SEAC

Spongiform Encephalopathy Advisory Committee

ANNUAL REPORT 2005

v4 including chair's comments

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Foreword

The format of the SEAC annual report has changed substantially this year. Since summaries of all the committee's deliberations and the majority of the discussion papers, statements and minutes are now accessible via our website (www.seac.gov.uk), this report simply aims to provide an overview of the committee and its work in 2005.

The UK BSE epidemic continues to decline and the number of human vCJD cases, thankfully, also appears to be in decline. However, there are still many uncertainties. It is critical to ensure that, as scientific understanding of transmissible spongiform encephalopathies (TSEs) develops, appropriate measures are in place to minimise future risks to human health and animal welfare. It is the role of SEAC to keep a watching brief on any scientific development relating to TSEs and to provide independent advice to the relevant Government Departments.

The committee considered a number of important issues this year. The small numbers of BSE cases in animals born after 1996 (Born After the Reinforced Ban (BARB) cases) provide a challenge to the eradication of the disease. Close examination of clusters of BARB cases suggest that these animals may have been infected from the persistence of the BSE agent in residual feed in storage bins. There is no evidence to indicate a non-feed related cause for these cases.

Surveillance of TSEs in sheep continues to provide reassurance that BSE is unlikely to be present in the national flock. However, as part of the surveillance for BSE in sheep, a number of cases of atypical scrapie have been identified in the UK and elsewhere. Such cases are distinguished from classical scrapie by an unusual form (less protease resistant) and neuropathological deposition of abnormal prion protein. Although there is an overlap in the range of genotypes affected by classical and atypical scrapie, the latter also occurs in genotypes that are considered to be resistant to classical scrapie. As data emerge, potential implications of atypical scrapie for human health and animal welfare are being closely monitored.

The incidence of vCJD in the UK showed a peak in mid 2000 and has since declined, with a total of 159 cases reported by December 2005. However, considerable uncertainty about the potential course and size of the human epidemic remains. In particular, SEAC is concerned that a number of subclinical carriers of vCJD infection may exist. Such carriers could develop clinical disease at a later stage, or infection could remain at a subclinical level. There is no test available currently to identify infection in the living so they could act as reservoirs for human-to-human vCJD transmission via medical interventions such as blood transfusion or surgery. Every appropriate effort is being made to minimise such risks.

Despite many research advances, uncertainty remains about the precise nature of TSE infectivity, and the precise role of the prion protein in neurodegeneration and clinical disease.

There are a number of key issues where clarity is urgently needed. It is my view that over the next year or so key issues, which SEAC and its Subgroups will need to consider, include:

(i) atypical scrapie and its potential implications for animal health and welfare, the National Scrapie Plan (NSP), and human health

(ii) the prevalence of vCJD in the UK population and the likely size of the current vCJD epidemic taking into account emerging data

(iii) the risk of secondary vCJD infection via medical interventions such as blood transfusion and surgery and the risk of a secondary epidemic of vCJD arising through secondary transmission

(iv) the precise nature of TSE infectivity and its implications for the development of ante-mortem diagnostics.

I would like to thank Professor James Ironside (Deputy Chair), Professor Ian McConnell, Professor Graham Bulfield and Mr Colin Browne who left SEAC during 2005 for their time, energy and commitment, and their rigorous input into the deliberations of the committee and its Subgroups. I am pleased to welcome Professor James Nicoll onto the committee.

The committee continues to be reliant upon access to early research findings. I would particularly like to thank all the researchers who have kindly presented their work to the committee prior to publication.

Finally, I would like to thank the SEAC Secretary and Secretariat for the truly excellent scientific and administrative support they provide, and the current members of SEAC and its Subgroups for their extraordinarily valuable insights and hard work. Without their contributions SEAC would be unable to be effective.

Professor Chris Higgins

Chair of SEAC

About the Committee

SEAC is an independent expert advisory committee that provides scientific advice to the UK Government on TSEs such as BSE, scrapie and vCJD. The committee's deliberations may be initiated by requests for advice from Government Departments, the Devolved Administrations, SEAC members or enquiries from members of the public. The Chairman of SEAC may convene Subgroups to examine specific issues in greater detail. Subgroups have clear terms of reference and are required to report to the main committee.

SEAC meets around 5 times a year with the majority of its business conducted at public meetings. Agendas, summaries, discussion papers and minutes of meetings are published on the SEAC website. Since September 2004, recordings of meetings may be viewed via the website. There are occasions when the committee considers certain information, such as pre-publication material or confidential medical data in reserved business sessions. Summaries of these discussions have been made available on the website from November 2004. Once the information considered in these sessions has been published, full details of the discussion and the relevant papers are placed on the website.

SEAC website (www.seac.gov.uk)

The website carries

- information about the committee's history, terms of reference and current membership
- agendas, discussion papers and minutes of meetings
- committee statements
- register of committee members' interests and the SEAC code of practice
- SEAC's annual reports from 1997 onwards and reports of independent reviews of SEAC that took place in 1997 and 2002
- information about the membership and work of the SEAC Subgroups.

Main issues considered by SEAC and SEAC Subgroups

SEAC met five times in 2005. An overview of the main issues considered and recommendations made is given below:

SEAC 86

- The implications of recent research on projections of the vCJD epidemic. The committee recommended that the newly convened SEAC Epidemiology Subgroup conduct a comprehensive assessment of the nature and future profile of the vCJD epidemic.

- BARB review. Professor William Hill (University of Edinburgh) consulted the committee on the scope of his independent investigation of the causes of BSE cases born after the reinforced feed ban. The committee suggested a number of areas for investigation.

- BSE in goats. The committee considered that there is no evidence of BSE in the current UK goat herd, but a risk of BSE cannot be excluded until further surveillance results are assessed. A watching brief should be kept. A case of possible BSE in a historic TSE case in a Scottish goat along with other suspect cases of BSE in goats that may arise in the future should be investigated further, including strain-typing bioassays possibly in parallel with some non-BSE like TSE goat cases.

SEAC 87

- Use of prion reduction filters for blood. The committee recommended that new prion filtration methodologies for the reduction of transmission risks via blood transfusion should be independently evaluated for their efficiency and reliability.

- The early phase of vCJD infection in blood transfusion recipients and the potential risks of vCJD transmission from transplantation of organs / tissues from donors that received blood transfusions. The committee considered that relevant data are extremely limited but suggest that in the early phase of infection, significant prion replication is unlikely to occur and that, therefore, tissue levels of abnormal prions following recent transfusions are likely to be related to the blood supply to each specific tissue. A risk of transplant associated transmission of vCJD exists from tissue/organ donors that have not received blood transfusions. The additional risk as a result of a donor having received a recent blood transfusion is likely to be very small. The risks of transmission of vCJD from organ donors that received blood transfusions prior to donation could be reduced by screening donors for the presence of abnormal prion protein prior to transplantation, washing tissues to remove residual blood before use, and avoiding the pooling of

tissues from different donors to be transplanted into one or more individuals.

- A report from the SEAC *ad hoc* Epidemiology Subgroup on UK BARB cases. The committee endorsed recommendations from the Subgroup on areas of further study.

- The age at which vertebral column from cattle could become specified risk material (SRM). The committee considered that a change in the classification of vertebral column as SRM from 30 to 12 months would make a very small to negligible difference in risk, even to the small number of people who consume beef on the bone.

- An exposure assessment of the use of category 3 animal by-products[1] in fertiliser. The committee concluded that TSE infectivity on land, as a result of the application of fertiliser containing category 3 animal by-products, would be extremely low. However, because of the heterogeneous nature of infectivity and the uneven spread of fertiliser, TSE infectivity levels might be higher in some geographical locations than predicted. Controls to ensure that category 3 material is processed separately from higher risk material should be audited. A watching brief should be kept on chronic wasting disease in North America and BARB cases of BSE in the UK to assess likely involvement of environmental persistence of TSE agents in the epidemiology of the diseases.

SEAC 88

- Research on abnormal prions in milk from cattle experimentally infected with BSE. The committee concluded that the results of this research, together with previous epidemiological and experimental research provided no evidence for the presence of BSE associated abnormal prion protein in, or for transmission of, BSE via milk. The milk samples should be retained to allow possible future analysis.

- Differential diagnosis of suspect BSE cases. The committee considered that, given the large number of clinical conditions of cattle that might resemble BSE, it was disproportionate to attempt to definitively diagnose all suspect BSE cases that are not confirmed as BSE. However, it was crucial to ensure that possible atypical cases of BSE in cattle, should they occur, are not missed.

- Sequencing studies on the prion protein gene of BARB cases in Great Britain and Northern Ireland. The committee considered that there is no genetic reason to suppose that BARB cases are any different than pre-

[1]Category 3 animal by-products are low risk material most of which is fit for human consumption but not intended for human consumption.

August 1996 cases. Data from Great Britain and Northern Ireland BARB cases should be combined, if possible, for statistical analysis.

- Report from Professor Hill on his independent investigation of the causes of BARB cases[2]. The committee welcomed the report and agreed with the main conclusions.

- Research into atypical cases of scrapie. The committee considered that issues around atypical scrapie should be addressed with high priority because of potential implications for human and animal health and policy implications for the NSP. Studies including infectivity, transmissibility, biochemistry and epidemiology of the atypical scrapie cases are crucial. It was recommended that the SEAC Sheep Subgroup consider the available scientific evidence in more detail and establish what further scientific research is needed.

SEAC 89

- The strategic areas of the European Commission TSE Roadmap with the aim of altering or relaxing TSE control and surveillance measures. The committee concluded that:

    - since removal of SRM is a primary TSE related public health protection measure, amendments to SRM controls should only be reviewed in light of emerging scientific findings on the distribution of TSE infectivity

    - all the constituents of animal feed, including the sources of those materials, should be examined carefully in assessing the potential TSE risks related to possible transmission of TSEs

    - effective surveillance to ascertain BSE infection prevalence is a very important public health protection measure and an effective system of TSE surveillance should be maintained

    - changes to legislation in any one strategic area might impact on other areas, therefore no single strategic area should be considered in isolation

    - there should be a watching brief on emerging science that may impact on any of the measures under consideration and since changes to controls may impact on the effectiveness of other controls, control measures should not be considered in isolation

2 http://defraweb/animalh/bse/pdf/hillreport.pdf

  - in the event of any changes to TSE legislation it would be important to communicate effectively to consumers the reasons for change.

- A hypothesis on possible human origins of BSE. The committee considered the hypothesis plausible but not the most likely origin of BSE.

- Research on natural transmission of BSE in an experimental sheep flock. The committee noted that transmission had occurred naturally within the experimental flock but it was not possible to determine from the information available the precise route of transmission. The committee recommended that appropriate calculations be done to ascertain whether or not the study could inform on the potential mode of transmission and whether or not the transmission rate might be able to self-sustain an epidemic within a flock. BSE had not been found in ongoing surveillance for scrapie, therefore there is no evidence that BSE currently exists in the national sheep flock.

- Research on the distribution of abnormal prion and TSE infectivity in the peripheral nervous system of cattle with BSE. The committee concluded that preliminary data did not warrant re-examination of SRM regulations. Studies on the distribution of abnormal prion protein and infectivity would be important to conduct on tissues from animals at the preclinical stage of BSE infection. Such studies would inform assessments on the level of risk posed by these tissues and the effect of SRM controls.

SEAC 90

- Epidemiological information on the vCJD epidemic and biochemical characterisation of abnormal prion protein from vCJD cases.

- The SEAC Epidemiology Subgroup statement on the vCJD epidemic. The committee welcomed and endorsed the statement and concluded there is an urgent need for studies to ascertain the prevalence of vCJD infection in the UK population.

- Epidemiological information on clusters of BARB cases. Clusters may have been infected by the persistence of the BSE agent in residual feed in storage bins. This feed may have been manufactured before the 1996 UK feed ban or imported before the 2001 EU feed ban. There is no evidence to indicate a non-feed related cause for these cases.

- Risk assessment of vCJD infectivity in blood. The committee noted that the data are very limited and strongly recommended that robust research is undertaken to examine infectivity levels through the incubation period and the distribution of infectivity in blood components.

- Studies in transgenic mouse models to examine human-to-human transmission of vCJD and the correlation between abnormal prion protein

concentrations and TSE infectivity. The committee concluded that development of such transgenic models helps to inform on transmission risks for humans and the influence of genotype on vCJD infection. New research suggests there is no clear correlation between abnormal prion protein concentrations and the titre of TSE infectivity in some animal models. Abnormal prion protein may not always be a good surrogate marker for infectivity and the implications of this for rapid diagnostic TSE tests should be considered.

New publications

SEAC commented on the following new scientific research papers:

- Bellworthy *et al*. (2005) Natural transmission of BSE between sheep within an experimental flock. *Vet. Rec.* 157, 206. (SEAC 89)

- Buschmann & Groschup (2005) Highly bovine spongiform encephalopathy-sensitive transgenic mice confirm the essential restriction of infectivity to the nervous system in clinically diseased cattle. *J. Infect. Diseases* 192, 934-942. (SEAC 89)

- Castilla *et al*. (2005) Detection of prions in blood. *Nat. Med.* 11, 982-985. (SEAC 89)

- Heikenwalder *et al.* (2005) Chronic lymphocytic inflammation specifies the organ tropism of prions. *Science*. 307, 1107-10. (SEAC 86)

- Iwamaru *et al*. (2005) PrP^{Sc} distribution of a natural case of bovine spongiform encephalopathy. In *Prions. Food and Drug Safety*. Springer-Verlag, Tokyo, 2005. (SEAC 89)

- Ligios *et al.* (2005) PrP^{Sc} in mammary glands of sheep affected by scrapie and mastitis. *Nat. Med.* 11, 1137-1138. (SEAC 90)

- Safar *et al.* (2005) Diagnosis of human prion disease. *Proc. Natl. Acad. Sci. U S A.* 102, 3501-3506. (SEAC 88)

- Slate (2005) Molecular evolution of the sheep prion protein gene. *Proc. R. Soc. B.* 272, 2337-2344. (SEAC 90)

SEAC statements

SEAC published the following statements in 2005:

- Maternal transmission of vCJD;

- Early phase of vCJD infection in blood transfusion recipients;

- Vertebral column: age at which specified risk material;
- Hypothesis that BSE originated from a human TSE;
- SEAC response to the SEAC Epidemiology Subgroup statement on the vCJD epidemic.

SEAC ad hoc Epidemiology Subgroup on UK BARB cases

The SEAC *ad hoc* Epidemiology Subgroup on UK BARB cases met on 13th April 2005 to consider analysis of the results of a case control study set up to investigate the possible causes of BSE in BARB cases. The Subgroup made a number of recommendations for further epidemiological research on BARB cases. The recommendations were endorsed by the main committee at SEAC 87. The work of this Subgroup is now complete.

SEAC Epidemiology Subgroup

The SEAC Epidemiology Subgroup met on 11th May and on 30th September 2005 to consider the nature and future profile of the vCJD epidemic, taking into account new research and the possibility of human-to-human transmission and the likelihood of a self-sustaining epidemic. The Subgroup issued a statement on the vCJD epidemic, which was endorsed by the main committee at SEAC 90. The Subgroup made a number of recommendations:

- The planned testing of samples under collection for the National Anonymous Tonsil Archive should be progressed with all possible urgency
- Serious consideration should be given to abnormal prion testing of samples from a range of tissues collected from autopsies
- Enhanced clinical surveillance for vCJD in the elderly should be considered
- Clinical monitoring and, with patient consent, post mortem vCJD tests should be considered on individuals from groups at risk of vCJD
- Work underway to develop population level models for the surgical and blood routes of vCJD transmission with a view to developing a combined model to explore the effect of interactions between these routes should continue to be supported.

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