Agreed version

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

Minutes of the 71st meeting held on 21 November 2001 at DEFRA, Conference Room A, Whitehall Place West, London

Members:	**Professor P Smith (Chairman)** **Professor A Aguzzi** **Professor R Anderson** **Professor C Bostock** **Mr R Bradley** **Professor R Carrell** **Professor J Collinge** **Dr D Cunningham** **Professor J Ironside** **Mr P Jinman** **Professor C Masters** **Professor I McConnell** **Dr J Safar**
Technical Advisors:	**Mr P Soul (DEFRA)** **Dr H Gates (DEFRA)** **Dr J Stephenson (DH)** **Dr N Connor (DH)** **Dr S Dixon (FSA)** **Ms A Conroy (FSA)**
Observers:	**Professor C McMurray (DARDNI)** **Dr M Simmons (NAW)** **Mrs L Shepard (HSE)** **Dr N Coulson (DEFRA)** **Dr S Baxter (SEERAD)** **Dr A Allman (BBRSC)** **Dr K Finney (MRC)** **Dr D Matthews (VLA)**
Secretaries:	**Dr M Bailey (DEFRA)** **Mr A Harvey (DH)** **Mr D Carruthers (FSA)**
Secretariat:	**Dr L Harbron (DEFRA)** **Mr H Needham (DEFRA)** **Dr A Leigh (DH)** **Mr M Hall (DH)** **Dr I Hill (FSA)**

Also in attendance:	**Dr D Salisbury (DH- Item 2)**
	Dr L Tsang (MCA- Item 2)
	Dr M Kavanagh (MCA- Item 2)
	Mr N Cleary (DEFRA- Item 5)
	Dr M Stack (VLA- Item 6)
	Dr M Brueton (Consultant gastro-enterologist-Item 8)
	Mr P Comer (DNV Consulting- Items 8 & 9)

Item 1- Chairman's introduction

1.1 The Chair formally welcomed Professor Robin Carrell and Dr Deirdre Cunningham to their first Committee meeting as full Members. They bring expertise to the Committee on protein chemistry and public health respectively. The appointment of a geneticist was in progress, and it was hoped that an appointment would be made prior to the next Committee meeting in February 2002.

1.2 Apologies for absence were received from Professor Harriet Kimbell.

Item 2- vCJD update

Number of cases

2.1 The Committee conducted its regular review of epidemiological information on vCJD. The Committee was informed that the total number of definite or probable vCJD cases in the UK stood at 112, of whom 10 were still alive.

2.2 Sixty of the 112 cases were male and 52 were female. The mean age at death was 29 years and at onset was 27 years. In 2001, so far, 18 people had died, compared to 28 in 2000. It remained the position that all of the cases tested for their prion protein (PrP) genotype, 96 in total, were Methionine/Methionine at codon 129 of the PrP gene. In 2001, so far, 35 people had died of sporadic CJD in the United Kingdom.

2.3 The Committee noted an analysis from the Public Health Laboratory Service, which showed that the increase in the number of vCJD cases since 1995 continued to be significant, on average increasing at a rate of 22 per cent per year for onsets and 27 per cent per year for deaths. This analysis is available on the National CJD Surveillance Unit (NCJDSU) website.

Geographically associated cases

2.4 The Committee was informed that a number of geographically associated cases were being investigated in conjunction with the National CJD Surveillance Unit (NCJDSU), the Communicable Disease Surveillance Centre/Public Health Laboratory Service, the London School of Hygiene and Tropical Medicine and the Department of Health. A protocol had been agreed to ensure consistency of investigation of such cases. This is available on both the NCJDSU and the Department of Health websites.

2.5 One investigation in Leicestershire had been completed, seven were currently underway and four others were due to start early in 2002. The

Committee was informed that the investigations had not, as yet, considered whether there was any correlation between areas of the country with a high incidence of scrapie in sheep and those areas where geographically associated cases had been found. The NCJDSU confirmed that this issue would be addressed in future though interpretation would be complicated by the known incomplete notification of cases of scrapie.

2.6 The Committee was informed that the NCJDSU had identified five geographically associated cases of vCJD who had lived in or near Southampton. Analysis of their medical records had shown that two had received oral polio vaccine (OPV) in 1994 from the same batch of vaccine. There were no other vCJD cases known to have received OPV from this batch. The Committee noted that at an early stage of the vaccine manufacturing process not only this batch, but also the original bulk vaccine and indeed the production of up to 60 million doses of the vaccine by the manufacturer had involved the use of UK-sourced Foetal Calf Serum (FCS) in the 1980's. The Committee noted that this vaccine product had been removed from use in October 2000 when the Department of Health had been informed of the details of the manufacture. The Committee was informed that analysis of the available data indicated that, whilst other vCJD cases had received polio vaccine from other batches from the same manufacturers, they appeared to be no more likely to have been administered this particular product than healthy individuals. However there were difficulties with retrospective tracing of vaccinations, as the batch numbers of the vaccines used had not always been noted on the patients' records.

2.7 The Committee recommended that the Department of Health encourage GPs to log batch numbers of vaccines, using new technology to assist where appropriate. This would greatly aid future investigations. The recording of batches by bar coding was presently being explored.

2.8 The Committee noted the conclusions of the Committee on the Safety of Medicines (CSM) and its Ad Hoc Expert Working Group (the membership of which is annexed) who had evaluated in June and October 2000 the safety of the OPV that had been exposed in the past to UK-sourced FCS. The Ad Hoc Working Group and the CSM had concluded it was very unlikely that there would be any BSE risks from the use of this UK-sourced FCS, taking into consideration (i) the nature of the material used (with no infectivity being detected in bovine blood, including foetal calf blood, as measured by bioassay), (ii) the manufacturing process, including the fact that the diploid cell line MRC-5 derived from fibroblast cells was considered unlikely to propagate the BSE agent, if at all present, and (iii) the enormous dilution of FCS during the production process. In addition, the CSM had concluded there was at present no scientific evidence to suggest that (a) vaccines currently authorised for use in the UK were unsafe with respect to the use of animal derived products in their

manufacture; and (b) there were any BSE related issues for established cell lines or seed lots used for the production of current vaccines authorised in the UK.

2.9 SEAC concluded that the observation that two vCJD cases had received OPV from the same batch did not provide a reason to change the CSM's recent assessment of risk from OPV. The Committee suggested it might be of value to conduct further scientific tests for abnormal prion protein and infectivity of the MRC-5 cell line. Appropriate experiments will be considered, and a report submitted to SEAC, together with any further epidemiological studies and the recent risk assessments conducted.

2.10 The Committee asked about the various enquiries carried out on animal-derived products used in all human and veterinary vaccine manufacturing. The Committee was informed that reviews had been performed by CSM and by the European Committee for Proprietary Medical Products (CPMP) and its Biotechnology Working Party, who had arrived independently at similar conclusions regarding vaccine safety for human use as the CSM. In addition, reviews had been undertaken by the United States Food and Drug Administration, through the FDA's Centre for Biologics Evaluation and Research, the FDA's TSE Advisory Committee and Vaccines and its Related Biological Products Advisory Committee. The Committee asked that, subject to the agreement of the responsible authorities, the review work undertaken to date should be provided to a future meeting, together with results of epidemiological analyses of CJD cases and vaccine history.

2.11 The Committee stressed the importance of vaccination in controlling infectious diseases. They emphasised that any theoretical concerns related solely to historic polio vaccine use and did not apply to current vaccine products. The Committee were of the view that any historical theoretical risk must be balanced against the overwhelming benefits that would have resulted from the vaccination programme, as a fundamental public health protection measure.

Item 3- Scrapie Brain pool experiments- Update on current position and audits of samples

3.1 Members were updated on experiments conducted at the Institute of Animal Health (IAH) to examine a pool of scrapie brains collected in the early 1990's for evidence of BSE. SEAC had previously recommended that the material should be examined by DNA analysis to assess whether the pooled brain material may have been contaminated with bovine tissue. The Laboratory of the Government Chemist (LGC) had been asked to perform the work. Their results were completely unexpected as the analysis detected only bovine material in the sample. SEAC had intended to meet on the 19 October to

consider the experiment in detail. However, in view of the result, the meeting was cancelled.

3.2 Two audits had been commissioned by DEFRA to examine procedures at the IAH. The reports had not yet been completed, and hence the chain of events was still unclear. However, Members considered that it was unlikely that the audit results would change the view that the experiment, because it had used material collected for a different purpose, was flawed and that, if bovine material was present in the material, it would be uninterpretable. Members agreed that any other experimental work using pooled scrapie brain material should be assessed to ensure that the provenance of the material was secure and the experiments remained valid.

3.3 Members expressed the view that this case was not a good example of the way in which developing science should be handled. It had been damaging that the SEAC meeting scheduled for 19 October had become such a high profile event. Members considered that the release of preliminary information by the FSA from incomplete experiments in the summer had raised expectations of possible conclusions from the experiment. This in turn had forced Ministers to make an early statement immediately after the LGC results became clear. Data would normally be subject to peer review before being made public.

3.4 Members agreed that there were important implications in terms of obtaining access to pre-publication scientific data in future. If scientists thought that preliminary work presented to SEAC may be placed in the public domain prematurely, it was likely that scientists would in future be cautious about presenting pre-publication information to the Committee. Members agreed that this would seriously hamper SEAC's capacity to give meaningful and timely advice. More generally, the majority of scientists rely on individual project grants, and the release of preliminary data could inhibit publication, which in turn may affect future funding. This may also influence scientists not to put pre-publication material before the Committee.

3.5 Members agreed that recent efforts to increase the transparency of SEAC's deliberations were important and largely beneficial. However, SEAC agreed that Government Departments needed to make a distinction between work that was complete but not yet published and work which was incomplete and, as a result, could not be reliably interpreted. Some Members considered that the FSA's commitment to openness in particular could create difficulties for the working of the Committee. Members agreed that the Chairman of the Food Standards Agency should be invited to the next meeting to discuss this issue.

Item 4- Review of SEAC's recommendations on sheep since 1996

4.1 The Committee briefly considered a paper setting out SEAC's recommendations on sheep since 1996 and the action taken to date. The recommendations would be considered at SEAC's next meeting in February 2002, together with the outcome of the DEFRA workshop on sheep TSE research taking place in December, at which all projects in the current sheep research programme would be reviewed. The aim would be to identify gaps in the programme and re-assess priorities. Members noted that a SEAC sub-group convened to consider sheep research and surveillance had published a summary of their discussions in April 1999. Members would consider the merits of convening a similar sub-group to review current progress at their next meeting.

4.2 There was some concern about whether the provision of information would be adequate to enable SEAC to consider all aspects of ongoing sheep research. However it was noted that SEAC's primary role was to take an overall view of the programme rather than consider individual projects in detail, which was the remit of research sponsors. Members also agreed that surveillance to investigate the prevalence of TSE's in the national flock was a vital component of the current sheep TSE programme, particularly in view of the uncertainties that remain in this area. Proposals to carry out abattoir surveillance would be discussed under agenda item 7. However Members agreed that the overall surveillance programme should also be critically reviewed.

Item 5- Update on genotyping of sheep under the National Scrapie Plan (NSP)

5.1 Members were updated on progress on the National Scrapie Plan, a long term programme to increase the level of genetic resistance to scrapie within the national sheep flock. The programme had recently been launched to purebred pedigree flocks on a voluntary basis. To date, approximately one third of eligible flocks had expressed an interest in the scheme.

5.2 Members were invited to consider proposals to accelerate the scheme as put forward during the recent consultation exercise. These included extending the NSP to the non-registered pure bred sector and to scrapie affected flocks.

5.3 Members endorsed any moves to accelerate the eradication of TSEs in sheep, but emphasised the importance of ongoing research to determine whether genetically resistant sheep were capable of carrying and transmitting the infectious agent. Members noted that an ongoing programme of work was underway to address this issue, including examining the spread of TSE infection in the tissues of sheep of different breeds and genotypes at various time points after experimental challenge. However the experiments were not

complete and hence currently it was not yet possible to draw any definitive conclusions from this programme of work.

5.4 Members recognised that action on scrapie affected flocks would be particularly beneficial. However, SEAC agreed that any plans for targeted action should be formulated with the industry to ensure that all suspect scrapie cases are notified and affected flocks participate. Members also suggested that restocking following slaughter due to foot and mouth provided an opportunity to accelerate the NSP by encouraging farmers to restock with resistant animals. However it was noted that there would be difficulties in excluding animals from imports on the basis of genotype as European trade rules did not allow this, and one of the key difficulties speeding up the scheme was the relative scarcity of resistant animals which would also apply to imported sheep

Item 6- Ongoing research

Testing of Individual sheep scrapie brains

6.1 Members were updated on ongoing research to strain type current scrapie cases for evidence of BSE. Previous experiments had indicated that a highly consistent pattern has been seen in the incubation periods and brain pathology in a panel of mice inoculated with isolates from cases of BSE, vCJD, feline spongiform encephalopathy in domestic cats (FSE) and some other naturally occurring or experimentally induced TSEs associated with exposure to the BSE agent. A typically BSE pattern is associated with characteristic incubation periods in RIII mice (320 days post inoculation) and C57-black mice, which progress to clinical disease approximately 100 days later. Other mice strains within the panel typically contract disease at similarly consistent, but extended, time points.

6.2 The Committee noted that 183 individual scrapie brains had been inoculated into panels of mice. To date, 176 isolates had passed the 320 day incubation period in the RIII mice. Thus none of these isolates showed the incubation period characteristics that had previously been associated with BSE-derived strains.

6.3 However Members stressed that the significance of the current data had to be interpreted with caution as there were many unknowns. It was possible, for example, that the strain characteristics of BSE might change on sub-passage from one sheep to another, or if BSE and scrapie agents were present together in the same animal. Hence, although the experiments on individual sheep scrapie brains had demonstrated no evidence of BSE in sheep so far, it was not possible to interpret fully these preliminary results. Members considered it paramount to try and establish a yardstick for determining the presence, or otherwise, of BSE in sheep

Analysis of sheep scrapie brains using Western blot techniques

6.4 Members were presented with preliminary work conducted at the Veterinary Laboratories Agency (VLA) to strain type scrapie isolates using a Western blot technique. Such molecular techniques have the advantage that they allow agent strains to be differentiated more rapidly than by using mouse panels.

6.5 Although the technique had not yet been validated, there was preliminary evidence that the technique was able to distinguish scrapie and BSE in sheep. However, the test required additional refinement before it could be used as a reliable and robust test.

6.6 Although the Committee was encouraged by the work presented by the VLA, some Members expressed frustration about the limited development of molecular techniques to differentiate between TSE agents in sheep. While recognising the complexities of assessing scrapie strains within the myriad of different breeds and genotypes that make up the UK sheep flock, the view was expressed that more work needed to be done to refine Western blot techniques in order to distinguish strains from sheep in an manner that was reproducible and unequivocal. This had been achieved with bovine BSE and with vCJD and other human prion diseases.

6.7 SEAC agreed that it was important to Western blot as many known scrapie isolates from sheep of different breed and genotypes as possible in order to build up a matrix of information from existing scrapie strains. In parallel, there was a need to assemble similar information on sheep experimentally infected with BSE. Members requested an update of what sheep genotypes and breeds had been examined to date at the next meeting.

6.8 Because of the importance of developing strain typing techniques for use in sheep, Members considered setting up a SEAC working group to carry strain typing work forward. However, in the first instance it was agreed to be more beneficial for scientists in relevant research groups to meet and to discuss how best to move this work forward rapidly. Collaboration between researchers employing molecular strain typing techniques in human disease and scientists at the VLA could be beneficial in refining techniques employed to analyse sheep isolates. Members wished to be updated on progress at their next meeting.

Item 7- Proposals for TSE sheep surveillance

7.1 The Committee considered DEFRA proposals for future sheep surveillance work. In order to comply with new EU regulations, the UK plans to carry out two separate sheep surveys beginning in January 2002. An abattoir

survey would monitor approximately 20,000 sheep over 18 months of age slaughtered for human consumption for evidence of TSE infection in brain tissue using an appropriate diagnostics test. A second survey would examine 3,000 fallen stock, which for the purposes of the survey are defined as sheep that have died or are slaughtered that are not fit for human consumption.

7.2 Epidemiologists had been consulted about appropriate sample sizes required to detect the true prevalence of scrapie in the abattoir survey with a degree of confidence. However the Committee expressed some concern that constraints prohibited the examination of larger numbers of sheep. Currently there was a requirement under EU law to destroy the entire carcase of an animal that had tested positive for a TSE. As a result, all parts of the body of the tested animals had to be retained pending the outcome of each test. Given that currently there is no evidence of BSE in the UK sheep flock, and that the vast majority of animals entering the food chain would not be tested, Members agreed that there should be no need to retain the carcases pending results of each sample. Although Members understood that Government was currently constrained by European legislation, they recommended that the relevant legislation be reviewed in order to facilitate the monitoring of increased numbers of sheep for evidence of TSE infection.

Item 8- FSA issues

Baby food and the advice given by SEAC in 1996 on the relative susceptibility of babies to vCJD

8.1 In view of recent interest in the use of lamb in baby food and the theoretical possibility of BSE infection in sheep, the Committee was asked to review its earlier advice, given in 1996, that infants and children were not likely to be more susceptible than adults to infection with the BSE agent. To help the Committee in its deliberations, a consultant paediatric gastro-enterologist had been invited to help review the current state of knowledge on this question.

8.2 It was explained that there were three issues: digestion of protein, access of proteins to the mucosa and the permeability of the intestine. Damage to the mucosa could occur in various ways, resulting in increased permeability. Infants in the first few months of life were more susceptible to gastro-intestinal infections during which their mucosa might become more permeable to proteins.

8.3 Concern was expressed that the intestines of new-born babies may be more permeable as they have a special need to take up antibodies from their mothers' milk. It was reported, however, that such increased permeability should no longer occur by weaning age, when infants would normally be receiving baby food.

8.4 Members noted that there was some epidemiological evidence that most infections with BSE in cattle had occurred early in life. Furthermore, vCJD had so far affected young adults more commonly than those in other age groups. It was not clear if this was due to age-dependent susceptibility or to age-related exposure. There is little experimental data on variation in age-related susceptibility to TSE infection in different animal species. There was limited published, and unpublished, information on age-related susceptibility in mice which was complex to interpret and differences between mouse and human immune systems in new borns limited any generalisations that might be drawn from this work.

8.5 As there were very few studies relevant to the question of age-related susceptibility that had been undertaken, the Committee did not consider they had sufficient data to give a definitive view. There were theoretical grounds for supposing that in some circumstances infants could be more susceptible in the first few months of life. But any increased susceptibility would be most likely to exist in the early months of life. Although many infants would not be exposed to sources of TSE through diet at that time, the Committee felt a prudent approach might be adopted. It was recommended that further experimental research was required on age-related susceptibility to infection with TSE agents.

Sheep risk assessments – areas of weakness in data

8.6 The Committee received a progress report on work commissioned by the FSA to assess the potential risks of BSE in sheep. A number of areas were identified where further data would improve the sheep risk assessment work currently underway. First, more details on the consumption patterns for lamb were needed, to include such factors as age, gender, geographical and cultural variations. Secondly, more data were needed on scrapie in sheep, including prevalence data over time, by age and flock type/geographical localisation. More data were also needed on the tissue distribution and quantitative titre changes of scrapie infectivity within sheep, by age, and on the transmission routes for scrapie (as if BSE were in sheep it is likely that its transmission characteristics would be similar to those of scrapie). In addition, the demography of the national sheep flock was considered to be poorly documented.

Item 9- Risk assessment on theoretical BSE risk from burning and burial of sheep

9.1 Members briefly considered a risk assessment that had been commissioned by DEFRA to examine the potential public health risks from the disposal of sheep carcases under contingency plans in the event that BSE were

to be identified in UK sheep. The report concludes that, even if BSE were present in the sheep, the infectivity that would result from burying or burning a large number of sheep carcases, such as in the recent FMD outbreak, would be very small.

9.2 It was noted that the risk assessment is heavily reliant on the input values used. These were often based on limited experimental data, although the proposed surveillance program would provide important information on scrapie prevalence that would improve the accuracy of the assessment. Members were invited to consider the risk assessment and send comments to the secretariat.

Item 10- Committee business

10.1 Members considered procedures for disseminating SEAC advice. Currently, the Committee releases a public summary after each meeting but, in the increasing drive for openness, these had become increasingly lengthy. Minutes of each meeting were also circulated for Members use, although these were not published.

10.2 In line with other Government Advisory Committees, and to further increase transparency of SEAC deliberations, Members agreed to dispense with the public summary and publish the draft minutes following each meeting. Members would be invited to comment prior to publication, and the minutes would not be fully ratified until Members had signified their agreement at a subsequent Committee meeting. The agreed minutes would then be re-circulated.

10.3 Members agreed that, on occasion, sections of Committee minutes should remain confidential. This would include SEAC's consideration of pre-publication research. In this case, an appropriate confidential section would be circulated to Committee Members only.

10.4 A paper on future plans for open meetings was circulated. However due to lack of time, Members did not get an opportunity to discuss this. Members were invited to send comments to the secretariat.

Item 11- Any Other Business

11.1 Members requested that the next SEAC meeting should include an update on progress with respect to reducing the potential risk of the transmission of vCJD through the use of contaminated surgical instruments.

11.2 FSA announced that they would be holding a public stakeholder meeting on 18 December to review the precautionary measures in relation to sheep. The

Chair would be attending and an open invitation was extended to other SEAC members.

SEAC Secretariat
December 2001

Membership of Ad Hoc Expert Working Party

Chair: Professor G W Duff MA BM BCh PhD FRCP FMedSci
Professor of Molecular Medicine, Sheffield University
(Chair of Biologicals Sub-Committee)

TSE Experts:

Dr Moira Bruce MBE BSc PhD
Head of Pathology and Pathogenesis Section, Institute for Animal Health, Edinburgh
(Member, CSM Biologicals Sub-Committee)

Mr J W Wilesmith BVSc MRCVS (**SEAC member**)
BSE Epidemiology, Central Veterinary Laboratory, MAFF
Visiting Professor, London School of Hygiene and Tropical Diseases

Professor R Will MD FRCP
Director, National CJD Surveillance Unit, Western General Hospital, Edinburgh

Professor P Smith DSc FMed Sci (**Chair, Spongiform Encephalopathy Advisory Committee**)
Professor of Epidemiology, London School of Hygiene and Tropical Diseases

Dr Christine Farquhar BSc PhD
Animal Health Institute, Neuropathogenesis Unit, Edinburgh

Dr R Knight BM BCh FRCP
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Dr G C Schild CBE DSc FIBiol FRCPath FRCP(E) FRCP
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Vaccinology, Immunology, Paediatrics and General Practice

Professor Roger Jones BM BCh DM FRCP FRCGP MFPHM FMed Sci
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Committee on Safety of Medicines

Professor A Breckenridge CBE MSc MD FRCP F Med Sci (**CSM Chairman**)
Professor of Clinical Pharmacology, Liverpool University Medical School

Professor M Kendall MB ChB MD FRCP
Professor of Clinical Pharmacology, Birmingham University Medical School

Principal Assessor

Dr L Tsang (Head, Biologicals and Biotechnology, Medicines Control Agency)

Department of Health (Observer)

Dr D Salisbury (Head of Immunisation, Department of Health)

List of scientific papers supplied to SEAC Members by the Secretariat between 18 September and 21 November 2001

Paper by P Rudd. M Wormald, David Wing, Stanley Prusiner and Raymond Dwek, "Prion Glycoprotein: Structure, Dynamics, and Roles for the Sugars", published in Biochemistry, 2001, Volume 40, pages 3759 – 3766.

Paper by V R Martins, A F Mercadante, A L B Cabral, A R O Freitas and R M R P S Castro, "Insights into the physiological function of cellular prion protein", published in the Brazilian Journal of Medical and Biological Research, 2001, Volume 34, pages 585 – 595.

Paper by Joanna Masel and Vincent A A Jansen, "The measured level of prion infectivity varies in a predictable way according to the aggregation of the infectious agent", published in Biocimica Et Biophysica Acta, 2001, Volume 1535, pages 164 – 73.

Scientific paper by Brigid Wenz, Bruno Oesch and Martin Horst "Analysis of the risk of transmitting bovine spongiform encephalopathy through bone grafts derived from bovine bone", published in Biomaterials, 2001, Volume 22, pages 1599 – 1606.

Paper by Angela McLean, "a scientific opinion on Risk Solutions' report Audit of Possible Contamination with BSE in the Meat and Bonemeal Study" , pages 1 – 9.

Letter by by M E Bruce, I McConnell, R G Will and J W Ironside " Detection of variant Creutzfeldt – Jakob disease infectivity in extraneural tissues" published in The Lancet, Volume 358, pages 208 – 209.

Paper by Frank Bastian and John W Foster, " *Spiroplasme sp.* 16s rDNA in Creutzfeld – Jakob Disease and Scrapie as Shown by PCR and DNA Sequence Analysis" published in the Journal of Neuropathology and Experimental Neurology, 2001, Volume 60, pages 613 - 20.

Paper by M H Anil, S Love, C R Helps, J L McKinstry, S N Brown, A Philips, S Williams, A Shand, T Bakirel and D Harbour, "Jugular venous emboli of brain tissue induced in sheep by the use of captive bolt guns", published in The Veterinary Record, 2001, Volume 148, pages 619 – 620.

Scientific article by Beverly K Pierson "Will scrapie in sheep in Great Britain disappear?", published in Trends in Microbiology, Volume 9, page 260.

Paper by I V Baskakov, G Legname, S Prusiner and F E Cohen, “Folding of Prion Protein to Its Native a-Helical Conformation Is under Kinetic Control” published in The Journal of Biological Chemistry, 2001, Volume 276, pages 19687-19690

Paper by E Asante and J Collinge, “Transgenic Studies of the Influence of the PrP structure on TSE Diseases”, published in Advances in Protein Chemistry, 2001, Volume 57, pages 273-311.

Article by Stu Borman, “PCR for Prions”, published in Chemical Engineering News, 2001, Volume 79 page 9.

Paper by D R Brown, C Clive and S J Haswell, “Antitoxidant activity related to copper binding of native prion protein” published in Journal of Neurochemistry, 2001, Volume 76, pages 69-76.

Paper by A N Hamir, J M Miller, M J Schmerr, M J Stack, M J Chaplin, R C Cutlip, “BRIEF COMMUNICATIONS Diagnosis of preclinical and subclinical scrapie in a naturally infected sheep flock utilizing currently available postmortem diagnostic techniques” published in the Journal of Veterinary Diagnostic Investigation 2001, Volume 13, pages 152-154.

Letter by M A Ferguson-Smith, published in British Medical Journal, 2001, Volume 322, pages1544-1545.

Paper by A C Frosh, R Joyce and A Johnson, “Iatrogenic vCJD from surgical instruments”, published in British Medical Journal, 2001, Volume 322, pages 1558-1559.

Paper by R C Cutlip, J M Miller, A N Hamir, J Peters, M M Robinson, A L Jenny, H L Lehmkuhl, W D Taylor, F D Bisplinghoff, “ Resistance of cattle to scrapie by the oral route” published in The Canadian Journal of Veterinary Research, 2001, Volume 65, pages 131-132.

Paper by D Gavier-Widen, G A H Wells, M M Simmons, J W W Wilesmith and J Ryan, “Histological Observations on the Brains of Symptomless 7 – Year-old Cattle”, published the Journal of Comparative Pathology, 2001, Volume 124, pages 52-59.

Article by S Cousens, P G Smith, H Ward, D Everington, R S G Knight, M Zeider, G Stewart, E A B Smith-Bathgate, M-A Macleod, J Mackenszie and R G Will, “ Geographical distribution of variant Creutzfeldt-jakob disease in Great Britain, 1994-2000” published in The Lancet, 2001, Volume 357, pages 1002-1007.

Paper (translated from German) by G Bohmler, " The detection of bovine protein in sausages" published in Fleischwirtchaft, 2001, Volume 6, pages 103-105.

Paper by A J E Green, E J Thompson, G E Stewart, M Zeidler, J M Mackenzie, M- MacLeod, J W Ironside, R G Will, R S G Knight, "Use of 14-3-3 and other brain-specific proteins in CSF in the diagnosis of variant Creutzfeldt-Jakob disease", published in Journal of Neurology, Neurosurgery and Psychiatry, 2001, Volume 70, pages 744-748.

Paper (translated from French) by Pierre Sarradin and Frederic Lantier, "Have sheep gone "mad"?" published in Biofutur, 2001, pages 42-46.

Paper by W A Cooley, J K Clark, S J Ryder, L A Davis, S S J Farrelly, and M J Stack, published in the Journal of Comparative Pathology, 2001, Volume 125, pages 64-70.

Paper by M Jeffrey, S Martin, J R Thompson, W S Dingwall, I Begara-McGorum and L Gonzales, "Onset and Distribution of Tissue PrP Accumulation in Scrapie-affected Suffolk Sheep as Demonstrated by Sequential Necropsies and Tonsillar biopsies" published in Journal of Comparative Pathology, 2001, Volume 125, pages 48-57.

Editorial by Cheryl Donnelly, "Key issues confronting the contact lens industry", published in Contact Lens and Anterior Eye, 2001, Volume 24, pages 52-58.

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