four thousand) increase in claims for symptom-based syndromes, including ME/CFS. No other disease category surpassed these rates of increase. UNUM's "CFS Management Plan" states: "UNUM stands to lose millions if we do not move quickly to address this increasing problem". The latest estimate (January 2007) of the economic impact of ME/CFS in the US is between \$22–\$28.6 billion annually; in Japan it is \$10 billion annually.
5. Significant published evidence supports the tenet that ME/CFS is an inflammatory autoimmune disorder that progresses to a complex multi-system neuro-endocrine-immuno-microvascular disorder with cardiac involvement. It devastates the lives not only of patients themselves but also of their families. For a short summary of the 8th International (ME)CFS Clinical and Research Conference held in Ft Lauderdale, Florida in January 2007—at which yet more evidence was presented that comprehensively destroys the psychiatric paradigm so tenaciously adopted by NICE and the UK Medical Research Council—see www.meactionuk.org.uk/Facts_from_Florida.htm

EXECUTIVE SUMMARY

6. In defiance of the substantial biomedical evidence submitted to its Guideline Development Group (GDG), NICE is recommending an inappropriate and potentially dangerous behavioural modification regime as the only management strategy for those with ME/CFS.
7. NICE's recommended management regime is promoted by a group (mainly psychiatrists) who have undeclared but undeniable competing financial interests. Their influence has resulted in a biased and unrepresentative consideration of the international peer-reviewed evidence upon which NICE is relying to support its national Guideline that purports to be "evidence-based" when it is nothing of the sort.
8. The evidence here submitted draws attention to the intentionally selective advice that NICE receives from its chosen advisors, who for almost two decades (ie before NICE was set up in 1999) have dismissed and/or ignored the biomedical evidence that is germane to the issues under consideration.

9. NICE maintains that its recommended psychotherapy regime is also promoted in its Guidelines for other organic diseases. This is untrue. This proposed Guideline for “CFS/ME” seems to be unique: in none of a sample of 12 existing Guidelines for organic disorders does NICE propose psychotherapy as the treatment of choice—it is only in the case of ME/CFS that cognitive behavioural therapy and compulsory graded exercise therapy (CBT/GET) is proposed as a specific treatment. If, on medical advice, patients refuse—or are simply too sick to participate in—this regime, their State and medical insurance benefits are already being withdrawn and some patients face destitution. Facing insuperable odds, a significant number of ME/CFS patients have committed suicide.

10. In the case of ME/CFS, NICE has failed to comply with the AGREE (Appraisal of Guidelines Research and Evaluation) Instrument to which it is party.

FIRST TERM OF REFERENCE

Why NICE’s decisions are increasingly being challenged

11. The alleged “independence” of NICE: NICE was set up—and is funded—by the Department of Health, to which it remains accountable. A common perception is that NICE is far from “independent” and that its *raison d’être* is to provide a shield for Government and Ministers who seek to preserve an untarnished reputation when unpalatable cost decisions have to be made, and who can then reassure the electorate that they are relying on ostensibly “independent” advice.

12. The evidence on which NICE has relied for the production of its “CFS/ME” Guideline has been provided by a small and unrepresentative group of self-styled “experts” and their adherents who study a heterogeneous patient population, resulting in flawed conclusions: Within their own discipline, Wessely School psychiatrists are regarded as mavericks. They are known colloquially as the “Wessely School” after their prime mover Professor Simon Wessely of Kings College Hospital and the Institute of Psychiatry (ref: Hansard [Lords] 19 December 1998:1013). Key members are Professors Michael Sharpe, now at Edinburgh, and Peter White of St Bartholomew’s, London (who holds the “CFS/ME” reins at the Department for Work and Pensions, whose own forthcoming DWP Guidance about “CFS/ME” has been rejected as unfit for purpose by a coalition of ME charities). The work of the Wessely School on “CFS/ME” has been stringently criticised in the international literature for flawed methodology; for use of a heterogeneous patient population (studies using mixed populations are not useful unless researchers disaggregate their findings); for selective manipulation of others’ work, claiming it supports their own findings when such is not the case; for their focus on the single symptom of “fatigue” whilst ignoring other significant signs and symptoms associated with the cardiovascular, respiratory, neurological and immunological systems; for generating conclusions before generating the data to support such conclusions; for advising Government bodies that the reported biomedical abnormalities “should not deflect the clinician away from the biopsychosocial approach and should not focus attention towards a search for an “organic” cause”, and for their recommendation that no advanced tests should be carried out on “CFS/ME” patients when it is those very tests that reveal the unequivocally organic nature of the disorder. It is only when dealing with “CFS/ME” that these psychiatrists are regarded by Government bodies and the medical insurance industry as “experts”. These psychiatrists are on record as being actively involved in social engineering via the deliberate creation of “psychosocial” illness. They believe that the biomedical approach to healthcare (ie that ill-health and disability is directly caused by disease and its pathological processes) is (quote) “a blind alley” and that the correct approach is the psychosocial one, in which “aberrant” thoughts, feelings and behaviour can be “modified” by their own brand of cognitive behavioural therapy with graded exercise (CBT/GET), resulting in restoration of health and productivity. Such a retrograde belief is fallacious, as the regime in question has been shown to be ineffective, yet NICE ignores the evidence submitted to it showing that even the proponents of its recommended regime are themselves on record as acknowledging that:

- (i) it is not remotely curative;
- (ii) modest gains may be transient and even illusory;
- (iii) these interventions are not the answer to ME/CFS;
- (iv) patients have a tendency to relapse; and
- (v) evidence from randomised trials bears no guarantee for treatment success (ref: www.meactionuk.org.uk/Concerns_re_NICE_Draft.pdf).

For a detailed review of Wessely School indoctrination of State agencies, and the impact of this on social and welfare policy, see www.meactionuk.org.uk/Proof_Positive.htm .

13. NICE has limited itself to—and based its recommendations for the management of “CFS/ME” on—a flawed 2005 Systematic Review from the Centre for Reviews and Dissemination at York, whose lead author was persuaded to change her mind between her 2001 article in the *Journal of the American Medical Association (JAMA)* and her 2005 Review for NICE: This may amount to scientific misconduct since the same author has remarkably different approaches to the same data in the two documents concerning the recommended psychiatric management regime favoured by NICE (CBT/GET). In 2001, she found methodological inadequacy; study withdrawals with high drop-out rates; unacceptability to patients of the regime in question; the exclusion of severely affected patients from all studies; the reported improvements

of the management regime may be illusory, with little lasting benefit, and an acknowledgement that the data had been corrupted. These findings were published in one of the world's most prestigious medical journals (JAMA), yet in her York Review for NICE, the same author disowns her own previous findings on exactly the same data; she excludes the many reports of adverse events and signally fails to address the safety and effectiveness of the recommended interventions (a remit with which she was specifically charged). A possible explanation for this volte-face is that the advisers to the non-medical York Review Team who prepared the Review for NICE were prominent members of the "Wessely School" (ie advisors to Government Departments, including the Medical Research Council, and the medical insurance industry). For an analysis by Hooper and Reid of the 2005 York Systematic Review upon which NICE is relying, see www.meactionuk.org.uk/FINAL_on_NICE_for_Gibson.html.

14. The advisors upon whom NICE relies have been shown to have undeclared vested interests: These psychiatrists and their adherents are heavily involved with the medical insurance industry, including UNUM Provident, Swiss Life, Canada Life, Norwich Union, Allied Dunbar, Sun Alliance, Skandia, Zurich Life and Permanent Insurance, as well as the re-insurers Swiss Re, at which Peter White is Chief Medical Officer. For the way in which these psychiatrists deal with ME/CFS claims, see www.meactionuk.org.uk/Notes_on_the_Insurance_issue_in_ME.htm. For an exposition of their commercial conflicts of interest in relation to the Department of Work and Pensions, see www.meactionuk.org.uk/Obs_on_DLA_Handbook_for_Gibson.html. Wessely is further involved with PRISMA, a multi-national health-care company working for insurance companies. In its company information, Wessely is listed as a Corporate Officer; he is a member of the Supervisory Board and in order of seniority he is higher than the Board of Management (for more information, see www.meactionuk.org.uk/What_Is_ME_What_Is_CFS.htm). A recent Report, known as the Gibson Report, by a group of Parliamentarians (including Dr Richard Taylor, who is also a member of the Health Select Committee) states: "There have been numerous cases where advisors to the DWP have also had consultancy roles in medical insurance companies. Given the vested interests medical insurance companies have in ensuring CFS/ME remains classified as a psychosocial illness, there is a blatant conflict of interest here. The Group finds this to be an area for serious concern and recommends a full investigation by the appropriate standards body" (For a summary of the Report findings, see www.meactionuk.org.uk/Summary_of_Key_Points_in_Gibson_Inquiry_report.htm). It is a matter of concern that NICE's chosen advisers on its "CFS/ME" Guideline Development Group include Dr William Hamilton, who has a published track record of believing "CFS/ME" to be a behavioural disorder. Moreover, he has spent 15 years working for the medical insurance industry and is currently Chief Medical Officer for a major medical insurance company, the Exeter Friendly Society. It was he who drew up the company policy that specifically excludes those with "CFS/ME" from eligibility for sickness benefit. Another member of NICE's GDG is psychologist Dr Hazel O'Dowd who also subscribes to the "behavioural disorder" model. However, she has recently published a paper that ought to cause NICE to reconsider its recommendations, as it showed that group CBT did not bring about the anticipated improvements. Another NICE GDG member is Dr Fred Nye, who was forced to make a public apology after his Department issued an advertisement for therapists informing applicants that "CFS" patients have "perpetuating illness behaviour"; that they experience "barriers to understanding" and that therapists will be required to "modify patients' predisposing personality style". Had such attributions been ascribed to those with multiple sclerosis, there would have been a national outcry. For an analysis of legitimate concerns about the NICE draft Guideline on "CFS/ME", see www.meactionuk.org.uk/Concerns_re_NICE_Draft.pdf.

15. NICE's advisors have an indisputable track record of denigrating patients with "CFS/ME": Members of the "Wessely School" have a long track record of denigrating patients with ME. See, for example, "Denigration by Design?" at <http://25megroup.org/denigration%20by%20design/denigration%201.htm> and also "The Mental Health Movement: Persecution of Patients?" by Hooper et al at www.meactionuk.org.uk/Select_CTTEE_FINAL_VERSION.htm. This includes in Appendices I and II a selection of quotations from the published works on patients with "CFS/ME" of Professors Wessely and Sharpe respectively, so Select Committee members can judge this denigration for themselves. The "Wessely School"—and now NICE itself—dismisses and/or ignores the substantial body of international scientific evidence which comprehensively proves them to be wrong in their assertions that "CFS/ME" is primary mental disorder (see, for example, the 174 page document "Illustrations of Clinical Observations and International Research Findings from 1955 to 2005 that demonstrate the organic aetiology of ME/CFS" by Hooper, Marshall and Williams at www.meactionuk.org.uk/Organic_evidence_for_Gibson.htm. See also the document "ME exists: True or False?" at www.meactionuk.org.uk/ME_Exists_-_True_or_False.htm). It is beyond reason that so many documented physical abnormalities in people with ME/CFS should simply be disregarded and/or denied and ascribed to a "behavioural" disorder by NICE, including the following: abnormalities of the central nervous system, of the autonomic and peripheral nervous systems, of the cardiovascular, respiratory and immune systems; evidence of muscle pathology; neuroendocrine abnormalities; defects in gene expression profiling; abnormalities in HLA antigen expression; evidence of persistent virus activity, with abnormalities in the 2-5 synthetase / RNase-L antiviral pathway; disturbances in oxidative stress levels; gastro-intestinal, reproductive and visual dysfunction, all of which are dismissed—and even actively suppressed in the UK—by Wessely School psychiatrists in their advice to Government bodies, and to NICE.

16. The evidence about “CFS/ME” upon which NICE relies has been proven to be biased in favour of current Government policy to create nationwide centres for psychotherapy: It is well-known that, on the advice of Lord Layard, in order to remove people from Incapacity Benefit, Government favours cognitive behavioural therapy for all chronic ill. This is borne out by the negative stance taken by the MRC when considering research applications into the organic aetiology of ME/CFS—documentary evidence exists showing that the MRC internally classifies “CFS/ME” as a mental (behavioural) disorder; by NHS Plus in its published Policy Document of October 2006 (“Occupational Aspects of the Management of CFS: a National Guideline” [DH publication 2735539], whose external advisors were psychiatrists Professors Michael Sharpe and Peter White), and by NICE’s own entrenched position about its preferred management regime, namely behavioural therapy, which has already been promoted and disseminated throughout the NHS as “effective treatment for CFS” in its “Effective Health Care” Bulletin of 23 May 2002 by the York Centre for Reviews and Dissemination. Given the existing extensive implementation of this policy and the relentless dissemination of its alleged efficacy by its proponents (for example, the assiduous advertising of a lecture at the Institute of Psychiatry on 28 February 2007 by Professor Trudie Chalder—a staunch advocate of the behavioural model of ME/CFS who works with Simon Wessely—promoting NICE’s advocacy of behavioural and exercise “therapy” for ME/CFS), unless legally compelled to change direction in line with the international evidence that has been so effectively downplayed by its advisors, NICE is unlikely to do so. This would be to the serious detriment of between 120,000 and 240,000 very sick people in the UK (figures given in the Chief Medical Officer’s Report of 2002), which is a prevalence five times that of HIV/AIDS. For comparison, there are about 83,000 people in the UK who suffer from multiple sclerosis. According to the US Centres for Disease Control, four million Americans have ME/CFS (see <http://listserv.nodak.edu/cgi-bin/wa.exe?A2=ind0701d&L=co-cure&T=0&P=5201>), which is more than those who suffer from multiple sclerosis, lupus, lung cancer and ovarian cancer combined. In the US, lung cancer alone has a prevalence of 350,000 (ie about half that of ME/CFS).

17. NICE fails to adhere to its own terms of reference: NICE is a party to the Appraisal of Guidelines Research and Evaluation Instrument (the AGREE Instrument) so is obliged to conform to certain standards in the production of its Guidelines, which in the case of this Draft “CFS/ME” Guideline it has signally failed to do. The NICE Guidelines are intended to be “systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances”. Their purpose is “to make explicit recommendations with a definite intent to influence what clinicians do”. Because the intent is to influence what clinicians do (which immediately impacts on patients), there are rigorous criteria (currently 23) which policy makers and Guideline developers must observe in the production of a Guideline. The most important criteria in relation to the Draft Guideline on “CFS/ME” are:

- There should be an explicit statement that all group members have declared whether they have any conflicts of interest: there is no evidence in the Draft Guideline that GDG member Dr William Hamilton has made any such declaration.
- The patients to whom the Guideline is meant to apply should be specifically described: the Draft Guideline fails this criterion as there is no such disorder as “CFS/ME”: the Wessely School believe that “CFS” is synonymous with neurasthenia, which is a classified mental disorder at ICD-10 F48, but ME/CFS is a classified neurological disorder at ICD-10 G93.3 and fibromyalgia is a classified soft tissue disorder at ICD-10 M79; to lump these different disorders together as one single disorder (as the MRC does in its on-going “CFS” trials led by Wessely School psychiatrists) is in defiance of established WHO taxonomic principles, particularly as research from Spain presented at the Ft Lauderdale International Conference emphasised that ME/CFS and fibromyalgia are two genetically distinguishable illnesses.
- The Guideline Development Group should include individuals from all the relevant professional groups: the Draft Guideline fails this criterion: whilst mental health professionals are well represented on the Guideline Development Group, and whilst there is a neurologist and an immunologist listed, their experience of patients with ME/CFS is not known. Conspicuous by their absence are a virologist, a clinical allergist, a microbiologist, an endocrinologist, a pharmacologist, a rheumatologist, a molecular biologist, a biochemist, a biostatistician, and experts in vascular medicine, nuclear medicine and genomics, all of whose input is essential to understanding the nature of ME/CFS.
- The patients’ views and preference should be sought and the patient/carer members must have equal status on the GDG: the Draft Guideline pays lip-service to the need to listen to patients’ and carers’ views but then entirely ignores them when they have been submitted.
- The health benefits, side effects and risks should be considered when formulating the recommendations: the Draft Guideline fails in this respect. All relevant patient surveys consistently report that a high percentage of patients are made worse by exercise therapy. Failure to report such adverse events may constitute research misconduct.
- The potential cost implications of applying the recommendations should be considered: the Draft Guideline fails this criterion. Assessment of cost-effectiveness must be carried out in respect of maximising health gain so that resources are not employed in interventions that are not cost-effective, but it is already known that the only recommendations in the Draft Guideline—CBT/GET—have very limited (and certainly not lasting) benefit and are not in any way curative, as

recognised by even its keenest advocates. Moreover, there is substantial evidence that patients with ME/CFS are actually made worse by these recommended interventions. Further, the cost implications of recruiting, training and supervising an army of behavioural therapists needed to deliver NICE's recommendations will be considerable. Given that its recommended intervention is already known to have no lasting benefit, how can NICE's recommendations be considered cost-effective?

- There should be an explicit link between the recommendations and the supporting evidence: the Draft Guideline fails this criterion: the alleged "evidence-base" is exceptionally weak yet NICE gives it more weighting than the patients' evidence, when there should be equal weighting.
- The Guideline should be editorially independent from the funding body: the funding body for NICE is the Department of Health; does NICE pay its editorial and other advisers with funding received from the Department of Health? If so, funding is not independent. If not, from where does it get any additional funding?

Whether public confidence in NICE is waning, and if so why

18. Public confidence in NICE is indeed waning: Given the extent and high calibre of the biomedical evidence known to have been submitted to—but ignored by—NICE, it is obvious that NICE's remit is to produce policy-based evidence instead of evidence-based policy. Its cavalier disregard of so much credible biomedical evidence justifies the public lack of confidence in NICE.

NICE's evaluation process and whether any particular groups are disadvantaged by the process

19. Patients with ME/CFS are at risk of being actively damaged by NICE's biased evaluation process: for NICE's evaluation process to exclude the evidence that its recommended regime is potentially harmful puts those with ME/CFS at immediate and unacceptable risk.

20. Patients with ME/CFS are disadvantaged by NICE's consultation process: for its own convenience, NICE insists that all comments on its Draft Guideline be submitted online, but many patients with ME/CFS do not have a computer or may be too sick to use one. This means that a significant proportion of the patients' voice is excluded, which is in breach of the AGREE Instrument to which NICE is party.

The speed of publishing guidance

21. The time taken by NICE to produce any of its Guidelines is unacceptably slow: in the case of ME/CFS, it is now over five years since the publication of the Chief Medical Officer's Report of January 2002 and still no Guideline has been produced.

Remaining Health Select Committee Terms of Reference

22. We have no comment to make concerning the Health Select Committee's remaining terms of reference.

Professor Malcolm Hooper

March 2007

Evidence submitted by Dr Chris Hyde (NICE 76)

EXECUTIVE SUMMARY

In circumstances where the total price of new health care innovations exceeds growth in health care budgets, scrutiny of value for money is essential. If NICE is performing this role in Technology Appraisal successfully, highlighting even a minority of innovations where the additional costs do not seem to be matched by the demonstrable health benefits, will bring it into conflict with both the public and drug manufacturers. The committee must thus take care not to judge the value of NICE by its popularity.

Scrutiny should instead be directed at whether the balance between benefits, harms and costs in cases which NICE has not supported make sense to the Committee. The Committee will need support with this because quantifying health benefit, side-effects and cost is often complex. Despite this it should be possible for the main elements of the argument for or against a health technology being cost-effective to be presented in a way where the Committee can make their own judgement on whether the conclusions reached by NICE are reasonable.

In my experience the decisions by NICE are reasonable and generally give the benefit of the doubt to the health technology being appraised.

Greater resources should be devoted to explaining the nature of the evidence underpinning NICE's Technology Appraisal systems more widely.

 INTRODUCTION

1. I have worked in health care for 20 years. During that time I have acquired a variety of experience which is potentially relevant to my evidence. I am a medically qualified Doctor and worked in hospitals for several years. I have also trained in public health and have worked in health authorities helping to commission health care for local populations.

2. Currently I am a researcher who helps provide the summaries of evidence which feed into the decisions which NICE makes. The university I am employed by receives funding from the NHS Health Technology Assessment Programme for developing these summaries, however my post is not dependent on this funding. I have attended NICE appraisal committee meetings and appeals, but I am not part of NICE and am not involved in the final decisions it makes. Finally I am a parent of young children and have been a carer.

EVIDENCE

3. The Committee posed a series of questions. My evidence consists of reflections on each of these.

Why are NICE's decisions increasingly being challenged?

4. My understanding is that NICE has a number of roles and that it is mainly the decisions of Technology Appraisal arm which are contentious and subject to challenge. My perception is that the advice NICE offers in the form Clinical Guidelines and Interventional Procedures Guidance although not immune from criticism, is rarely formally contested.

5. Two things set the Technology Appraisal arm apart. First it is the stream of guidance which specifically sanctions use of specific new technologies. Second it is the only stream which considers value for money in which the benefits, side-effects and costs are weighed against alternative approaches. This is essential in a situation where the total price of new health care innovations exceeds growth in health care budgets.

6. Both factors suggest why NICE's decisions in Technology Appraisal are challenged, both because it is required to make decisions which prevent a new technology being made widely available and because it uses a criterion (cost relative to benefit) which is not universally accepted as one which should govern decisions about availability of health care. Unfortunately it is self evident to those aware of the true costs of health care, which the NHS rightly protects most patients from, and the scale of health innovations, that such decisions must be made.

7. The only way NICE could avoid conflict with patients and drug companies, is if it made no negative decisions, thus NICE's growing unpopularity might be regarded as a marker of success rather than failure. One would certainly be suspicious if it was popular.

8. Concerning the apparent *increase* in decisions being challenged, I suspect this is due to the fact that negative decisions take years to achieve because appeals can be mounted, and the nearer the end of the appeal process the greater the volume of criticism.

9. Greater clarity borne of a number of years of experience, could also explain an increase in negative initial decisions made by NICE, as could random fluctuation in the cost effectiveness of new health care products being introduced, as the licencing system is primarily aimed ensuring that drugs meet minimum criteria of safety and effectiveness, allowing marked variation in the extent of effectiveness and cost-effectiveness.

Is public confidence in the Institute waning, and if so why?

10. This is difficult to gauge because it may not be clear to many members of the public exactly what NICE's role is. Given this the contention that NICE has ever had true public confidence is open to question.

11. However, irrespective of this it is inevitable that if NICE is performing this role successfully, highlighting even a minority of innovations where the additional costs do not seem to be matched by the demonstrable health benefits, it will be brought into conflict with the public. This in turn could be interpreted as waning of public confidence, whereas more truthfully it might just reflect that as the number of negative decisions rises over time, the more people are directly affected by the unpopular decisions NICE has to make.

12. One issue is clear is that NICE does not have the capacity to counter media campaigns supported by drugs companies. Whether NICE should try to do so is debatable, but what is certain is that greater coverage of views reflecting the drug manufacturers perspectives will inevitably make it appear that public confidence is waning. How much of media coverage on a particular topic is inspired or supported by drug companies may be amenable to measurement.

Are any particular groups disadvantaged by NICE's evaluation process?

13. Having observed the evaluation process relatively independently, I would suggest that no group is greatly disadvantaged.

14. Relatively however, although NICE have tried hard to solicit and incorporate patient views, the technical complexity of the submissions and the debate often make it challenging for truly representative patient perspectives to be incorporated into their decisions.

15. Greater resources devoted to facilitating understanding of the available evidence by patients and patients groups could be valuable. There is certainly no funding to translate the summaries of evidence we provide to NICE into lay language, so the feasibility of this could again be usefully explored.

Speed of publishing NICE guidance?

16. In my experience the slow progress with the guidance, although frustrating, is usually commensurate with the complexity of the decisions being made. Delays are usually to allow greater opportunity for consultation.

17. Speed of guidance is often as much compromised by filibustering techniques by drug manufacturers as delay attributable to NICE's processes.

18. Concerning the time taken to produce the systematic reviews and health economic models, these are produced much more quickly than would normally be achieved if the same summaries of research were produced in normal academic practice where contracts would usually be between one and two years. In the NICE process, the usual period to produce the technology appraisal is six months.

19. Recently NICE has tried to streamline procedures in the Single Technology Appraisal (STA) process. Experience with this is still limited so it is unclear whether it will actually achieve quicker guidance, especially where a negative decision is made by NICE.

20. There is also concern that time saved by not having an independent academic report on effectiveness and cost-effectiveness may lead to important issues being overlooked in the appraisal process. Again only greater experience with the new STA process will allow an accurate assessment of this to be made.

The appeal system

21. I have attended appeal hearings on three topics. In all cases the process appeared to me to be on balance fair.

22. The unlimited resources which appellants can invest in preparation for the appeals procedure more than outweighs any possible bias in the way the procedures are organised and conducted.

Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)?

23. This is a highly respected system of developing clinical guidelines in Scotland.

24. However, as indicated in B3, comparing the work of SIGN with the component of NICE's advice which attracts most criticism, the Technology Appraisal component, is inappropriate.

25. SIGN would most reasonably be compared with the Clinical Guidelines produced by NICE, which rarely attract adverse comments, and would thus externally be judged to perform to the same high standard as SIGN

26. As a corollary, it should be noted that SIGN do not sanction use of specific new technologies or not, nor do the SIGN guidelines make any recommendations based on information about value for money—are the costs of the new technology justified relative to the demonstrable health benefits?

Implementation of NICE guidance

27. A key problem with implementation is that specific funds are not made available to match each decision. A favourable decision to make a technology available must be funded by diverting resources from another area of health care. This will inevitably lead to variation in the extent and speed with which a new recommendation is implemented in different PCTs depending on the amount of flexibility in the health budget in a given locality at a given point in time

28. Support at a local level to explain and educate about the nature of the decisions made by NICE may improve implementation. This is for the same reasons the patient groups may struggle to understand the evidence considered by the NICE appraisal process (see 14).

29. However, given sufficient support I believe it is possible for non-experts to understand the key features of the arguments which lead NICE to concluding that some new technologies may be considered cost-effective and others not.

C. RECOMMENDATIONS

30. The success of NICE should not be judged by its popularity.

31. Generally it performs its functions well and it should continue to be strongly supported.

32. However, there should be more resources to explain the nature of the evidence to patients, the public and health care workers both during the NICE process and as part of the dissemination of the decisions.

Dr Chris Hyde

March 2007

Evidence submitted by Doris Jones (NICE 37)

EXECUTIVE SUMMARY

ME/CFS is a neurological illness, which affects an estimated quarter of a million patients in the UK; a quarter (ca.60,000) are severely affected and about a tenth are children. The cause or causes of this disease have not yet been fully established. NICE was requested to prepare guidelines on diagnosis and management of this condition following the publication of the Chief Medical Officer's Report on CFS/ME in 2002. The draft guideline (in two versions) was released for consultation in September 2006, but was unanimously and comprehensively rejected by eight major UK ME/CFS Charities and many others. The main reasons for this are that the principal recommended management approaches of Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) have been shown to be ineffective and potentially harmful respectively. Extensive and compelling input from patients and experts supporting the physical/organic nature of the condition has been largely ignored in preparing these draft guidelines. Instead a biased so-called "biopsychosocial" model of the disease has been suggested, largely based on a flawed 2005 Systematic Review of RCTs. It has been shown that NICE in preparing these draft guidelines has failed to comply with numerous conditions laid out in the AGREE Instrument, although it is a pity to this.

1. This memorandum is submitted as an individual.

2. I am an independent researcher and writer, with a particular interest in ME/CFS and related disorders. I have conducted a large-scale post-graduate multifactorial study into ME and a number of smaller studies; I was a Reference Group Member of the CMO's Working Group on CFS/ME and have contributed to the NICE draft guideline on CFS/ME as a member of the wider consultation group. I am also a carer of a person with ME for 27 years.

3. INTRODUCTION

In September 2006 the National Institute for Health & Clinical Excellence (NICE) published a draft guideline in two versions for consultation on "Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (or encephalopathy): diagnosis and management of CFS/ME in adults and children"—the full version consisting of 269 pages and the "NICE Guideline" of 48 pages. This draft guideline has been unanimously rejected by eight major UK ME/CFS Charities in a statement released on 19 December 2006. In addition many formal responses by stakeholders were supplied to NICE by the end of the official consultation period in November 2006—all those by patient group stakeholders expressing severe criticisms of these draft guidelines in many respects. NICE has now decided to postpone publication of the final guideline from April to August 2007 due to a huge number of responses and feedbacks. At a meeting of the APPG on ME on 22 February 2007 Professor Peter Littlejohns said that NICE was still considering these responses and feedback, but he indicated that there was unlikely to be a further consultation, adding that even if the final guidelines were rejected by all UK ME/CFS Charities, they would still be published. This situation is causing great concerns amongst the ME/CFS community, their official representatives and many caring professionals and clinicians.

Problems in compiling these particular guidelines are due in part because of confusion over the definition of the target population. NICE in their draft guideline refer to "CFS/ME" patients which is not the same as the definition relating to "ME/CFS" patients—the former relates to patients suffering from a variety of fatiguing illnesses, the latter to patients who suffer from a neurological disease, classified by the WHO under G93.3 and described in detail in the Canadian Clinical Guidelines on ME/CFS, published in 2003 in the *Journal of Chronic Fatigue Syndrome*. Important in this context is the fact that in the UK there has been very significant influence by a certain group of psychiatrists, who in many published articles, books and documents have unjustifiably stressed the psychological nature of the condition and have recommended behavioural management/treatment approaches, ie Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET). These views are not supported by experiences of patients, who have consistently stressed the physiological/organic nature of the disease. Whilst there is some divergence of views on the appropriateness of these approaches amongst some UK ME/CFS Charities, it has been recognized that a joint approach in dealing with these issues now is vital because of potential long-term serious detrimental

health effects for many patients. Therefore a memorandum endorsed by 10 UK ME/CFS Charities and regional support groups has been supplied to the Health Committee for their current inquiry into NICE, and a separate submission has been made by the 25% ME Group on behalf of those most severely affected. There may be other separate submissions by ME/CFS Charities or organisations for their inquiry into NICE.

4. CONTENTS OF THIS MEMORANDUM

The Contents of this memorandum relate to four terms of reference of the Committee's Press Notice No.11—Session 2006–07 issued on 2 February 2007:

- (a) Why NICE's decisions are increasingly being challenged.
- (b) Whether public confidence in the Institute is waning, and if so why.
- (c) NICE's evaluation process, and whether any particular groups are disadvantaged by the process.
- (d) The speed of publishing guidance.

5. SPECIFIC COMMENTS RELATING TO TERMS OF REFERENCE

(a) *Why NICE's decisions are increasingly being challenged*

NICE has been heavily criticized for decisions made on drug treatments and drug availability; one recent example being that of drug availability for cases of early onset of Alzheimer's Disease, another that of the availability of the drug Herceptin for Breast Cancer cases. The case for ME/CFS patients is different: Here drug treatment is largely ineffective and can be detrimental (eg due to frequent severe sensitivity to drugs and chemicals and potential serious adverse reactions to many). For this group of patients behavioural approaches in the form of CBT and GET have been recommended as first-line management approaches. However, both are fraught with problems: CBT has been shown to be largely ineffective in numerous patient surveys, and GET has been reported to be potentially harmful for a significant number of patients, particularly those who are severely affected. NICE was advised of these concerns and although detailing the results of two patient surveys in the "full draft" on p58, has largely ignored these findings in its overall recommendation. In preparing the draft guideline NICE has relied heavily on a "Systematic Review of the CFS/ME Medical Evidence Base" carried out in 2005 by the Centre for Reviews and Dissemination at the University of York; but this review focused almost entirely on RCTs applying CBT and/or GET; it was severely flawed in many respects—a detailed critique was sent to NICE in January 2006 see section (iii) Key Item 8 below and was acknowledged. Whilst minor adjustments were made to the updated version of this "2005 York Review" when it was published in the Journal of the Royal Society of Medicine in November 2006 (ie adverse events and patient drop out of RCTs were mentioned), many other legitimate and justified criticisms were ignored.

NICE's decisions with regard to recommendations made in the draft guideline on CFS/ME are challenged in part because in this instance the Institute has not complied with a number of conditions set out in the AGREE INSTRUMENT (Appraisal of Guidelines Research and Evaluation—The AGREE Collaboration, September 2001), to which it is party. The purpose of this Instrument is to provide a framework for assessing the quality of clinical practice guidelines; it was specifically designed for new guidelines (which applies to the Guideline) and is intended for Policy Makers and Guideline Developers (ie NICE and the Government in this instance). One key reference of this document is an article entitled "Development and Application of a generic methodology to assess the quality of clinical guidelines" published in the International Journal for Quality in Health Care, 1999;11:21-28, and one of its authors is Professor Peter Littlejohns (now Clinical and Public Health Director at NICE). This "Instrument" consists of 23 key items, organised in six domains, each designed to capture a separate dimension of the guideline quality.—It can be shown that a significant number of these key rules/clauses have not been adhered to by NICE in preparing the CFS/ME Draft Guideline. Below are five of these:

- (i) Key Item 3: "There should be a clear description of the target population to be covered by the guideline". This has not happened in the draft guideline on CFS/ME issued by NICE in September 2006. The terminology "CFS/ME" does not describe a recognised specific and classified disease entity, but encompasses a range of fatigue illnesses, including psychological disorders like depression and anxiety; it is a term promoted by certain UK psychiatrists who maintain that it should be regarded as a "biopsychosocial" disease, which is amenable to behavioural modification techniques (ie CBT + GET). By contrast "ME", "CFS" as well as "PVFS" (Post Viral Fatigue Syndrome) are classified by the WHO as a neurological disease and "ME/CFS" as described in the 2003 Canadian Guidelines provides the best description of patients who suffer from this condition. This crucial issue is not addressed in the NICE draft guideline.
- (ii) Key Item 5: "Information about patients" experiences and expectations of healthcare should inform the development of clinical guidelines, eg involve patients' representatives' etc. Although some patients and patient representatives were part of the GDG and testimonies of their experiences were recorded in the full draft report prepared by NICE, these details are not fully reflected in the key recommendations on the management and treatment of these patients. In

various parts of this draft it is stated that GET is inappropriate for the severely affected and a better concept in these cases would be “activity management”. However, on p257 of the full draft it clearly states that the severely affected should receive the same management regime as that of any person with “CFS/ME”. More importantly, most of the caveats and restrictions indicated in the full NICE draft are omitted from their condensed 48-page version. GPs and healthcare professionals are unlikely to read a 269 page NICE guideline; they may not even have time to read a 48 page version and most probably will rely on a leaflet-type publication consisting of a few pages (similar to the NHS Plus leaflets on Occupational Aspects on the Management of CFS issued in October 2006, where none of these caveats and restrictions are mentioned). Summary details of four patient surveys on over 3,000 patients in total and originally submitted to the CMO’s Working Group on CFS/ME in 2001, were provided to members of the GDG on at least two occasions—first in January 2006 and again during the summer of that year. The details of these surveys show very clearly that CBT was found to be largely ineffective and GET was the most harmful of a range of management techniques and treatments, which patients had tried. By contrast, an approach referred to as “Pacing”, ie patients pacing activities according to their perceived energy levels, alternating with rest periods, was reported as most helpful by a large majority of patients, but other methods (including bed rest) as well as alternative treatments were also found to be more helpful than either CBT or GET. One survey reported counselling as being helpful to patients. These details were evidently considered by the GDG (results of two surveys were listed on p58 of the full draft), but given a very low weighting in their considerations. It is important to remember that neither CBT, GET, PACING nor COUNSELLING are curative approaches in treating these conditions.

- (iii) Key Item 8: “Details of strategy used to search for evidence to be provided, including search terms used, sources consulted and dates of literature covered. Sources could include electronic data bases (eg Medline etc), databases of systematic reviews (eg Cochrane Library etc), hand searching journals, reviewing conference proceedings and other guidelines”. NICE used the October 2005 Systematic Review carried out at the Centre for Reviews and Dissemination at the University of York. However, this review was shown to be severely flawed in many respects and a detailed critique entitled “Inadequacy of the York (2005) Systematic Review of the CFS/ME Medical Evidence Base” prepared by M Hooper and H Reid was sent to the GDG in January 2006; this was acknowledged by Nancy Turnbull, Chief Executive and Project Lead, National Collaborating Centre for Primary Care, in January 2006, but again most of many justified criticisms were ignored by NICE in their draft guideline. Instead a version of this flawed 2005 York Review was published by Chambers et al in the November 2006 issue of the Journal of the Royal Society of Medicine. As mentioned in the Introduction, some adverse events and patient drop out rates were mentioned in this published review, which also referred to some new papers.
- (iv) Key item 10: “Description of methods used to formulate recommendations—formal consensus techniques (eg Delphi etc)”.—The “Delphi” method was used for these draft guidelines, but the consultation method and process were highly unsatisfactory: Initially a copy of the 2005 York Systematic Review (which dealt almost exclusively with RCTs on CBT + GET approaches) was sent electronically to a number of volunteer parties, including patients and carers, to be studied in detail, in readiness for a questionnaire which would follow. This 488-page pdf document could not be accessed by many people and paper copies had to be supplied to many in the wider consultation group. These proved to be almost impossible to handle for many sick patients and the contents were virtually impossible to study properly by them, to enable assimilation of the relevant information. The questionnaires which followed (some electronic, some in printed format) were incomplete—they only covered a small proportion of all questions considered by the GDG, were poorly or misleadingly worded and the printed versions contained incorrect instructions relating to approx a third of all questions; they were sent to a relatively small number of people (399), completed by only 219 including 119 ME/CFS patients. Compared to an estimated number of 240,000 sufferers this translates to 0.05%. In the full draft NICE acknowledges on p203 that patients were “uncertain” about its recommendation on CBT, that they “disagreed” about GET and clearly preferred Pacing (p204). Therefore the feedback obtained by this method was largely unreliable and importantly, insignificant in magnitude.
- (v) Key Item 20: “Recommendations may require additional resources in order to be applied, eg need for more specialised staff, new equipment . . . These may have cost implications for health care budgets. There should be a discussion of the potential impact on resources in the guideline.” This is an important failing in this draft guideline, because that issue has not been addressed. It has been pointed out to NICE representatives at 5 October 2006 “Implementation Planning Meeting” for this draft guideline that arrangements to administer CBT alone for approximately 180,000 mildly or moderately affected ME/CFS patients would cost in the region of £180 million (based on an estimated cost of approx £1,000 per person). There is already a shortage of suitably trained psychotherapists to administer this particular management technique for patients suffering from various mental disorders. To extend this regime to ME/CFS patients would be very costly to the NHS—and that for a regime, which is known to have no long-lasting benefits for patients. It would be far more appropriate to allocate such funding for comprehensive, biologically-based care

that is available, for example, to MS patients, especially for the most severely affected ME/CFS patients within the framework of the so-called “FINE trials”, which indicate the need for “Specialist Medical Care”.

(b) *Public Confidence in NICE is waning—why?*

A huge amount of information supporting the physical/organic nature of ME/CFS has been supplied to NICE during the development period and the consultation process. Much of this emanated from American or Canadian research. Virtually all of this was ignored by them in preference of a “biopsychosocial model” of the disease, as advocated by certain UK psychiatrists. This is an overtly biased decision taken by NICE, favouring government policy strategies instead of being based on medical and scientific evidence. At the APPG meeting on 22 February 2007 the two representatives from NICE were provided with a synopsis of research presented at the International Fort Lauderdale Conference on ME/CFS held in January 2007, entitled “Facts from Florida” by Margaret Williams, together with summarised details of some specific problems which have emerged from research shown and discussed by 250 clinicians and researchers from 28 different countries at this event. A short selection of these specific problems includes the following:

- (i) The cardiac index of ME/CFS patients is so severe that it lies between heart attack patients and those in shock.
- (ii) Brain imaging shows reduced cerebral blood flow (especially in areas involved in ANS functioning, sleep, concentration and pain).
- (iii) There is evidence of “arteriolar vasculopathy” (a blood vessel disease)—affecting all body organs.
- (iv) Various specific viruses are involved in this disease: HHV-6, EBV, Enteroviruses (ie echovirus, coxsackie virus and polioviruses). There is evidence of chronic inflammation.
- (v) In contrast to most other countries, the UK government is resistant to funding any biomedical research into ME/CFS and favours studies into behavioural modification regimes in these patients. Previous CBT/GET programmes were based on a false assumption that avoidance of activity, illness severity and increased attention to symptoms caused perpetuation of symptoms, but in reality are the result of the illness. . . These approaches do not work—ME/CFS patients do not have dysfunctional beliefs, but instead function at maximum activity levels, and exercise makes some worse. Any benefits are short-lived.

The confidence of ME/CFS patients in the NICE process of preparing these draft guidelines and in their consultation is therefore non-existent.

(c) *NICE’s evaluation process*

Many shortcomings were identified in the consultation process for the CFS/ME draft guidelines. For more details see Key Item 10 under Section 5(a)(iv) above.

(d) *Speed of publishing guidance*

NICE’s process of producing this guideline has taken an extraordinarily long time—over five years since the publication of the CMO’s report, which recommended that NICE prepare such a guideline. The entire process of developing the guideline was complex, laborious, cumbersome and protracted, but above all patients’ views and those of knowledgeable clinical experts in the field were almost completely ignored. In the meantime a number of so-called “Specialist Centres” were established where ME/CFS patients are supposed to receive specialist care, but regrettably all that is on offer at these centres are CBT and/or GET approaches. Some patients are randomly allocated to a structured PACING regime within the framework of an ongoing part MRC-funded “PACE Trial”. All this is highly unsatisfactory because none of these regimes are in any sense curative, CBT is largely ineffective and GET is often harmful. Whilst there may be few “official” complaints from patients about treatments provided at these centres sent to the main charities, it is known that many are very concerned about the options offered.

At the APPG meeting on 22 February 2007 Professor Peter Littlejohns, one of the two representatives from NICE present at this meeting, acknowledged that the previously adopted “hierarchy of evidence” should be reconsidered, which presumably means that they may now give greater credence and weighting to patient evidence. He also confirmed that serious flaws in the 2005 York Systematic Review had been stressed in many responses which NICE received to the draft guideline. It is to be hoped that all these facts will finally convince NICE that a major re-write of this draft guideline is necessary, and so is further consultation with patient group representatives. It is astonishing that NICE should have adopted such an intransigent stance with regard to patient evidence, at a time when the government’s own guiding principle for the NHS is that it must be patient-led, as outlined in the 2001 DoH booklet “The Expert Patient”, which was endorsed by the CMO himself. A serious look at these crucial issues by the Health Select Committee would be most welcome.

I would be prepared to give oral evidence to the Committee in support of the above complaints about NICE's preparations of their draft guideline on CFS/ME and the consultation process adopted in this instance, should this be required.

Doris M Jones

March 2007

Evidence submitted by Gay Lee (NICE 03)

I am a ward sister in a hospice and would like to say that I find some of the decisions taken by NICE difficult to understand and, like other people, am beginning to lack confidence in the institute, especially over the issue of drugs to be prescribed by the NHS.

An example is drugs used in the early stages of Alzheimer's Disease. NICE is not supposed to be making decisions on the basis of cost alone but on clinical effectiveness. As far as I can see, it uses the argument that, statistically speaking, because only a minority of patients benefit from the drugs (albeit a large minority), it is not cost-effective to supply all patients with them—ie the cost is too high because too few patients benefit.

My view is that this should not be an issue of randomised controlled trials and statistics. It should be about giving drugs to (however few) patients who will benefit—and undoubtedly some do. The most cost-effective way to manage this would be to try all patients on the drugs and then monitor their effectiveness and promptly take those patients off the drugs who are not benefitting from them but letting the rest continue. If this keeps symptoms in check for a longer time for some, then this will benefit the NHS in the longer term.

This principle should apply to all drugs which are shown to be effective for some patients. It is worth mentioning a similar situation from my own direct experience: we use a lot of drugs to treat symptoms in palliative care on a pragmatic basis—by trial and error. This would seem to be common sense, as individual metabolisms are likely to react differently to any given drug in an unpredictable way. This is illustrated by the fact that randomised controlled trials almost never have a 100% success rate even when a drug is proved to be beneficial for a majority of subjects—there will always be some who benefit and some who don't because no two human beings are unique!

Gay Lee

18 February 2007

Evidence submitted by Michael Lee (NICE 13)

EXECUTIVE SUMMARY

1. The submission is directed towards the first three items of the Committee's Investigation, namely:
 - why NICE's decisions are increasingly being challenged;
 - whether public confidence in the Institute is waning, and if so why; and
 - NICE's evaluation process, and whether any particular groups are disadvantaged by the process.
2. Cost benefit, based on Quality Adjusted Life Years (qalys), is now the standard method of appraising therapies adopted by NICE. Cost benefit in health originated mainly from issues relating to economic market theory and pharmaceutical products, where prices were fixed well above marginal cost. The technique attempted to demonstrate that even so, the benefits that flowed from improved health far outweighed the costs. The discipline was developed academically with the introduction of the concept of a qaly to measure benefits on a single standard across many different health applications.
3. The value of qalys in assessing product issues is open to question. In terms of simple economics, a qaly does not satisfactorily emulate prices. The absence of any point elasticity in qalys, defining the rate at which supply and demand change in response to price level changes, severely constrains its value as a price surrogate in a distributive system. More problematically, a qaly fails to relate to patient care. The obvious impact on care of the elderly and chronically sick, suggests questionable medicine. The qaly system finally implies one model of health provision and funding. Qalys relate to a centralised top-down target setting structure of the health service where the lines of practice and development are determined by a central authority. The contrast is a patient-centred service where the variety of needs and demands presented by patient is decided individually by the doctor within the context of the doctor-patient relationship. Patient satisfaction, under this approach, becomes the key to evaluation.
4. In the context of pricing NHS supplies, a variation on the marginal cost model of the industry may be derived from consideration of uncertainty, coupled with modern theory of the firm, which now are generally accepted as the dynamics producing profits in a competitive market system. The unknown may be equated

with uncertainty, and so integrate research and technological progress into the dynamic market model. The approach would describe the workings of industry more effectively, and so may provide a more satisfactory backdrop for a regulatory framework.

RECOMMENDATIONS

5. In regard to NICE, the scope for evaluation of benefit needs to be widened and based upon patient satisfaction rather than the single narrow standardised concept of the quality.

6. In terms of the relationship of NICE to the PPRS, the concept of an alternative model of the industry beyond that of marginal cost pricing, shaped on uncertainty, the unknown and the theory of the firm may prove more fruitful.

QUALIFICATIONS AND EXPERIENCE

7. I am a consultant economist, B.Sc(Econ) graduate of the London School of Economics, and professionally qualified as Fellow of the Institute of Management Consultancy. My practice is incorporated as Lee Donaldson Associates Ltd (LDA), consultant economists.

8. In April 1962, I was appointed as a founding director of the Office of Health Economics, with responsibility for research especially the cost benefit studies: I remained a member of the OHE Editorial committee until 1992. I subsequently joined Professor Nathaniel Lichfield's planning consultancy, which explored aspects of cost benefit in planning; and later, was appointed economic adviser in the Engineering Industry Training Board, with responsibility for research, especially into effectiveness of the Board's work.

9. I established my practice in 1971, and retired from active involvement in the late 1980s. Professional studies included report for the then PEP (subsequently Policy Studies Institute) on private health, commissioned by the Health Department. I subsequently acted as the Department's consultant on the private sector until 1984, submitting evidence to the Royal Commission on the National Health Service. In 1981, I was appointed as specialist consultant adviser to the Secretary of State for Health as part in the Department's investigation into NHS funding.

10. I have retained a close link with the NHS since retirement through establishing and largely funding an arts in health charity Poems in the Waiting Room (PitWR). The registered charity supplies short collections of poems for patients while waiting to see their doctor. The current mailing totals some 750 NHS clinics, mainly in general practice. Bizarrely, to meet the Culture Department stipulations, LDA undertook a cost benefit analysis of PitWR in 2006. Regular contact with NHS doctors, staff and patients provides a valuable NHS overview. A Bristol doctor wrote that "PitWR is the one thing in the NHS no one complains about . . ."

COST BENEFIT

11. The discipline cost benefit was introduced into the NHS by the OHE in 1962. Its foundation was prompted by political development in the United States affecting international pharmaceutical firms. The US Senate Anti-Trust and Monopoly Subcommittee, chaired by Senator Estes Kefauver (1903–63) held hearings on the pharmaceutical industry between 1959 and 1963. The Senator had a distinguished record on promotion of industrial competition. He focussed on the paradox that the industry, as an advocate of the free market, did not act according to the core market proposition that prices should equal marginal costs, which, in a theoretical situation of perfect competition, produces the greatest social benefit.

12. The American industry responded by adopting cost benefit studies, which then were attracting growing interest in economics, and which purported to guide situations lacking price discipline, especially in the public sector. They demonstrated that the benefits flowing from the introduction of new drugs, in lives saved and income produced, far outweighed sums in pricing pharmaceuticals in excess of marginal costs. Further, the revenue flows produced by the enhanced price levels sustained the continued benefit of the industry's research.

13. US companies operating in the UK, especially those who developed the then new range of broad spectrum antibiotics, feared the Kefauver argument might bear adversely on their NHS markets. The OHE was established by the Association of the British Pharmaceutical Industry (ABPI) in April 1962 to undertake cost benefit studies, published as OHE pamphlets. The OHE produced studies of tuberculosis, childhood diseases, pneumonia, poliomyelitis, diabetes and the like: it also considered NHS structures, reviewing the hospital system and general practice.

14. In the mid 1960s, the Health Department promoted the Department of Health Economics at York University. The Department was to develop a rigorous academic structure of health service cost benefit and to develop the subject within the context of public service cost benefit, which then was seen as an integrated feature of the National Plan.

QUALITY ADJUSTED LIFE YEARS (QALYS)

15. The central outcome of York's research has been the concept of quality adjusted life years (qalys). The qaly rapidly became favoured by public sector and spending control bodies (HM Treasury 2003 The Green Book: appraisal and evaluation in central government. Annex Two). The qaly was seen as coping with questions that health impacts are rarely a question simply of lives lost or saved, but need to take account of life changes, especially changes in the quality of life. The qaly weights life expectancy for health-related quality of life over time.

16. The objective is to create a matrix of information that may act in lieu of the market where relative prices determine distribution of expenditure and effort. The cost of any therapeutic process is compared to the assumed marginal value of qalys generated. Cost benefit requires a single standard unit to enable comparison to be between widely diverse procedures and morbidities. The process lies at the heart of the National Institute of Clinical Excellence (NICE)'s work.

PRICE THEORY, PATIENT CARE AND CENTRALISED FUNDING

17. Although appealing in theory, cost benefit and the qaly as a substitute price system is open to question; there are three areas of criticism.

18. In simple terms of economics, a qaly does not satisfactorily emulate prices. The absence of any point elasticity in qalys, defining the rate at which supply and demand change in response to price level changes, severely constrains its value as a price surrogate in a distributive system. The lack of transactions involving a transfer of resources from consumer to supplier deprives the qaly of all incentive power. An absence of relative or opportunity costs or choice deprives the qaly system of the competitive element that fuels effective markets. A price is the market tool bringing supply and demand into balance and clearance. A qaly is a complex bureaucratic tool which in no way automatically adjusts either supply or demand; it induces no response but only a central control decision to approve or to refuse supply.

19. More problematically, a qaly fails to relate to individual patient care. The obvious impact on care of the elderly and chronically sick, suggests questionable medicine. Happily, doctors provide care from the given the resources available and their professional assessment of its effectiveness. The broad pattern of expenditure on health reflects medical science and the profession's response to patients' needs. Qalys act only on the margin, to constrain the rate of change. Argument that the entire NHS budget should be reappraised, subject to qaly analysis and redeployment accordingly has found little or no response. (see for example Williams Alan 2004 What could be nicer than NICE? Office of Health Economics) Medical ethics override the qaly concept.

20. The qaly system finally implies one model of health provision and funding. Qalys relate to a centralised top-down target setting structure of the health service where the lines of development and practice are predetermined by a central authority. Patient care needs to be rationed; qalys provide the key to care and seeks to ensure it goes, like the ministrations of the stockman, to those who might produce the greatest economic returns. The contrast to central control is a patient-centred service where the variety of needs and demands presented by patient is decided individual by the doctor within the context of the doctor-patient relationship. Patient satisfaction, under this approach, becomes the key to evaluation.

COST BENEFIT AND RESEARCH AND NEW MEDICINES

21. The public response to NICE decisions substantiates these criticisms of cost benefit and qalys. Recent cases concern breast cancer or Alzheimer disease. With breast cancer, the value arises not from the reduced one or two percent risk in terms of lives saved, but from the reduction in widespread anxiety and uncertainty for 100% of sufferers. With Alzheimer, the treatment brings relief and short extension of a diminishing life, but the major benefit flows to loving kin and carers. Neither factor features in qaly cost benefit. The public are little persuaded either by the concept of qalys or cost benefit analysis as part of the NHS control machinery.

22. The diversity of therapeutic benefit underlie the weakness of cost benefit which technically requires reduction to a single feature. The broad range of health care, either therapeutic or prophylactic bears on features such as fears and uncertainties, pain and forbearance, with patients' needs varying regarding not simply age and life expectancy, but in terms of family responsibility, employment duties and prospects and a host of personal social factors. This diversity of impact was a major source of early disillusion in the value of cost benefit in a health context.

23. Recent NICE history suggests a treadmill has been created. NICE cost benefit produces answers with qalys and their value for money. The range of matters excluded causes adverse reaction by patients affected. Their endeavours to obtain the treatment by popular publicity and lobbying achieves reversal of the decision. A qaly based cost benefit becomes rapidly indefensible regarding patients' needs or satisfaction. Further new treatments will seek approval for use in the NHS. The treadmill of NICE decision, public outcry and reversal will turn again. Over time, this routine will produce general anxiety about the NHS and its reliability to provide effective health care.

MARGINAL COSTS AND PHARMACEUTICAL PRICES

24. The main issues referred to NICE concern pharmaceutical products, where the NICE analysis provides a backdrop to the ABPI/Health Department Pharmaceutical Products Regulation Scheme (PPRS). The paradox identified by Kefauver, that theoretical greatest benefit flows when prices match marginal costs, underlies much of the argument. Marginal costing, although a strict economic concept has a basic appeal to common sense that prices should just be the cost of making a product. Under marginal cost price competition, profits, excess or otherwise, would not exist.

25. The presence of uncertainty and the theory of the firm are two market features that now shape current discussion of markets and profit. The conventional explanation for the presence of profit, standard in current text books is the impact of uncertainty. (The seminal thesis is by Knight (1885–1962) especially *Risk, Uncertainty and Profit* (Boston 1921)). The concept of uncertainty introduces the flux of time into the static marginal cost price model. Sources of uncertainty include market changes such as swings in consumer taste, difficulties in commodity supply, change in accessibility, variations in regulations and the like. Response to major changes by suppliers opens prospect for substantial profit or loss.

26. The Knightian concept of uncertainty, as a major variation of the marginal cost price model, needs to be distinguished from risk. Risk is characterised by probability, which opens the feasibility of treating it as an insurable cost. True uncertainty is radically distinguished from the calculable risk; with uncertainty, there is no valid basis of any kind whatsoever for classifying instances. It may be defined as an event whose amplitude or periodicity is incalculable.

27. Associated with the concept of uncertainty, which modifies the classical model of perfect competition, is the presence of the firm. Under marginal cost pricing, the functioning of the market is seen as organic, as a naturally self-adjusting system without conscious organisation. Theoretical discussion, especially since the late 1980s has stressed theories of the firm as a major feature of markets, especially regarding transaction costs and bureaucracy. (The seminal work in the theory of the firm is by Coase (1910–94). His study *The Nature of the Firm*. *Economica*. November 1937). Briefly, the Coasian firm is seen as the surrender by individual workers of entrepreneurial rights of direct market access in exchange for a contract of employment; the market is replaced by the firm, the organism by organisation. The motive or driving force is the operation of risk (which is insurable but not always acceptable), and, by extension, uncertainty. The firm's scale provides a degree of security.

28. The Coasian firm can be developed from a simple passive or negative response to uncertainty towards a proactive organisation, actively extending the area of certainty and creating a structure capable of coping with major market changes. Profits ensure the continued life of the organisation, forming a core over and above immediate daily market pressures.

29. This model can be extended further to cover the research based corporation. Research concerns proactive extension of knowledge into the unknown. The unknown may be equated directly with uncertainty, with identical impact on profits or losses for those who successfully deal or fail to respond.

30. Take for example, a new and fanciful pharmaceutical product. Call it Flutac. It is the specific remedy for all forms of influenza, including avian flu. Taken thrice within twenty-four hours, the pill reduces temperature, alleviates headaches, relieves aches and pains and, eliminates entirely the attacking virus, while providing immunity for twelve months against any form of flu virus. It is of course simple to demonstrate substantial cost benefit and a multitude of qalys from a treatment priced at say £30.00; annual world-wide sales would produce upwards of some £10 billion gross revenue. Work on this product is encouraging. To date, a pill can be provided which satisfies the first three items. The ingredient for the fourth and last item, the elimination of the virus, is at present unknown.

31. Flutac would generate substantial profit, excessive or otherwise. These would emerge irrespective of any statutory rights are regulatory system, which only modify the extent and rate of profitability. As the knowledge embodied in the product is disseminated widely and competition develops, these profits would be eroded by competitive market forces and fall eventually to marginal cost. This is the typical research product market cycle.

32. Therefore the unknown can be equated with uncertainty in a dynamic market model to explain the existence of profit, modifying the static marginal cost model. Coupled with the Coasian firm, as the vehicle to safeguard against risk and uncertainty, the research corporation is organised to explore the unknown. Under this model, technical change and research are no longer exogenous, but an integral part of the market, and its driving force.

33. In discussions of uncertainty, there is an implicit assumption that the news is always bad, although there is never wholly an ill-wind. Discovery of the unknown through systematic research is generally seen, in contrast, as a desired objective, although it would be a wholly beneficent breeze that blows no ill. The unveiling of the unknown by the research based pharmaceutical firm is a proactive approach to uncertainty, where the conditions and consequences of uncertainty are sought, rather than avoided or averted.

34. The postulated model of the research firm links directly with the concept of product competition and product differentiation (originating mainly from RH Chamberlain (1899–1967) *The Theory of Monopolistic Competition*. Harvard 1933), which has a well established place in the discussion and management of market structures. The ideas of product differentiation have proved valuable in exploring issues of pharmaceutical profits and pricing.

35. The model derived from the Knightian concepts of uncertainty as the core of profitability in a market economy is similar to pharmaceutical firms unveiling the unknown. The model provides a more integrated backdrop to development of the PPRS than the NICE approach of treating discoveries as exogenous and acceptable in terms externalities in cost benefit measured by qalys. In regard to regulation and public sector needs, the model coupling the unknown with the uncertain, giving rise to profit may provide a more effective framework for regulatory systems bearing on the industry.

Michael Lee

16 March 2007

Evidence submitted by Professor Ragnar Lofstedt and Frederic Boudier, King's College London (NICE 31)

SUMMARY

The King's Centre for Risk Management, King's College London is a centre of excellence in research and teaching on risk communication and management topics. The evidence is based on ongoing research within the pharmaceutical policy area where we are closely liaising with regulators, stakeholders, industry, media and academics.

1. This response to the Select Committee's inquiry into NICE focuses on two of the seven topics raised namely "why NICE's decisions are increasingly being challenged" and "whether public confidence in the Institute is waning";

2. In summary we would like to point out that we live in a post trust society, where regulators and industry are increasingly being questioned by a distrustful public. Public opinion itself is increasingly fragmented into diverging, sometimes antagonistic, views; therefore we will refer in this memorandum to "publics" in the plural form. In such an environment decisions by any government body such as NICE will be questioned. NICE is, in other words, a victim of present trends. The Institute also has not been helped by high profile cases where publics have been refused drug products because of cost grounds set by NICE, which have then been amplified by the media. To make matters worse there is a strong adversarial and somewhat hostile relationship between NICE and a number of the key drug manufacturers.

3. What NICE needs to do now is to explain in a clearer fashion to the publics and other stakeholders why rigorous cost-benefit analysis need to be placed on new drug products before they become available in the UK. Secondly, it needs to develop a proactive dialogue with the pharmaceutical industry to avoid the present spat of law-suits and general back-stabbing.

Why NICE's decisions are increasingly being challenged

4. Because of a large number of regulatory scandals ranging from BSE to tainted blood in France and foot and mouth disease, we live in a post trust society where the publics no longer trust regulators, policy makers or industry. NICE's (like other Government bodies) decisions are increasingly being challenged as a result of this.

5. One of the key components of trust is fairness. At the present time a number of UK publics and stakeholders do not see themselves as treated fairly by NICE. For example, why should their loved ones be refused cancer drugs on cost grounds such as Herceptin, considering the fact that had they been living in other Western nations this product would have been available? Why does NICE's super secret economic formula supposedly differ from that of our poorer neighbours? This is not seen to be fair.

6. NICE's decisions make great media stories. There are pictures of the dying granny that has been refused a cancer drug by the drug watchdog NICE, followed by in-depth heartbreaking quotes from the granny's relatives that this is simply unjust. As the public ages and as their needs for expensive drug products increases and as government health spending slows down, the number of media stories surrounding NICE's decisions are bound to increase still further. To complicate matters, NICE does not have many neutral highly trusted third parties to defend it in the media. It is not very popular to come out and defend an economic decision condemning someone's relative to death.

7. The public's expectations in the UK health service has increased since Labour came into power. Since 1997, government figures indicate that spending on health is now 90% higher in real terms than it had been in 1997 ensuring that overall UK health spending has gone up as a proportion of GDP from 6.8 to 9%. Under such circumstances the publics are less tolerant to why they cannot be prescribed drugs such as Herceptin. One of the primary reasons to why NICE is receiving so much media attention is a resource

problem. The UK government does not have all the funding it needs to get the pharmaceutical products that the public wants. Particularly as the UK public is increasingly ageing overall, and as the treatments that they need are getting more expensive, a larger amount of funding for pharmaceuticals need to be provided.

8. It is inherently difficult for any one to explain to the general publics that regulators and institutes need to establish costs per life and cost per life years in determining everything from whether a road should be widened, to whether a train should be fitted with the latest safety technologies to whether a drug should be allowed to come on the market. Many individuals see such cost per life pricing as more or less immoral and therefore it is not surprising that regulators and policy makers do not like publishing formulas of how such a cost per life saved was developed in the first place nor what the actual figure is. NICE's formula is also secret. In addition, statements such as "QALY is best that NICE could come to" come across as being arrogant. The technical nature of cost/benefit analysis is not easy to grasp. In particular people do not necessarily make a clear difference between affordability and value for money. When NICE rejects affordable drugs (eg Exelon or Reminyl) it is essential that the decision be explained in plain language, using simple analogies. Secrecy and perceived arrogance breed distrust (transparency breeds trust).

9. Drug companies want to be able to sell any drug they produce at the going market price. They do not want to be dictated to by a government body whether a drug is actually cost effective or not, as this will decide whether one of their drugs can be put on that country's market in the first place, naturally impacting their profit calculations. Drug companies are also concerned that decisions taken by one medical regulator may dictate how other insurance companies and drug regulators in other jurisdictions will react. For example, the perception in industry circles is that NICE is being used by US insurance companies to decide which drugs their patients will be allowed to take. Such copy-cat decisions will reduce profitability of individual products still further. Hence there is no wonder that drug companies will actively contest specific cost effective decisions taken by NICE.

Whether public confidence in the Institute is waning

10. Public confidence in a number of government institutions has declined over time (if measured between prior to the BSE scandal to the present time). NICE was established in 1999, in the aftermath of these destructive regulatory scandals, therefore in a context of already declining trust. NICE could be seen as part of that trend, although this would need to be supported by scientific evidence.

11. There are a number of short and medium term measures that can be introduced to address the public confidence issue:

- NICE should consider establishing an external academic advisory board composed of Europe's leading economists who would advise NICE with regard to the economic formulas that it presently uses to decide whether a drug should be allowed on the market or not. Such an advisory board would deflect any possible flack that NICE may receive for not approving one drug over another.
- NICE should, in a proactive sense, develop a constructive dialogue with industry and other stakeholders. One possible way to facilitate such a dialogue would be to hold a yearly industry forum where NICE and industry could explore in an off-the-record format regarding decisions taken over the past year and what issues/drug products need specific attention in the following year.
- NICE should ensure that its arguably controversial economic formula is scientifically peer reviewed.
- NICE needs to better explain to patient groups, patients, publics, medical bodies and others to why there is a need to calculate the value for money with regard to pharmaceutical products. Such explanations are especially needed to address the crucial "fairness" issue.
- A sense of fairness implies caring for those vulnerable. Although NICE should constantly reinforce that it is defending the public interest, it should also provide obvious demonstration that special attention will be paid to the need of children and the elderly. Any decision to refuse access to a drug benefiting children or the elderly should be carefully explained in order to avoid sending the wrong messages. NICE should be prepared to face challenging reactions from the publics.
- In addition to fairness, NICE should improve its communication skills and focus on combined demonstration of humility and competence. This is especially important, given the technical nature of most cost/benefit decisions. One way to go is to develop simple messages in plain language.

Professor Ragnar Lofstedt and Frederic Boudier
King's Centre for Risk Management, King's College London

March 2007

Evidence submitted by Dr Tom Marshall, University of Birmingham (NICE 05)

EXECUTIVE SUMMARY

1. NICE's greatest strength is the transparency of the process by which it reaches decisions. Given the areas in which it works it is inevitably likely to attract criticism. NICE's strongest defence is therefore to be more transparent about how decisions are taken.

2. I am a Senior Lecturer in Public Health at the University of Birmingham. I have research interests in the organisation of primary care services for prevention of cardiovascular disease. I am a member of the NICE Clinical Guidelines Group on Lipid Lowering.

STATEMENT

3. Clinical guidelines are a strong influence on clinicians' decisions—for example to prescribe or undertake diagnostic investigations. Because of this they are a powerful tool for resource allocation within the NHS. A decision to recommend a particular treatment can mean allocating hundreds of millions of pounds per annum.

4. As a member of a NICE Clinical Guidelines Group I have a generally favourable impression of the process by which NICE reaches decisions. Committee members represent a range of stakeholders including clinicians, academics and patients. All committee members are required to make declarations of interest. Attempts are made to use scientific research to inform all decisions. Research evidence is sought to answer explicitly pre-defined questions using reproducible methods. Research evidence is appraised using explicit criteria. Attempts are made to model the costs and benefits of different decisions. All committee members have the opportunity to comment on the interpretation of research evidence.

5. This contrasts sharply with the methods used to produce other guidelines with which I am familiar. The Joint British Societies' recommendations for prevention of cardiovascular disease are currently regarded as the definitive statement on prevention of cardiovascular disease in primary care. They are written by a narrow range of stakeholder organisations: British Cardiac Society, British Hypertension Society, Diabetes UK, HEART UK, Primary Care Cardiovascular Society and The Stroke Association. All of these stakeholders represent medical professionals. All but one represents the views of secondary care specialists. There is no patient representation. Neither the public nor those who commission or pay for of health care are represented in the process.

6. Most of these stakeholders receive funding from the pharmaceutical industry. For example the Primary Care Cardiovascular Society is funded by AstraZeneca, Bristol-Myers Squibb/Sanofi-Synthelabo, Merck Sharp & Dohme, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Pharmacia & Upjohn and Roche Products.¹⁷⁰ The British Hypertension Society is funded by Boehringer Ingelheim, Bristol Myers Squibb/Sanofi, Menarini, Merck Sharp & Dohme, Novartis, Pfizer, Servier and Takeda.¹⁷¹ All of the participating stakeholders have an interest in increasing resource allocation towards cardiovascular disease prevention.

7. The processes by which decisions are reached in these guidelines are unclear and although decisions are based on scientific evidence, this evidence may be being cited selectively. No attempt is made to estimate the benefits of following the guidelines' recommendations. No attempt is made to estimate the costs of following the guidelines' recommendations.

Why NICE's Decisions are Increasingly Being Challenged?

8. NICE takes decisions that have substantial resource implications for key stakeholders. It is inevitable that NICE will have these decisions challenged by other stakeholders. Were NICE's decisions unchallenged by other stakeholders it would be reasonable to assume that it was not taking appropriate decisions.

9. NICE takes decisions that may have substantial personal implications for individual patients. At the margins, some of these decisions are very difficult. Again, it is to be expected that individuals will challenge these decisions in order to obtain treatment that they feel may offer them benefits.

10. The NHS is often inflexible about alternative means of funding treatment. For example, if a drug is not funded, often the NHS will not permit patients to receive the treatment in an NHS facility even if it is privately funded. If a patient feels strongly they want a treatment that NICE has not recommended they have no alternative but to lobby NICE and the NHS. If the NHS were obliged to accept partial funding from philanthropic organisations it would provide an alternative to challenging NICE.

¹⁷⁰ http://www.pccs.org.uk/About_PCCS/sponsors.asp Last accessed: 14 February 2007.

¹⁷¹ [http://www.bhsoc.org/pdfs/Text_for_BHS_website_re_Friends\(April%202006\).pdf](http://www.bhsoc.org/pdfs/Text_for_BHS_website_re_Friends(April%202006).pdf) Last accessed 14 February 2007.

Public Confidence in the Institute

11. Public confidence in NICE is likely to reflect the way in which it is represented in public debate. NICE's greatest strength is the fact that it makes decisions using an explicit process, bases those decisions on scientific evidence and takes account of a wide range of views.

12. Greater public awareness of the transparency of NICE's decision-making process could result in greater public confidence. It would also help if greater emphasis were placed on the need to choose between services and that a decision to provide one service means a decision not to provide something else.

Are any Particular Groups Disadvantaged by NICE's Evaluation Process

13. The creation of an "orphan" status for rare illnesses has privileged rare conditions over common conditions. More lives could be saved at lower cost by prescribing simvastatin to individuals currently considered ineligible for treatment than by prescribing expensive treatments for rare conditions. The aim of creating orphan status was to make development of treatments for rare conditions rewarding to industry. However the effect may be to increase the price of health care for rare illnesses and to create perverse incentives. For example this encourages the creation of subcategories of illness (so that they become rare and hence acquire orphan status). A better solution would be to reduce the costs of developing treatments, by reviewing the regulatory requirements for rare conditions. For example, if a specified proportion of know sufferers (or their guardians) give their consent, the regulatory requirements for bringing a new treatment could be relaxed.

Comparison with the Work of the Scottish Intercollegiate Guidelines Network (SIGN)

14. The transparency of the NICE process compares very favourably with that of SIGN.

The Implementation of NICE Guidance

15. Implementation of NICE guidance in my area of interest is dependent on the decisions of GPs. It is very likely to be influenced by incentives provided in the Quality and Outcomes Framework. Implementation is therefore largely dependent on the extent to which the Department of Health incorporates NICE recommendations into.

16. Implementation of NICE technology appraisal recommendations is a matter for the local NHS. Technology appraisal recommendations represent a national view. As the local NHS lacks a political mandate it is difficult for them.

Dr Tom Marshall

Senior Lecturer in Public Health, University of Birmingham

March 2007

Evidence submitted by Dr Catherine Meads, University of Birmingham (NICE 08)

EXECUTIVE SUMMARY

This submission is from a systematic reviewer for the NICE guidance programme. The main issues it addresses are that the work to assess treatments is complicated and time consuming, explaining results to a lay audience is difficult and may not be happening adequately at the moment and that groups without a strong lobby are missing from the decision making process. NICE is vital to protect patients from expensive new treatments that are no better than currently used alternatives.

I work within a team at the University of Birmingham Department of Public Health and Epidemiology to produce Technology Assessment Reports for the NICE guidance programme. The work that we do for NICE includes systematic reviews of the published and unpublished evidence on a particular topic and an economic model. In the past I have worked on the reports on Coronary Artery Stents and Photodynamic Therapy for Age-Related Macular Degeneration and am currently leading on Structural Neuroimaging in First Episode Psychosis and Use of Tumour Necrosis Factor Alpha Inhibitors for Crohn's Disease Multiple Technology Assessment Reports. I also teach academics how to perform systematic reviews of the evidence at masters' degree level. Some of these students are now either working at NICE or in Evidence Review Groups producing technology appraisal reports for NICE. I have no financial investment in any drug or device company.

FACTUAL INFORMATION AND RECOMMENDATIONS FOR ACTION

1. This submission is largely based around my experience of the NICE process that I witnessed while I was doing the technology appraisal on Photodynamic Therapy for Age Related Macular Degeneration (PDT for AMD).

2. The UK drug licence for photodynamic therapy with verteporfin was based around a subgroup analysis on a particular subgroup of patients in a single randomised controlled trial (RCT). When the second relevant RCT was published, the subgroup analysis no longer appeared to be a true estimate of the effectiveness of the treatment. This suggested that the drug licensing process was based on a subgroup analysis that was developed for the reporting of the first trial (predominately classic AMD) rather than a clinically accepted subgroup known before the trial was conducted (classic wet AMD).

3. Whilst doing the systematic review we encountered some very difficult academic issues around how to measure vision and how to measure quality of life in patients with vision loss. This was needed in order to establish the cost effectiveness of treatment.

4. The issues that arose were very complicated so getting them across to a lay audience was very difficult. I listened to press coverage of this topic when it was covered, particularly on BBC Radio 4, and they struggled to present the necessary detail required to really understand the issues.

5. At the same time it came to my attention that patient groups were receiving information about photodynamic therapy that was overemphasising the clinical effectiveness of the drug and not giving due weight to the known potential side effects (blindness in a small percentage of patients) and the uncertainties around the effectiveness of treatment. Patient groups had also not been told that the potential budget impact to the NHS was enormous and that there were insufficient ophthalmologists to administer the treatment.

6. The general impression I was given from press articles was that photodynamic therapy would “save vision” and “improve vision”. However, it was only ever shown from the RCT results that photodynamic therapy could slow the rate of vision loss in some patients who had the wet form of AMD.

7. It appears to me that public confidence in NICE may be waning. This could be due to two main factors. Firstly the information needed to really understand the issues properly is complicated so explaining it to a lay audience is tricky. I am unsure that NICE has really been able to tackle this area adequately because I do not know if they have the remit or staff to do it. Secondly, some drug companies are providing some funding for patient groups, and at the same time letting them have promotional material for their products. The patient groups are not having access to independent appraisal of this evidence. So when NICE pronounce on a particular topic, it does not tally with what patient groups have been told so they tend to complain, particularly if they are told they cannot have a treatment they think they should have.

8. The types of people who are currently disadvantaged by the NICE process are those who do not have a strong lobbying voice. For example, in PDT for AMD, it may have been more cost effective and may have benefited far more people if the money that could have been used for PDT instead had been used for much more extensive rehabilitation services for people going blind. However, the rehabilitation services do not have a strong lobbying voice so this perspective was lost to the decision-making process.

9. With regard to the speed of publishing guidance—I am more concerned that the guidance is correctly based on the best evidence available rather than rushed through. The issues involved in many of the Technology Appraisals are very complex and can't be evaluated without sufficient time for thought. I think that it is entirely appropriate that there is an appeals process.

10. If we didn't have NICE then what would have happened for photodynamic therapy would have been considerable pressure from the drug company to ophthalmologists to provide this treatment for all patients with wet AMD irrespective of whether they would really benefit from the treatment. They would also not have considered what services would not have been offered because the money was being spent on PDT. Some ophthalmologists would have provided the treatment; some would not, resulting in postcode prescribing and other more basic essential services without groups to lobby for them being squeezed out. It is essential that NICE provides a way to impartially assess these very expensive new treatments because they aren't necessarily any better than our currently available treatments.

Dr Catherine Meads
University of Birmingham

7 March 2007

Evidence submitted by Sandra Simkin (NICE 50)

1. *Why NICE's decisions are increasingly being challenged?*

My experience of NICE is that they are very selective about what it is that they do and they are unduly influenced by the professionals. However I am completely at one with them over the need to restrict untried and untested drugs to the public, even when people have go information on drugs that they think will help them. The Select Committee and NICE should be looking at the unfettered way in which drugs are marketed. The companies are trawling the drugs that are in preparation with a huge media hype long before they are in anyway tested to be of benefit or more specifically to be of harm to patients.

2. *Whether public confidence in the Institute is waning, and if so why?*

NICE takes forever on its deliberations and has no teeth to enforce a guideline once it has been established. The new guideline on HMB has had little impact on doctors prescriptions—and I know this because I am still receiving calls from women ill advised to have a hysterectomy. If there is no way to police the guideline there is little point in going to the trouble of creating one. Some prosecutions of doctors and sackings for ignoring guidelines would restore some public confidence in the system. As far as rebellion on drugs decisions are concerned NICE are fighting an insidious PR and marketing programme of Dugs companies which always puts a gloss on their medicines. Unfortunately our NHS has sold out to the Pharmaceutical companies through sponsorship and goodie bags given out to GPs and hospital doctors like smarties and there is intense pressure to prescribe drugs and every effort is made through the media to get to patients demanding to have them. There should be strict controls over what the Pharmaceutical companies are able to do and their contacts with individual doctors and institutions should be policed.

3. *NICE's evaluation process, and whether any particular groups are disadvantaged by the process?*

Yes the patient's voice is almost drowned out in the process. There is a process whereby stakeholder reps can put up to work on the Guideline Development Group. I was not selected but one Group that was selected rarely if ever sent any representation to the meeting. I believe that I was not selected because I had been too confrontational about hysterectomy and had written a book against it and was extremely well informed about the subject. Brigitte York from the Fibroid Network was very committed and I have no problems about her appointment. The third person was just a member of the public who had experience of the procedure but no special knowledge or information. Brigitte often felt that she was on her own as a patient rep on the CDG because the other 2 patient reps did not have her knowledge or commitment. Together we would have made a dream team as we had both personally already sifted through hundreds of medical papers to have got to where we were. I made representation to NICE when my application to the GDG failed because I definitely felt at the time that they were trying to suppress the patient input into the guideline. There should be more not less patient input into the guidelines.

4. *The speed of publishing guidance?*

Very slow in deliberation. The process is very academic. Some points could be taken as read and not investigated to the nth degree.

5. *The appeal system? What appeal system?*

6. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)?*

No knowledge of this.

7. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)?*

If a guideline is made by NICE it must be implemented fully and policed to flush out doctors who are not complying, or refuse to, or who are ignorant of the guideline because they are not doing their job properly. Ignorance of something is not an excuse in law and should not be so in medical practice. If NICE guidelines are made in good faith and all parties are involved including patients then whatever the clamour through the media the guideline must be explained and adhered to. Giving into patients who are demanding an untested drug because they have heard about it on the news does nothing to strengthen the respect for and value of the work done by NICE. If NICE was more genuinely representational the public might have more

respect for it. Its decisions are never properly explained. NICE really needs some PR as it seems to be losing ground to the Drugs companies. I for one regret this.

Sandra Simkin

Campaign Against Unnecessary Hysterectomies

23 March 2007

Evidence submitted by Dr Keith Syrett, University of Bristol (NICE 48)

EXECUTIVE SUMMARY

Increasing challenges to NICE decisions may be understood as instances of the “legitimacy problem” which arises when access to healthcare resources is explicitly restricted. NICE has sought to address this problem through commitment to due process and, in respect of the “social value” dimension of its work, through development of deliberative mechanisms. However, there remains a need to engage in a comprehensive debate about rationing in the NHS in order to secure public acceptance of the authority of limit-setting bodies such as NICE.

1. The author is Senior Lecturer in the School of Law at the University of Bristol. He has published a number of articles on the National Institute for Health and Clinical Excellence in scholarly journals in the UK and worldwide and has written more widely on the relationship between the rationing of healthcare resources and public law.

2. This memorandum will seek to address the first question in the Committee’s terms of reference: that is, “why NICE’s decisions are increasingly being challenged” and will seek to outline proposals to diminish the frequency of such challenges. It also pertains to the issue of why public confidence in the Institute may be lacking.

3. The controversy which has been generated by NICE’s work—especially (but not exclusively) its technology appraisal role—may in large part be traced to the perception that the Institute functions to “ration” care within the NHS. This view is, in some respects, misleading. Strictly speaking, the remit of the Institute is to consider clinical and cost-effectiveness of treatments and services and not to make judgements on affordability, the latter remaining the responsibility of government. Moreover, it has been demonstrated that technology appraisals have resulted in an additional cumulative cost of £800 million p.a. or approximately 1% of all expenditure upon the NHS.¹⁷²

4. Nonetheless, as observed by the Committee in its previous report on NICE, the imposition of an obligation of mandatory funding attached to technology appraisal guidance has resulted in a blurring of the distinction between cost-effectiveness and affordability, such that the Institute may be regarded as “essentially making decisions about how money is spent in the NHS”.¹⁷³ This concatenation of the two concepts is exacerbated by a lack of public understanding of issues of health economics, such that the public regard the application of health economic metrics (such as QALYs) by NICE as being indiscriminately “about money”. The confusion also creates a space within which patient groups and drug companies may seek to advance their interests through the media and other channels. Here, invocation of the negative discourse of “rationing” serves as a rallying cry for the construction of a community of opposition to the NICE preliminary or final appraisal.¹⁷⁴ The view that NICE is a “rationing” body is accordingly widespread.¹⁷⁵

5. The perceived status of NICE as a “rationing” body renders it open to contestation on grounds of legitimacy. In understanding this issue, the work of Norman Daniels and James Sabin is highly instructive.¹⁷⁶ These authors have identified a “legitimacy problem”, which may be defined by means of the question: why should patients or clinicians accept the authority of a particular priority-setting body to make moral decisions which limit access to healthcare and thus adversely affect individual well-being? This problem arises because there is no consensus as to the ethical principles which might underpin decisions which function to restrict access to healthcare. In view of this moral disagreement, “suspicion, distrust and even resistance [will] often greet efforts to set limits on access to medical services”.¹⁷⁷ Hence, a stakeholder

¹⁷² Audit Commission, *Managing the Financial Implications of NICE Guidance* (Wetherby: Audit Commission, 2005) at para.23.

¹⁷³ Health Committee, *National Institute for Clinical Excellence*, Second Report HC 515-I (2001-02) at para.106.

¹⁷⁴ See eg Pfizer Press Release, “Sad day for Patients with Alzheimer’s Disease” (11 October 2006), available at <http://www.pfizer.co.uk/template2.asp?pageid=379>.

¹⁷⁵ See eg the *Daily Mail*’s response to the Press Notice announcing this inquiry: “Drug rationing watchdog put in the dock by MPs” (3 February 2007); and further “NHS must pay for fat children to get surgery”, *The Observer* (19 November 2006), “Find the Balance”, *The Times* (27 May 2006). For academic analyses along similar lines, see R. Smith, “The Failings of NICE” (2000) 321 *BMJ* 1363; A. Maynard, K. Bloor and N. Freemantle, “Challenges for the National Institute for Clinical Excellence” (2004) 329 *BMJ* 227.

¹⁷⁶ See especially *Setting Limits Fairly* (New York: OUP, 2002).

¹⁷⁷ N. Daniels, “Accountability for reasonableness in private and public health insurance” in A. Coulter and C. Ham (eds.), *The Global Challenge of Health Care Rationing* (Buckingham: Open University Press, 2000) at 89.

who is disappointed at the outcome of a NICE appraisal will invoke an ethical principle (such as the “rule of rescue”) which conflicts with that which is applied by NICE (which may often exhibit utilitarian characteristics). The incommensurability of these positions is likely to be further exacerbated by media coverage, with particular emphasis being placed upon the notion of “putting a price on life” as human interest collides with “bureaucratic” decision-making. The conflict may be played out in a variety of fora, including the Institute’s own internal appeals process, the political arena, or by means of legal challenge.

6. The “legitimacy problem” has become acute because of the shift from implicit forms of rationing, in which allocative decisions were concealed behind a veil of clinical judgement, to explicit strategies, in which the financial implications of provision of particular services and treatments to a local or national population are visibly exposed to public view. The work of NICE in conducting technology appraisals is an illustration of this broader trend. The shift to explicit allocative strategies may be comprehended as an attempt by government to exercise more systematic control over healthcare expenditure, grounded in a commitment to deployment of the techniques of “evidence-based medicine”. This is intended to eliminate inefficacious and inefficient treatments and to reduce arbitrary variations (especially of a geographical nature) in access to services. However, it is widely acknowledged that explicitness generates instability both at an individual level and, more broadly, within the health system, as a consequence of the “ability of small groups to evoke public sympathy and support in contesting government decision-making . . . those who care deeply but are denied access will inevitably challenge the explicit judgement through the mass media and other ways, undermining support for purchasing decisions”.¹⁷⁸ According to the “legitimacy problem” thesis, this instability will manifest itself in a challenge to the moral authority of a body like NICE to make decisions which, in effect, limit access to care. The growing frequency of these challenges may simply be explained by the increasing visibility of the Institute and public and media awareness of the implications of its decisions, especially as it appraises treatments for a variety of diseases.

7. The “legitimacy problem” thesis enables us not only to understand why decisions reached by NICE are likely to be subject to regular challenge, but also offers a prescription for addressing the problem. Straightforwardly, NICE needs to make a convincing claim to legitimacy in order to minimise the conflict which its work will inevitably generate.

8. As the author has argued elsewhere,¹⁷⁹ analysis of the legitimacy of an administrative institution will tend to make reference to a limited and agreed set of values, comprising legislative mandate, accountability and control, efficiency, expertise and due process. Claims by NICE to the realisation of the first three values are likely to be unpersuasive. The vesting of wide discretionary powers in the Institute makes it difficult to argue that it is acting as a mere “transmission belt” for instructions provided by elected representatives in Parliament. Similarly, the relative independence of the Institute from direct ministerial control renders accountability mechanisms indistinct and attenuated. As regards efficiency, the consideration of the cost-effectiveness of treatments and services is central to the Institute’s work. But it is clear that this, in itself, is insufficient to ground legitimacy in view of the absence of a societal consensus that utilitarian principles are the correct basis for judgements on resource allocation in healthcare.

9. At first sight, the claim to legitimacy through expertise would appear to be the Institute’s strongest suit. In particular, those sitting upon the Technology Appraisal Committee, seen as the Institute’s key decision-making body, are expected to draw upon their experience and judgement in reaching conclusions as to whether a technology is to be recommended for use upon the NHS. The composition of this Committee, with membership drawn from the NHS, patient and carer organisations, health-related academic disciplines and the pharmaceutical and medical device industries, attests to a commitment to a technocratic form of decision-making. This is underlined by the assertion of the Institute’s Chairman and Chief Executive that “the scientific value judgements made by NICE remain, ultimately, those developed and enunciated by the knowledge, experience and expertise of the board members and its independent advisory bodies”.¹⁸⁰ Further, the methodology adopted by the Committee, which is based upon the techniques of health technology assessment, and the consequent dominance of the “technical” discourses of health economics and biomedicine within the Committee’s decisional processes, support the claim to legitimacy through the exercise of expert judgement.

10. However, as the Institute itself recognises, its claim to legitimacy through expertise in respect of “scientific value judgements” does not, in itself, provide a basis for the assertion of moral authority with regard to the dimension of its work which involves “social value judgements”, defined as those which “relate to society rather than to basic or clinical science: they take account of the ethical principles, culture and aspirations that should underpin the nature and extent of the care provided by the NHS”.¹⁸¹ If, as argued previously, NICE is engaged in rationing of healthcare resources (or perceived as such), it is readily apparent that its decision-making will carry such a social value component since, as has been noted, priority-setting is an “inescapably political process”.¹⁸² The consequence is that a claim to legitimacy in respect of this aspect of the Institute’s work must make reference to a value other than exercise of technical expertise.

¹⁷⁸ D. Mechanic, “Dilemmas in rationing health care services: the case for implicit rationing” (1995) 310 *BMJ* 1655 at 1658.

¹⁷⁹ K. Syrett, “NICE Work? Rationing, Review and the “Legitimacy Problem in the new NHS” (2002) 10 *Medical Law Review* 1.

¹⁸⁰ M. Rawlins and A. Culyer, “National Institute for Clinical Excellence and its Value Judgements” (2004) 329 *BMJ* 224 at 226.

¹⁸¹ NICE, *Social Value Judgements: Principles for the Development of NICE Guidance* (London: NICE, 2005) at para.1.1

¹⁸² R. Klein, “Puzzling Out Priorities” (1998) 317 *BMJ* 959 at 959.

11. It is therefore important to consider the extent to which NICE can successfully claim legitimacy on the basis of its compliance with principles of due process. Here, the framework of “accountability for reasonableness” which is developed in the work of Daniels and Sabin offers a well-regarded model for the attainment of legitimacy through procedural justice within this public policy context. The model establishes four conditions with which bodies making decisions which have the effect of limiting access to healthcare resources should comply. These are:

- (a) publicity: decisions and their rationales should be publicly accessible;
- (b) relevance: rationales should be based upon evidence, appeals and principles which fair-minded persons can accept as relevant to the problem of meeting the varied health needs of the population under resource constraints;
- (c) revision and appeals: opportunities must exist for revision and improvement of decisions in light of new evidence and arguments, and there must be mechanisms for challenge to decisions;
- (d) enforcement: voluntary or public regulation of the process to ensure that the preceding conditions are met.

12. Significantly, NICE has committed itself to a process of decision-making which seeks to comply with “accountability for reasonableness”, and has been praised for its success in this regard.¹⁸³ Why, then, are the Institute’s decisions increasingly subject to challenge? One answer might be that, in the context of allocative decision-making in healthcare, the “due process” claim to legitimacy (as captured in the “accountability for reasonableness” model) is also problematic. It is certainly the case that the Daniels and Sabin thesis has been subject to criticism,¹⁸⁴ but as NICE has acknowledged, it is not clear that any viable substitute theory exists.¹⁸⁵ In the light of this conclusion, it might be tempting to label the “legitimacy problem” as too intractable in the healthcare context, and to simply abandon any attempt at resolution. However, this would surely be an unsatisfactory response.

13. An alternative would be to argue that, notwithstanding the attempts made to give effect to “accountability for reasonableness”, NICE decision-making remains deficient when set alongside the Daniels and Sabin model. In this regard, it is important to appreciate that the four conditions outlined above are not intended to serve as ends in themselves. Rather, they perform an “educative” function in building public understanding as to the need for the rationing of healthcare resources and the criteria which should underpin such decision-making. “Social learning” of this nature may in itself engender legitimacy, as the provision of reasons for decisions builds public confidence in, and acceptance of, the decision-making process. However, Daniels and Sabin’s central claim is that compliance with the conditions of “accountability for reasonableness” acts as “connective tissue” to democracy more broadly, in so far as enhanced public understanding enriches debate and empowers the public to deliberate in a more comprehensive, informed and focused manner upon the rationing of healthcare within a range of democratic institutions and processes.¹⁸⁶ In this manner, the “accountability for reasonableness” framework feeds into theories of deliberative democracy, which contend that a process of communication and reasoned argumentation among citizens who are free from coercion and self-interest can contribute to the legitimacy of decisions made under conditions of scarcity, as is the case within health systems.

14. Once again, NICE has recognised the applicability of this theoretical work to its functions. It has sought to give practical realisation to deliberation by establishing the Citizens’ Council—described in an internal document as “a unique experiment in deliberative democracy for the NHS and seemingly for almost any healthcare system in the world”—to assist in identifying the social values on questions of rationing which are held by the British public.¹⁸⁷ The Council possesses a number of deliberative characteristics, notably its composition as a representative cross-section of the British population, and its mode of operation, which centres upon the hearing and weighing of evidence and debate and discussion within plenary and small group sessions.

15. However, a recent evaluation of the Council has reached a cautious conclusion as to its deliberative qualities.¹⁸⁸ Moreover, even if the Council is regarded as deliberative in character, it is arguable that its role within the Institute’s decision-making processes is insufficient to provide a basis for the legitimacy of the social value dimension of NICE’s work. It meets only twice a year for six days in total and the topics which it discusses are formulated by the Institute. Most crucially, it has no direct input into the technology appraisal process and its recommendations are not binding. It is therefore more accurate to view the Citizens’ Council as fulfilling an informational role: it “feeds data” (in this case on public values) to the

¹⁸³ See eg N. Daniels, “Accountability for Reasonableness” (2000) 321 *BMJ* 1300; C. Ham and G. Robert (eds.), *Reasonable Rationing* (Buckingham: Open University Press, 2003), Chapter.

¹⁸⁴ See eg A. Hasman and S. Holm, “Accountability for Reasonableness: Opening the Black Box of Process” (2005) 13 *Health Care Analysis* 261; T. Beauchamp and J. Childress, *Principles of Biomedical Ethics* (Oxford: Oxford University Press, 5th edn., 2001) at 258.

¹⁸⁵ NICE, above n.10 at para.2.2.5.

¹⁸⁶ N. Daniels and J. Sabin, “The Ethics of Accountability in Managed Care Reform” (1998) 17 *Health Affairs* 50 at 61.

¹⁸⁷ Cited in C. Davies *et al*, *Opening the Box: Evaluating the Citizens’ Council of NICE* (Milton Keynes: Open University, 2005) at 43; and see further, M. Rawlins, “Pharmacopolitics and Deliberative Democracy” (2005) 5 *Clinical Medicine* at 473-475.

¹⁸⁸ Davies *et al*, above n.16.

Institute, but it is the experts on the NICE board and advisory bodies who are the ultimate decision-makers. To this extent, the Institute's claim to legitimacy through its commitment to due process of a deliberative type is, it is submitted, unpersuasive.

16. An obvious means of addressing this deficiency in legitimacy, and hence of rendering NICE's decision-making more widely acceptable, would be to strengthen the "join" of the Citizens' Council to the main technology appraisal work of the Institute. This could be achieved by giving the Council a standing "consultee" status on all technology appraisals, thereby enabling it to submit evidence directly upon the social value implications of recommending, or restricting the availability of, given technologies. A reform of this nature would, however, entail far greater demands on the time of Council members, especially if the valuable work which the Council currently undertakes on broad ethical topics, such as the relevance of age to NICE decisions on availability of treatments and the role of the "rule of rescue", were to be continued. For this reason, it might only be feasible if membership of the Council were to be increased to ensure a pool of available deliberants whenever required which would, in turn, carry resource implications. Moreover, more direct involvement of the Council would be likely to increase the length of the technology appraisal process, which is already a source of significant criticism of the Institute. Finally, and perhaps most crucially, even the enhanced role for the Council outlined in this paragraph might be insufficient to stem challenges to legitimacy, since the ultimate decision on access to treatments would continue to reside with those professing technical expertise. This remains technocratic decision-making, not deliberative democracy.

17. A more radical solution is therefore needed. If, as argued here, a process of public deliberation is the key to resolving any problem of legitimacy from which NICE suffers, and thus minimising the prospect of challenges to its decisions, it would appear to be imperative to engage in a full public debate upon the scope of coverage which can appropriately and affordably be provided by the NHS. Such a debate will foster public understanding of the inevitability of limitations on access to healthcare and of the complexity of the ethical choices which must be made. Although consensus is likely to remain elusive in view of the persistence of moral disagreement in this field, the greater awareness of the need for rationing and appreciation of the rationality and weight of countervailing ethical principles which should emerge from the process of deliberation will serve to engender broader acceptance of decision-making of the type in which NICE is engaged.

18. The work of NICE has served to place questions of the rationing of healthcare more firmly on the public agenda, and in that respect has prepared the ground for evolution of such a debate. Yet there remains an unwillingness to take the necessary further step of acknowledging the true nature of the task which it undertakes. This is reflected in NICE's disavowal of any role in respect of affordability—notwithstanding that the practical impact of a negative appraisal is almost always to restrict or exclude access to a particular treatment—and, more broadly, in its rejection of the term "rationing" to describe its work. In the latter respect, the Institute is merely following in the tradition of numerous politicians over the course of several decades, who have sought to diminish the inevitable electoral unpopularity which would attend deployment of the word, preferring instead the more neutral (and rational) terminology of "priority-setting".

19. Ultimately, it is the function of government, not of NICE, to initiate such a public debate (albeit that, once such a debate has commenced, the Institute is in a unique position to contribute both from a scientific and ethical perspective). However, an opportunity may exist in the context of current calls for the establishment of a constitution to enshrine the core values of the NHS.¹⁸⁹ Any debate upon such a document must inevitably engage with the issue of the comprehensiveness of the service which is provided. Of course, embarking upon an open and honest public debate upon the need for and criteria which should underpin the rationing of healthcare may cause short-term pain for the government in the form of criticism that it is "putting money before lives". Nevertheless, this author would contend that this is a pill worth swallowing if the longer-term consequence is to secure the legitimacy of bodies such as NICE which must play a central role in ensuring the affordability, as well as the efficacy, of publicly-funded healthcare services.

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March 2007

¹⁸⁹ See A Burnham, "A health constitutional", *Progress*, September 2006.

Evidence submitted by Peter Telford (NICE 32)

1. WHY NICE'S DECISIONS ARE INCREASINGLY BEING CHALLENGED

2. This arises out of several factors.

3. First, the appeal process cannot take into account up to date evidence so the decision is out of date and irrational to those consultants expert in this field who actually have to treat patients.

4. Second, the methodology of decision making at NICE involves people who may be accomplished at reviewing evidence and compiling a report but are not necessarily the best in their field and not all "cutting edge" experts in for example oncology.

5. Third, the mechanics of decision making involve a contentious concept which is termed a "QALY". This is a rough attempt to provide some objective approach to a complex matter of quality of life and the number of years of that quality of life which can be achieved as a statistical median for the proposed drug or treatment under review. QALY does not always provide the only or best way of assessing this. It is the measure of cost effectiveness but it can mislead in particular difficult and complex cases involving terminally ill patients or those whose life is already affected by a particular condition and who are not looking at a cure as such. The statistics of QALY also can lend themselves to decision made not on the basis of an individual's prospect of successful treatment but on an overall assessment which is to the disadvantage of particular groups of patients. For example, there will be those who with these particular drugs of Avastin and Erbitux would on the evidence pull through to operable status. These will be discarded because the majority would not reach that stage. This has to be wrong and nonsensical.

6. Fourth, the QALY cost of £20,000 (£30,000 in oncology) appears to move upwards in some cases and not at all in other cases. It also has not been increased to reflect high inflation in the medical sector let alone kept up with inflation in terms of the RPI for a number of years (2000).

7. An example of why a QALY has sometimes little or no meaning in a terminal bowel cancer patient's treatment can be given from direct personal experience.

8. It is admitted from the outset that Bowel Cancer is not as "sexy" a subject as Breast cancer might be to the publicity conscious but the following example is worth considering as I believe everyone can relate to this.

9. A patient with advance bowel cancer might commonly have an operation to remove part of their lower bowel or a stent inserted.

10. Let us consider the lucky patient with a stent. This stent is a narrow tube (one finger width diameter) which allows their stools or motions to pass, otherwise these would block up due to the size of tumour in the bowel. In order for the stool to pass, however, it must be almost liquid in consistency and large doses of laxative have to be prescribed. This causes embarrassment, misery and cramps. It can create a mood of depression. It also means that the type and range of food that can be eaten is very much reduced, with a ban on say broccoli, greens, tinned tomatoes and a host of other foods.

11. With the benefit of "normal" chemotherapy, the bowel tumour will hardly ever (less than 1% chance) reduce in size sufficiently so as to allow the stent to be removed (or remove itself). In the case of first line prescription of Avastin (Bevacizumab) in conjunction with "normal" chemotherapy, to a patient who had a stent fitted in September 2006, the bowel tumour reduced by half in volume after 3½ months which meant that the stent left the body, and the patient was and is able to pass normal motions in the normal way. The patient is now able to eat normally. This means that the patient is able to eat anti oxidant food (broccoli, greens, tinned tomatoes) and able to build the body back up to increase antibodies against infection. The quality of life in simply being able to live normally in this way cannot ever be underestimated.

12. In another patient who was unable to walk or move or carry items or care for his teenage son who had water on the brain requiring a stent operation to relieve the pressure on the brain. With the advantage of Erbitux, in combination with Irinotecan chemotherapy which had previously been given alone and failed to work, as third or last line of treatment, the patient's tumours in liver and lung have reduced to such an extent that he is now able to move around and look after his son who would otherwise be in the care of the social services.

13. WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING, AND IF SO WHY

14. To my mind and experience over the past eight months, it has waned and is waning rapidly.

15. Just to state that I became involved in the process of applying for the "banned" biological agent drugs Avastin and Erbitux for advanced bowel cancer treatment through a close relative being diagnosed with advanced bowel cancer in July 2006.

16. By the time diagnosis had occurred and a consultant oncologist advised treatment in August 2006, NICE had brought in their interim determination making the “Not Recommended” decision in both Avastin (Bevacizumab) first line chemotherapy and Erbitux (Cetuximab) third line use. It should be noted that the patient had paid privately to see the consultant as the time delay in the NHS would have meant waiting several weeks longer for that decision on treatment.

17. Following that recommendation for Avastin, the patient applied for, was refused and appealed the decision of the PCT to refuse Avastin first line use in combination with “normal” chemotherapy Oxaliplatin and 5FU. The appeal was refused on baseless grounds. The decision was then voided, and a fresh decision made again to refuse Avastin. That was appealed and again refused and only when judicial review proceedings were notified to the PCT was a decision made to approve Avastin in first line use. The basis of refusal was always the NICE “not recommended” interim determination. The basis of appeal was the exceptional grounds that in this particular case, the patient could not tolerate 100% of the side effects associated with the “normal” chemotherapy.

18. The basis for refusal in all subsequent appeals has always been the NICE recommendations.

19. The delay occasioned by this refusal and appeal process meant that effective combination treatment involving Avastin could not begin until October 2006. That was 3½ months after diagnosis. By then the CEA count had risen to 4,500.

20. The combination of Avastin with “normal” chemotherapy has meant the bowel tumour reduced in size by half and through lack of contact with the tumour, the stent removed itself and this patient can presently enjoy a relatively normal life in terms of bowel motions anyway.

21. The delay in treatment however, meant the patient lost her job. She would normally have been working and paying taxes. Instead she is in receipt of income support, housing benefit, and a car has been provided. She would have preferred to have been on her own two feet and working.

22. It is a story repeated with variations many thousands of times each year across the UK. In fact 30,000 times for bowel cancer. Each patient has on average five close relatives who are of voting age. These are in the main people who paid taxes for a health service to benefit not only themselves but those who cannot work.

23. Some patients have been able to benefit from a PCT deciding to provide primary care on the NHS (“normal” chemotherapy) whilst the patient pays privately to take the drug involved whether it is Avastin or Erbitux.

24. Some PCT’s refuse to allow this mix confusing themselves with the rules on “Public/Private” mix. Although the patient would be entitled to seek judicial review of this refusal of primary care, the patient is usually too ill, and too impoverished by buying one off drugs privately to be able to seek judicial review.

25. It would be very useful to clarify the position so that more PCT’s can understand that taking drugs privately does not mean the patient cannot have primary care on the NHS. It is not like a hip replacement situation, the patient is not asking for any NHS input in taking the drug privately. The patient by analogy will be able to take healthy foods privately without risking abandonment by the NHS of primary care and indeed patients often take both alcohol and smoke tobacco without losing primary NHS care.

26. It is anticipated that eventually there will be a case brought by way of judicial review to challenge this refusal of a PCT to provide primary care whilst the patient is taking either Avastin or Erbitux privately.

27. Since that first appeal, I have assisted pro bono a further 18 patients in their applications mainly referred via individual consultants and Bowel Cancer UK.

28. I cannot continue to do this indefinitely. I have published the results of my efforts and provided guidance for lay people and lawyers. I have referred my material en bloc to the Bar Council pro bono unit.

29. It would be helpful if a person could be paid to coordinate advice and representation nationally across all PCT’s on behalf of patients without relying on ad hoc charity work.

30. The table at the end of these submissions sets out the date of my application/appeal for exceptional funding; the patient (anonymised); the type of drug sought; the area of PCT; whether the appeal was successful/the time period of delay in deciding from first application/whether the PCT allows them to have normal chemotherapy on the NHS whilst taking the drug privately. Please note the delay includes time previous to my involvement.

31. Each patient has expressed the frustration at being refused a drug that can help them, not knowing the avenue of appeal or even that it existed, of not being helped by anyone in bringing an appeal, and at the same time, having to receive debilitating treatment for a life threatening illness.

32. Each carer has expressed the view that they wished to be able to take all steps they could to know that they had done as much as possible to help their loved ones.

33. In those appeals, only four have been fully successful, a further three have come to a private public arrangement with the PCT and the remainder have had their treatment limited.

34. Obviously, there will be other cases which probably deserve to be brought to a PCT appeal which have not been brought.

35. The pattern of success appears to indicate a postcode lottery system at work. Indeed one patient even indicated that he would be better visiting relatives in Italy to obtain the Erbitux.

36. I have been in contact with oncologists around the world and it is sobering to think that in Guatemala the public doctors there view with amazement the UK's refusal to treat with Erbitux third line.

37. Treatment in France, Germany, Spain and Italy all outstrip the UK's level of use and effectiveness on treatment. This is due in part to their use of these drugs.

38. On instruction from Bowel Cancer UK and Cancer Back Up I appeared at the NICE appeal in regard to Avastin and Erbitux headed by Professor Sir Michael Rawlins on 27 November 2006.

39. NICE in the appeal on 27 November 2006 expressed the view that not all clinicians might be as professional in their approach to prescribing these drugs as the two experts who were called to give evidence on behalf of the appeal.

40. It has been my experience in all 18 appeals that the clinicians have in the main been reluctant to prescribe drugs which they and the patients know can cause side effects, reluctant to prescribe until the right moment, and cautious in regard to whom they would lend their support, bearing in mind some patients just could not physically endure these additional biological agents. In other words, they have erred on the side of caution and have not taken an unprofessional approach to prescription. Indeed the figures for prescription of Erbitux in Wales in a small way are consistent with that picture in that the numbers being prescribed per year dropped slightly from 35 to 30 following the Welsh Assemblies decision to ignore the NICE recommendation.

41. As a result of stories like these those related to the unfortunates make decisions to enrol themselves on private medical insurance schemes. They lose their interest in themselves supporting and promoting a universal health scheme that does not provide sensible solutions to their life's problems.

42. People see the present restrictions from NICE as being a means to claw back money in NHS spending that has been wasted on inflated wages and wasted on computer systems.

43. The basis of most NICE "not recommended" decisions appears to people to be based on a lack of proof of effectiveness when the standard of that proof is set too high for what are new and groundbreaking treatments.

44. Also NICE look at the case as if everyone on the drugs would continue on the drugs for a full course of treatment whereas the new evidence rejected by NICE in Erbitux was to the contrary.

45. The perception of NICE is that it is a body which fails to trust expert clinical opinion.

46. Far from protecting the NHS, NICE decisions are seen as undermining the effectiveness of the NHS.

47. NICE'S EVALUATION PROCESS, AND WHETHER ANY PARTICULAR GROUPS ARE DISADVANTAGED BY THE PROCESS

48. The evaluation process involves QALY. Those disadvantaged are patients whose condition is not likely to result so much in curing the patient's condition or in saving of life but prolonging life and those whose quality of life is not amenable to a quantification of level but is likely to be variable through the proposed course of treatment.

49. It most certainly disadvantages those exceptional patients who may be able to respond so well that they are able to have surgery.

50. THE APPEAL SYSTEM

51. The present "appeal" system is not an appeal system in the sense of it having the power to hear new evidence. This is not necessarily wrong in law. I take the strong view that it is wrong in practice and leads to more problems than it solves.

52. The present system of appeal is based on the model of a judicial review.

53. The only legal avenue of appeal from the final decision of the appeal panel is itself by way of judicial review.

54. It thus follows that once a determination is made, there is no appeal which involves any new evidence at all, neither on appeal to NICE or on appeal by way of judicial review from NICE.

55. In fact the date on which the decision becomes out of date is in fact much earlier than that because there is a "cut off" date for the admission of evidence set long before NICE makes any reported determination.

56. The present appeal committee's job is a review only of the material which was before the original decision maker at the date of decision.

57. As such it only relates to checking if the internal procedures of that original decision were correct.

58. There are different ways of conducting an “appeal”. Some can be rehearing, some can be as this process is, review and others can be reconsiderations.

59. I would not recommend rehearing.

60. The present chosen method of limited review has advantages and disadvantages.

61. *Advantages*

62. The advantages are that the appeal committee do not have to do anything but look at the original material and even simpler than that, look at only those parts that fit into the limited criteria for these “due process” appeals. It makes the appeal committee’s task easier. In addition it prevents an appeal being brought as and when new evidence comes into being. It prevents the original decision being challenged (and even re challenged) and implemented simply because a new relevant fact has emerged. This enables a decision to in theory be promulgated without too much delay.

63. *Disadvantages*

64. The disadvantages closely mirror the advantages.

65. The disadvantages principally relate to the peculiar nature of oncology. It is to do with the fact that under this method of appeal, the decision can be very quickly out of date with the best practices in the real world.

66. There exists in the professional world of oncology a known and knowable consensus of expert professional clinical opinion which takes account of up to date information on the results of the myriad of ongoing medical trials.

67. What NICE decision subtly does is stifle “hands on” practice with new drugs. Apart from clinical trials, it is actual practice that eventually lets good results filter down as best practice. Without access to the new drugs the UK will always be second best and playing catch up to other countries. It is as if we are allowing NICE to state we need a perfect world and a perfect basis for a positive decision before approving any new treatment.

68. It also means that drug companies will not provide the UK’s best clinicians with their drugs so that the best clinicians may be drawn to practice elsewhere around the world.

69. From the moment the closure date for admitting evidence passes in the original decision makers process, the clock is running for the next piece of clinical trial information. By the time the original NICE decision maker has reported the determination, a substantial period of time has usually elapsed during which time relevant but inadmissible evidence about recent results in clinical trials has occurred. That schism between the real world and the determination can become wider once an appeal is lodged and heard and findings made on the appeal. With this further delay, further material can become available in the real world and the original decision, albeit in proper procedural format and albeit “right” on the original material, can lead NICE to make recommendations that any sensible person at the time of the final appeal, would not follow.

70. *Improvements*

71. Obviously, to keep the time from last evidence being admitted to determination and final appeal as short as possible would be beneficial.

72. The problems with that are that there are what are known as “reasonable” time periods of submission of evidence, sending it to the interested parties for comment, reports from expert committees to NICE, conclusions and report drawing, time period for notice of appeal, time period for setting down the appeal as the original committee will want to respond to the appeal notice, and then time for the appeal committee to consider and report back. There will always be delay. Where any of those processes can be taken out of the “process equation” or whether any particular time period can be shortened is not something I can accurately comment upon.

73. As a general observation, there remains an obligation for fairness in procedure such that it would appear that none of the above steps can be removed without causing unfairness and that the time limits set for each step (which cumulatively add up to so much time) cannot reasonably be cut much further without missing the opportunity for sensible evidence to be given and commented upon. There does not appear to me at least much scope for improving the time delay aspect of a decision.

74. There does appear to be another simpler way forward in improving the whole appeal process.

75. *A fair appeal*

76. A fair appeal process in the circumstances of rapidly changing oncology would allow in evidence “appertaining to the material facts as at date of decision” to be adduced at an appeal. This is a phrase common enough in legal parlance and is understood and defined by the Courts.

77. A proper appeal in my view would involve a reconsideration of the facts on the basis of the best available evidence.

78. The present system of decision making and review is one in which there is no opportunity to have relevant and material up to date facts considered in any appeal.

79. Judicial review of its very nature prevents new evidence. The evidence is limited to that which was before the original body.

80. Even if one were to successfully argue before a judicial review that the evidence before the appeal panel should have been taken into account, it would still not enable the judicial review body to come to its own conclusions on those facts. It could only refer the matter back for a fresh decision.

81. That really would prevent promulgation of decisions and create a “never ending” system of decision making.

82. The danger of a “never ending” system of decision making in changing the present terms of reference for a NICE appeal is met by the wording of the new procedural rule which would apply to admitting any new evidence which would apply when an appeal body reconsidering the matter looked at what evidence to take into account.

83. That wording would be similar to that used in appeals in other legal fields such as immigration.

84. “The appeal body may take into account evidence of material facts which appertained as at the date of decision”.

85. These other appeal bodies continue to function and do not suffer from a “never ending” process due to admitting new evidence because the new evidence is restricted to the relevant material issues and is not allowed to widen the debate or bring up new issues.

86. Thus the rule of admissibility is a discretionary one and not an absolute right to new evidence, the person seeking to place it before the appeal body has the onus of establishing it as relevant and material and as is the present position, the appeal body would take legal advice on whether it should be admitted.

87. The appeal process presently is limited to an essentially “due process” review; this means the merits of the decision are not reviewed. This artificial limit is not necessary. It means that when coupled to excessive delay in the process, the decision can become out of step with the reality of rapid technological advances. The fact that the appeal panel themselves are experts is somewhat wasted by their attendance on what is little more than observing that the original panel went through the right process and having made proper assumptions on the then available evidence, came to a decision by a logical and reasonable process.

88. It would be useful upon reconsideration on available relevant material evidence would be if the appeal panel could form their own view as to the recommendation.

89. In human rights law, under article 8, the right to a private and family life, the appeal authority must consider the facts as they are before them on the day of the appeal. This to my mind is akin to a rehearing and not necessary for NICE appeal committees and has many obvious disadvantages.

90. THE IMPLEMENTATION OF NICE GUIDANCE, BOTH TECHNOLOGY APPRAISALS AND CLINICAL GUIDELINES (WHICH GUIDANCE IS ACTED ON, WHICH IS NOT AND THE REASONS FOR THIS)

91. The NICE guidelines are followed by all PCT’s I have been involved with. Unfortunately they are not followed in the same way by all PCT’s. Some apply the guidelines as absolute rules which take precedence over clinical decisions by the consultant. Some treat them as the deciding factor when compared to clinical decisions. Only a few apply them properly as matters to be taken into account when looking at all the evidence and for them not to override clinical decisions in a particular case. Some PCT’s decide without legal assistance and others take legal assistance. The level and quality of legal assistance sought varies enormously. The PCT’s really do only get what they pay for in that respect.

92. It would be useful for there to be a National Guidance Manager who could oversee and help apply guidance for PCT’s.

93. THE SPEED OF PUBLISHING GUIDANCE

94. For the above reasons it can be seen that there is considerable delay built into the system. However, it is not so much the speed or lack of it but the way in which the decision makers go about their decision which is flawed. Increasing the speed will to my mind only increase the level of judicial reviews which will occur.

95. COMPARISON WITH THE WORK OF THE SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK (SIGN)

96. I have left this to last as I have no direct knowledge of this save to say that two PCT's have based their initial decision to refuse on the fact that the Scottish board had decided to make a "no" recommendation. One of these PCT's overturned the decision (Derby) and another did not (Uxbridge).

CONCLUSIONS

1. It would be very useful to clarify the position so that more PCT's can understand that taking drugs privately does not mean the patient cannot have primary care on the NHS.
2. It would be helpful if a person could be paid to coordinate advice and representation nationally across all PCT's on behalf of patients without relying on ad hoc charity work.
3. Obviously, to keep the time from last evidence being admitted to determination and final appeal as short as possible would be beneficial.
4. A fair appeal process in the circumstances of rapidly changing oncology would allow in evidence "appertaining to the material facts as at date of decision" to be adduced at an appeal.
5. A proper appeal in my view would involve a reconsideration of the facts on the basis of the best available evidence.
6. It would be useful upon reconsideration on available relevant material evidence would be if the appeal panel could form their own view as to the recommendation.
7. It would be useful for there to be a National Guidance Manager who could oversee and help apply guidance for PCT's.

Peter Telford

21 March 2007

Evidence submitted by Mr David Thomson (NICE 16)

1. SUMMARY

The comments given are from a patient's viewpoint and based on working as a lay member with NICE for over two years. There are finite resources available in the NHS for the care and treatment of patients. The allocation of these resources must be seen to be fair, consistent and equitable throughout the UK. For any given illness or condition, patients should have equal access to the same treatment and care regardless of their location within the UK. NICE and people associated with NICE, work very hard to produce timely decisions and papers which are fair, consistent and equitable within England and Wales. The NICE consultation process is excellent but inevitably time consuming. Patients' expectations are increasing and they make comparisons with treatments in England and Wales compared to say Scotland that is quoted by the press as having higher levels of funding. Parts of the press fuel any inconsistencies. It is suggested that NICE will come under increasing pressure as people live longer and the more successful the NHS becomes, the greater the competing demands for limited resources. The consequential impact on NICE is discussed including the increasing challenges arising from NICE decisions, the effect of these decisions on public confidence and possible ways of speeding up the publication of guidance.

2. PERSONAL BACKGROUND

I took an active interest in health issues after experiencing a heart attack in 2002. I joined the British Heart Foundation Hearty Voices network and I was appointed to the Patient and Public Involvement in Health Forum for the local Hospital Trust. I joined local heart support and cardiac rehabilitation groups. Although retired, I have close contacts with all age groups. To help others, I have written articles on health for the Database of Individual Patient Experiences (DIPEX) and NHS National Genetics. For over two years, I have been a lay member of the NICE Guideline Development Group on Post Myocardial Infarction and a lay member of a NICE Technology Appraisal Committee for six months.

3. WHY NICE DECISIONS ARE INCREASINGLY BEING CHALLENGED

3.1 The more successful the NHS is, the more problems NICE will face. In general, businesses welcome more customers but the NHS and NICE will face more problems and more criticism with the increasing number of patients (customers) requiring treatment and care. As a result there are likely to be further increasing demands on the finite resources and a reaction from those losing out.

3.2 Inevitably, NHS financial resources must be allocated according to need coupled with achieving maximum efficiency and savings in the NHS to effectively create more resources.

3.3 Allied to this is the progressive increase in expectation of patients and carers. This level of expectation appears to be fuelled by drug companies and charities that are becoming more proactive. Those losing out, shout out.

3.4 The use of a drug in any country is used as a lever against NICE. In particular, patients frequently quote Scotland, which the press says, has a higher per capita allowance for treatment and care than England. If this is correct, it leads to the question “Why is there not equity of treatment and care in the UK with equal opportunities for all patients regardless of location?”

3.5 Parts of the press regularly criticise NICE. This criticism is often based on comments from one or two patients and a comparison with the practice in other areas and countries.

3.6 Unfortunately, NICE may need to divert some resources from patient care towards countering the publicity from pressure groups and this will lead to a vicious circle.

4. WHETHER PUBLIC CONFIDENCE IN THE INSTITUTE IS WANING AND IF SO WHY

4.1 Most members of the public are not aware of NICE other than from the Press or media when it is either subject to criticism with glaring headlines or for example, a very short article regarding the introduction of a helpful new guideline. Unfortunately due credit does not seem to be attributed to NICE for the excellent work produced.

4.2 I talk to many patients and without doubt a major problem is the comparison with treatment and care in Scotland. The press fuels this dissatisfaction by quoting individuals who may move to Scotland in order to get certain drugs.

4.3 Another patient perception relates to the level of NHS funding between Scotland and England based on press quotes saying the level of funding is higher in Scotland. If this is the case, it is putting patients in England and Wales at a disadvantage. If the funding level is lower in England, then presumably NICE must be at a disadvantage compared to SIGN.

4.4 Patients, associated charities and the press react particularly strongly to NICE if a drug with a good reputation and in current use is withdrawn from future use for a group of patients.

4.5 A strong reaction impacting on public confidence in the NHS but not specific to NICE occurs if a drug with a good reputation is not available to patients in some areas.

4.6 NICE appears to consult fully with all interested parties and gives them an opportunity to comment on decisions.

4.7 My experience of NICE and those working with it, is a team of very skilled, highly motivated, caring people determined to do an excellent job for patients and the public.

4.8 NICE has an excellent international reputation.

5. THE SPEED OF PUBLISHING GUIDANCE

5.1 Speeding up publications can be achieved in the longer term by increasing the effort applied thus enabling more projects to proceed in parallel or individual projects to be moved quicker. This approach will give long-term benefits but it can be counter productive in the short term due to the required recruitment and training of additional staff. Also, the production level of existing highly skilled staff is often reduced as they become involved with the introduction of new staff. The management workload increases.

5.2 One trade off is between speeding up the publication of papers by reducing their size, and the time and care spent producing them, against increasing the risk of more appeals, which in turn consume time and effort.

5.3 Publishing could be speeded up by continuing present initiatives such as:

- Increase the number of parallel activities on a project thus reducing timescales.
- Concentrate on the recommendations, particularly key recommendations.
- Concentrate on significant recent changes to evidence rather than old evidence.
- Reduce the size of papers, thus reducing the effort to produce and read.
- Tailor papers to the management of patients and reduce academic type reference material.
- Increase the international collaboration on drug selection and share the knowledge.

David Thomson

17 March 2007

Evidence submitted by John Walsh (NICE 09)

1. I have been active in the field of patient and public involvement in health for a decade, that is to say during the whole of the National Institute's existence. As with the majority of initiatives within the ambit of DH, NICE had a somewhat ponderous start but for the past several years has performed well and certainly to the overall benefit of patients. Though demonstrating some of the collegiate-academic atmosphere that pervades medicine in Britain, it also exhibits a welcome adaptability: recent examples are the shortening of the consultation process for guidelines on the way to issue and the launch of the "Understanding NICE Guidance" series of publications.

2. Yet I have no doubt that public confidence in NICE has waned. My evidence is from involvement with patients—I have chaired the British Heart Foundation's patients group since 2003, chaired their national patients conference in 2005 and have frequent interaction locally, regionally and nationally with NHS patients.

3. Over the last three years—roughly the period of decline in public confidence—I have been involved in the work of NICE myself, as a lay member of a guideline development group. The contrast is complete: the way that NICE works merits the highest praise; it is an institution of which we should be nationally proud. Having observed the working methods closely and at length I can truthfully say that it is impossible to imagine how they could be improved. And I speak here as a patient as well as a student of organisational performance.

4. The one criticism that may merit sympathy on some occasions is of NICE's response time, but here too, I can see no way of doing the job more quickly while continuing to do it as well. (There is one other point of dissatisfaction, that I share, but where blame cannot be laid at NICE's door: how is it that, 300 years after the Act of Union, we citizens of the United Kingdom find ourselves with both a NICE and a SIGN? That is a question the Committee might like to ask itself.)

5. What are the reasons for this diametric difference between the reality and the public belief? I think there are two:

- (i) By virtue of its mission, NICE is unusual, perhaps unique, among bodies in the health field in that it can attract only bad publicity; its myriad "good deeds" are subsumed into practice un-noticed.
- (ii) It seems that a section of the press is bent on destroying public confidence in NICE. One is accustomed to the "good news is no news" rule that is general in the media, but we have seen lately a positively malevolent campaign that is causing distress to patients and that comprises editorial matter that amounts to no less than lies.

John Walsh

8 March 2007

Evidence submitted by Miss Rose A Woodward (NICE 98)

SUMMARY

I believe the NICE process is unnecessarily bureaucratic, it is not responsive to the needs of patients or the clinicians tasked with their care.

It takes no account of extant approvals and licenses from other Countries—ie the EU. It is slow, autocratic and trying to find someone who will take responsibility for the patients lives lost while it rumbles through its work, is as impossible as trying to get a life saving drug to a terminally ill patient before they die. That is the blunt truth of the situation. Where an approval and prescribing history exists for a drug then that drug should be fast tracked and seen to be fast tracked by the general public.

1. Why NICE's decisions are increasingly being challenged

Patients have realized that the NICE system does not take proper and full account of the rights and interests of patients. It does not consider the needs and interests of patients with the same weight it attaches to cost effectiveness. The process is not open and certainly not accessible or understandable to ordinary people. Patients and the public are not engaged with, they feel impotent against such an arrogant attitude and feel that recourse to the law represents their only way of calling bodies like this to account.

2. *Whether public confidence in the Institute is waning, and if so why*

Genuine members of the public are increasingly cut out of the process. Real Patient involvement is minimal and is considered tokenism. The process for a genuine and sincere patient who feels they have something to offer is so convoluted that, especially if you are a patient battling illness, the whole process seems designed to prevent your views being heard. The work of the institute is not generally advertised to the Public. Support Groups are not consulted. Cancer Networks are not consulted. the voice of the individual is not felt to be important:

“They will do what they want to do”.

Why should the public have confidence in an institution they cannot connect with and feel so distant from. The language used by staff in response to enquiries from members of the public is archaic and often incomprehensible ie scoping workshops, 14th wave pre appraisal drafts and remits?? Email responses are impersonal and could well just come from an automated system. It is impossible to have any effect on the system which is rigid and unresponsive to the needs of the very people it is meant to be serving.

3. *NICE's evaluation process, and whether any particular groups are disadvantaged by the process*

The obvious groups disadvantaged are those patients with a terminal illness. I am a kidney cancer patient. If my disease spreads the prognosis will be 8 to 12 months. The process for NICE to approve a drug has been quoted to me at 18 months to 2 years. Should I really feel this is an evaluation process that is responsive, proactive or one that cares whether I live or die? There must be a fast track process for treatments that are of benefit to terminally ill patients or those whose disease will progress. The absolute maximum time to approve or refuse a life saving drug should be 3 months.

4. *The speed of publishing guidance*

NICE must take into account the process of licensing and approvals that drugs have gone through in the European Union. If the treatments have been assessed by the EU then that prior process should count for something and the drugs should just go immediately to a final phase assessment. The drugs will have been evaluated. The same applies for other Countries who have licensed and approved drugs as safe and efficacious. What is the point of all the Countries in the EU subjecting the drugs to individual checks if it is obvious that they have already been assessed and approved by other Countries. See previous point number 3 for comments that while this process is slowly grinding towards a published document, patients needing the drugs will have died waiting.

5. *The appeal system*

This needs to be publicised in the National press, there needs to be statutory consultees. the appeal panel should comprise patients (not representatives of national charities but patients personally affected by the decision that will be made). Patients have the unique view which is just as valid as that of the health economist and that of the clinician.

6. *Comparison with the work of the Scottish Intercollegiate Guidelines Network (SIGN)*

I cannot comment on this—I have no direct knowledge of the this organisation.

7. *The implementation of NICE guidance, both technology appraisals and clinical guidelines (which guidance is acted on, which is not and the reasons for this)*

I cannot comment on this. I do not have any experience of which guidance is or is not acted upon, whether the guidance issued is mandatory or not—and nor do I suspect do other members of the public.

Rose A Woodward
Cancer Patient

23 March 2007

Pelvic Pain Support Network (NICE 04)

The Pelvic Pain Support Network supports patients with a wide range of conditions for which there is no NICE guidance. It is extremely difficult for these patients to access health professionals with expertise in these conditions. This creates inequalities in access to care.

The decisions are increasingly being challenged for several reasons:

- There are many gaps in the guidance. Areas that are not included tend to be of low priority despite their impact on quality of life.
- There is little room for patient choice in treatment.
- Guidance only takes account of research published in English.
- The guidance may already be out of date by the time it is published due to the length of time it takes to develop it.

Implementation is hit and miss due to lack of familiarity with guidance at local level and a lack of available data on patient need. The system is rigorous but it is a huge amount of effort which is not necessarily translated into practice for the benefit of patients. Development of guidance needs to be linked to training of health professionals many of whom are not familiar with the research. The Haute Autorite de Sante in France is a coordinated comprehensive model from which we could learn a great deal.

Pelvic Pain Support Network

March 2007
