

**SEAC: Annual
report
1999/2000**

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FOREWORD



Welcome to the third Annual Report of the Spongiform Encephalopathy Advisory Committee (SEAC). This report covers the period from 1 April 1999 to 31 March 2000.

In the last year, the BSE epidemic in cattle has continued to decline in line with expectations, but the numbers of cases of vCJD in the human population have shown a rising trend, although it is still too soon to predict how the epidemic will evolve. Increasing amounts of the Committee's time have been occupied with the consequences of infections in humans and on the identification and surveillance of TSEs in other species, particularly sheep. Public interest in the Committee is understandably high and we have continued to hold Press Briefings after every meeting of the Committee. SEAC will continue to explore ways of opening up their work to a wider audience.

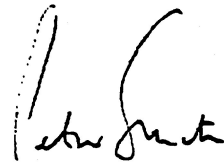
I have been the acting Chair of the Committee for most of the past year. I am grateful to fellow members of the Committee and to the Secretaries and the support staff in all three departments of the SEAC Secretariat for their insight and support in tackling some of the complex issues we have had to address. The Committee continues to be reliant upon access to early research findings and technical briefings on particular issues and I would like to thank those who throughout the year have helped the Committee in this way.

I would also like to pay tribute to the extensive contributions of the previous Chair, Sir John Pattison, who steered the Committee during a very demanding period, and also greatly thank those other Members who, for various reasons, left the Committee during the year.

I hope you find this report of interest. If you have any comments or suggestions, I would be grateful if you could send these to the [SEAC Secretariat](#), whose details can be found at the end of this report.

This report covers the year up to 31 March 2000 but is being published shortly after the BSE Inquiry was reported. There is much discussion in the Inquiry Report as to the way in which SEAC has functioned and

recommendations are made on the ways in which the committee might best advise government. Some of the changes suggested have already been incorporated into our working practices and in the coming months we will be giving careful consideration to all the relevant recommendations in the Inquiry Report.

A handwritten signature in black ink, appearing to read 'Peter Smith', written in a cursive style.

Professor Peter Smith
Deputy Chairman

PART I: ABOUT SEAC

TERMS OF REFERENCE

1. The Spongiform Encephalopathy Advisory Committee (SEAC) was established over ten years ago in 1990. The Committee's terms of reference were redefined in the SEAC review which was published in 1997¹ and are as follows:

“To provide scientifically-based advice to the Ministry of Agriculture, Fisheries and Food, the Department of Health and territorial Departments on matters relating to spongiform encephalopathies, taking account of the remits of other bodies with related responsibilities.”²

This revision was both to explain the purpose of the Committee and clarify the Committee's overlap with other bodies with related interests.

COMMITTEE BUSINESS

2. It is usual for the Committee to meet between four and six times a year to discuss TSE - related issues and to provide any necessary scientific advice to Ministers. It is standard practice for Ministers to consider SEAC's advice in deciding what action to take, and publish this advice when announcing their conclusions.

3. The Committee's work can come from a number of sources such as:

- specific requests for advice from Ministers
- results of research
- requests from a Member of the Committee
- specific requests for advice to individual SEAC members or to the Secretariat.
- the forward business plan as shown in this report.

4. SEAC continues to make efforts to increase the openness and transparency of its deliberations. This is the Committee's third Annual Report, and in

¹ How the review was implemented was covered in the first SEAC Annual Report 1997/98. Further information on this, and on the historical aspects of the Committee's work and recommendations can be found on the websites of its sponsoring Departments:
MAFF <http://www.maff.gov.uk/maffhome.htm>
DoH <http://www.open.gov.uk/doh/dhhome.htm>

² Since the publication of this report the Committee's terms of reference have been amended again to incorporate the establishment of the Food Standards Agency and devolution.

accordance with the recommendations of the SEAC Review 1997, the Committee has been publishing a [public summary](#) after each of its meetings since October 1997. Additionally, since November 1998, SEAC has held a press briefing after each meeting to present and discuss the summary with the aim of improving public understanding of the recommendations and conclusions of the Committee and how it reaches conclusions. The summary and the briefing also serve to highlight the facts and uncertainties surrounding aspects of the science of TSEs. Since March 1999 SEAC have attached to their public summaries a list of published papers distributed to Committee Members by the SEAC Secretariat³ since the previous meeting. The public summaries appear on the MAFF and Department of Health websites.

MEMBERSHIP

Membership of SEAC during the period covered by this report is given in [ANNEX I](#). A [current list](#) of Members can be found on the MAFF website.

5. The SEAC Review, published in July 1997, identified fields of expertise which should be represented on the Committee. These were epidemiology, microbiology, neurology, neuropathology, veterinary pathology, virology, genetics, veterinary medicine, public health practice, food toxicology/gastro-intestinal immunology and a representative of the public interest. It was emphasised that the composition of the Committee should be kept under constant review as more about TSEs becomes known.

6. Three Members left SEAC between April 1999 and March 2000. These included the then SEAC Chairman, Professor Sir John Pattison, who took up an appointment as Director of Research and Surveillance at the Department of Health. Another outgoing Member finished his second term of appointment to the Committee and the remaining member resigned because of other commitments. An open competition to replace the Chairman is still in progress at the time of writing this report. In the meantime the Deputy Chairman, Professor Peter Smith, is acting Chairman of SEAC. Three further Members have been appointed through open competitions and a fourth Member has been appointed after a recommendation from the CJD Surveillance Unit (CJDSU)⁴.

³ The SEAC Secretariat comprises three Secretaries. One each from MAFF, DoH and FSA. See paragraph 11 of this report for further details.

⁴ Because of the need to retain expertise from the CJDSU, in June 1999 the Unit was invited to act as a “nominating body” following an open advertisement of vacancies on the Committee.

7. New Members are appointed to the Committee in accordance with the code of practice for public appointments issued by the Commissioner for Public Appointments. Members of SEAC are usually appointed for a period of three years, although a second term (and in exceptional cases a third term) is acceptable. The Commissioner's code considers that a maximum period for 2 terms of office can be between 6 and 10 years.

CODE OF PRACTICE FOR MEMBERS

8. The Committee agreed a revised Code of Practice in July 1999. This amended version contained further guidance on the disclosure of Committee business after SEAC meetings and information on an indemnity offered by Ministers to Members of SEAC and related Committees in connection with the performance of Committee duties. A copy of the indemnity offered to SEAC Members can be found at [ANNEX III](#). The SEAC Code of Practice is written with regard to the seven principles of public life identified by the Nolan Committee in their report on Standards in Public Life and, in addition to the above, gives specific guidance on publication of work by SEAC Members, conflicts of interest and confidentiality. Copies may be obtained from the SEAC Secretariat.

REGISTER OF MEMBERS' INTERESTS

9. In accordance with the principles of public life identified by the Nolan Committee, details of commercial and non-commercial interests of SEAC Members which may conflict with their responsibilities as Members of the Committee, are put into the public domain. The register is at [ANNEX II](#).

CONFLICTS OF INTEREST

10. In addition to the register of Members' interests, Members are asked, at the beginning of each meeting, to declare any conflicts of interest with respect to individual items.

SECRETARIAT

11. Three Secretaries, one each from MAFF, DoH and JFSSG⁵, with support staff, co-ordinate the work of the Committee and arrange the financing of its activities. (Details of SEAC expenditure can be found in [ANNEX IV](#)). Addresses

⁵ The Joint Food Standards and Safety Group (JFSSG) was reconstituted on 1 April 2000 to form the Food Standards Agency.

for the [Secretariat](#) (including website addresses, for further information on the work of each respective Department) can be found at the end of this report.

SUB-GROUPS

12. With the approval of Ministers, the Chairman of SEAC can authorise the setting up of *ad hoc* sub-groups to discharge specific tasks. Sub-groups are chaired by SEAC Members, have clear terms of reference and are required to report to the main Committee. There is considerable flexibility about how sub-groups are set up, depending on the issue in question.

13. Expanded use of sub-groups, as recommended in the 1997 SEAC Review, has allowed the Committee to delegate the initial consideration of some of the highly specialised issues which require a substantial input from experts not on the main Committee.

14. During the year work has been carried out by sub-groups on vCJD, epidemiology and sheep surveillance.

Epidemiology sub group

15. A SEAC epidemiology sub-group was set up in September 1997, chaired by Professor Peter Smith. Details of membership are set out in [ANNEX VII](#). The sub-group reports jointly to the four UK Chief Medical Officers and SEAC. Its terms of reference are:

“To assess the information about the epidemiology of vCJD and develop as far as possible advice on trends in the disease”.

16. The sub-group met twice during the year of this report, in May 1999 and February 2000. SEAC subsequently agreed a report on the work of the Sub-Group covering the period up to February 2000, which was passed to the four UK Chief Medical Officers. This is attached at [ANNEX VIII](#). A key conclusion from that report is that it remains too soon to be able to make soundly based predictions about the future evolution of the vCJD epidemic.

Sheep Surveillance sub group

17. In April 1999, SEAC published a report from its subgroup on research and surveillance for TSEs in sheep. At the SEAC meeting in September 1999, Members considered progress on implementing the report's recommendations. As part of that process they agreed that an additional sub group should consider the

objectives and options for further surveys of TSEs in sheep. The sub group, chaired by Professor Peter Smith, held its first meeting in March 2000.

Its terms of reference are:

“To review current scrapie surveillance within the UK flock and advise on further surveillance mechanisms to improve understanding of the distribution and incidence of TSEs in sheep.”

Membership is given in [ANNEX VI](#).

WORKING GROUPS

ACDP/SEAC Working group

18. In addition to sub-groups, SEAC maintains a joint working group with the Advisory Committee on Dangerous Pathogens (ACDP), which is chaired by the ACDP Chairman. The terms of reference for this group are:

“To consider the risks from exposure to the agents of transmissible spongiform encephalopathies that may arise as a result of work activities, to develop guidance to minimise such risks and to provide advice as requested by the parent committees (ACDP and SEAC).”

19. During the period of this report the ACDP/SEAC working group met in July and November 1999 and February 2000. Full membership of the working group is given in [ANNEX V](#).

PART II: THE WORK OF THE COMMITTEE DURING THE YEAR

SEAC'S DISCUSSIONS DURING THE YEAR

20. Throughout the year SEAC examined current research within the field of transmissible spongiform encephalopathies. New results from work are presented regularly in the form of published papers and confidential pre-publication drafts. In addition, key results from current research are presented *ad hoc* during Committee meetings.

21. The Committee met four times between 1 April 1999 and 31 March 2000. During this period SEAC continued to monitor epidemiological data on vCJD and BSE. The number of BSE cases continues to decline although the rate of decline slowed in the period to 31 March 2000 as the tail of the epidemic is reached.⁶ The overall total of confirmed vCJD cases increased to 52. The complete texts of SEAC public summaries and advice given to Ministers can be found in [ANNEX IX](#).

⁶ Since the publication of this report the rate of decline has again increased.

Issues addressed by SEAC: April 1999- March 2000

A. CJD and Public Health

- CJD SURVEILLANCE
- CJD EPIDEMIOLOGY
- DIAGNOSTIC CRITERIA FOR vCJD
- VACCINES
- OCCUPATIONAL HEALTH
- HUMAN BLOOD AND BLOOD PRODUCTS
- CONTACT LENSES/ OPHTHALMIC INSTRUMENTS
- STERILISATION & DISPOSAL OF SURGICAL INSTRUMENTS
- RISK ASSESSMENT
- CJD RESEARCH PRIORITIES/ DIAGNOSTICS

B. Food Safety and the Protection of Animal Health

- BSE EPIDEMIOLOGY
- BSE SURVEILLANCE
- BSE-DIAGNOSTIC TESTS
- BEEF BONES - DORSAL ROOT GANGLIA (DRG) AND BONE MARROW
- REVIEW OF THE OVER THIRTY MONTH RULE
- BSE PATHOGENESIS - FOOD SAFETY
- SPECIFIED RISK MATERIAL (SRM)
- SHEEP RESEARCH & SURVEILLANCE
- PATHOGENESIS IN SHEEP
- STAIN TYPING IN SHEEP
- ANIMAL FEED
- ANIMAL FEED - PIG MBM
- MATERNAL TRANSMISSION

C. Environmental Issues

- DISPOSAL OF MEAT AND BONE MEAL
- RENDERING CONDENSATE

A. CJD and Public Health

CJD SURVEILLANCE

21. In February 2000, the Committee recommended that work to ascertain the sub-clinical prevalence of vCJD in the human population should be taken forward with all possible speed. This might, for example, include large scale surveys testing tonsil and appendix tissue for evidence of prion protein.

CJD EPIDEMIOLOGY

22. The Committee conducts a review of vCJD epidemiology at every meeting and regularly assesses current case data. In June, Members agreed that although at the time of the meeting there had been only one confirmed case in 1999, it was too early to draw any conclusions as to whether or not the increase seen in the last quarter of 1998 would be sustained.

23. In September 1999, the CJD Surveillance Unit reported results of analysis of the geographical distribution of vCJD cases. The results confirmed earlier analyses that there was no evidence of any geographical clustering of cases.

24. In February 2000, the Committee noted that although the final number of deaths from vCJD during 1999 was expected to show a fall from the number who had died in 1998, it remained too soon to make predictions with any confidence about the likely number of deaths in the coming years.

DIAGNOSTIC CRITERIA FOR vCJD

25. In June 1999, Members considered a report to develop clinical criteria for the diagnosis of probable cases of vCJD. Once these had been agreed they would form the basis of published statistics on the number of probable cases. Some suggestions for additions to the criteria were made, including the possible use of tonsil biopsy.

26. At the Committee's meeting in February 2000, Members endorsed the view of its Epidemiology Sub-Group that robust scientific criteria now existed that would enable live 'probable' cases to be separately identified from 'confirmed' cases of vCJD for the first time. The number of cases meeting these criteria could then be included within the data on vCJD published by the Department of Health.

VACCINES

27. In June 1999, the CJD Surveillance Unit performed an analysis of cases by year of birth to investigate a possible link of vCJD to childhood vaccines. The Committee noted the conclusion that it is unlikely that the cases of vCJD to date would have been exposed to BSE infectivity through the vaccines needed to immunise them as young children, since the vaccines would have been produced well before the BSE epidemic.

OCCUPATIONAL HEALTH

28. At its November meeting, the Committee received an update from the Advisory Committee on Dangerous Pathogens (ACDP) / SEAC Joint Working Group (JWG) relating to safe practices for working with TSE agents. SEAC endorsed the JWG's recommendation that recipients of corneal transplants should be added to the list within the ACDP/SEAC guidelines of those patients for whom special precautionary measures would be necessary in a health care setting.

HUMAN BLOOD AND BLOOD PRODUCTS

29. In September, the Committee reviewed the action being taken in the UK to reduce the theoretical risk of transmitting vCJD through blood and blood products. The Committee were pleased to note that following their earlier advice and that of the Committee on Safety of Medicines, all licensed blood products were now manufactured using non-UK plasma, and all blood collected in the UK would be leucodepleted from 1 November 1999. Having considered the available evidence, the Committee concluded that no further steps were currently necessary to ensure the safety of UK blood.

30. In February 1999, the Committee considered a publication suggesting that infectivity was detectable after disease onset in the plasma of mice experimentally challenged with a mouse-adapted human TSE. It also considered preliminary evidence which appeared to demonstrate that blood plasma, taken from mice with clinical disease caused by a mouse-adapted BSE agent and inoculated into the brains of disease-free mice, gave rise to clinical disease in some of the recipient mice. The Committee concluded that priority should be given to carrying out a study on mice infected with a mouse-adapted BSE agent at various stages before development of disease. However, the Committee did not recommend any measures in addition to those already in place to reduce any potential risk to public health from human blood and blood products.

CONTACT LENSES/ OPHTHALMIC INSTRUMENTS

31. In June 1999, the Committee considered the possible risk of transmission of vCJD through the re-use of trial contact lenses on subsequent patients. Members agreed that although relevant scientific data was limited and any potential risk was likely to be very low, the Department of Health should encourage opticians to adopt, as a matter of best practice, the single use of trial lenses followed by safe disposal.

32. In September SEAC considered whether the advice it had given in June regarding contact lenses should also apply to trial or diagnostic contact lens fitting sets and ophthalmic devices that come into contact with the eye. Members confirmed earlier advice and in addition recommended that trial or diagnostic lens fitting sets should also be confined to single patient use. In addition, as a precautionary step, the Committee further recommended that the components of ophthalmic devices that touch the cornea should be for single patient use, whenever practicable. The Committee also recommended that research is undertaken to investigate the binding of the PrP to glass and plastic surfaces and the possibility of reducing the risk of infectivity by using disposable films with components that touch the cornea.

STERILISATION & DISPOSAL OF SURGICAL INSTRUMENTS

33. In June 1999, Members received an update on work to follow up the recommendations made at previous meetings aimed at reducing the potential risk of vCJD transmission associated with surgery. The Committee noted that various aspects of the issue were under consideration and requested a full report for subsequent discussion on what had been achieved, with the identification of any constraints on progress.

34. In September, the Committee considered the report on action being taken by the DH to reduce the risks of iatrogenic transmission of vCJD through surgical procedures. The Committee confirmed its earlier view that rigorous implementation of washing, decontamination and general hygiene procedures were key measures in minimising the risk of infection. They noted that DH had recently released a comprehensive package of guidance for the cleaning and decontamination of instruments and that an audit was planned to verify compliance with this guidance.

35. Following the presentation of an updated risk assessment in September assessing the possible risk of transmission of vCJD from contaminated instruments, the Committee concluded that although the theoretical risk of

transmission could depend on a number of factors, it was likely to be greatest from operations involving central nervous system and ophthalmic tissue, followed by lymphoid tissue. The Committee considered that, wherever practicable, the use of disposable instruments for such surgery was to be encouraged. Tonsillectomies were identified as a discrete operation where specific practical steps might readily be taken and the Committee noted that DH was examining the feasibility of the use of disposable tonsillectomy instruments.

RISK ASSESSMENT

36. At the September meeting, the Committee were provided with updated information from mathematical risk assessment models for assessing the possible risk of transmission of vCJD from contaminated instruments. They noted that the huge uncertainty about the possible number of people who might be incubating vCJD remained a key factor in determining conclusions. The Committee recommended that a group of experts be convened to review the model and report back to the Committee.

CJD RESEARCH PRIORITIES/ DIAGNOSTICS

37. In September, the Committee considered research examining vCJD. They accepted that most of the major areas were being addressed and that it would take some time before many of the projects produced results. However, the Committee reiterated that the search for a diagnostic test using blood should be a key priority and recommended that the DH explore with urgency all possible means of securing such a test.

B. Food Safety and the Protection of Animal Health

BSE EPIDEMIOLOGY

38. Members regularly assess the status of the BSE epidemic. In June 1999, SEAC agreed that the number of cases of BSE was continuing to decline, albeit at a lesser rate than in previous years. The likely explanation was that the decline in 1996 and 1997 was more pronounced as a result of the culling of certain birth cohorts.

39. In November 1999, scientists from the Wellcome Trust Centre for Epidemiology of Infectious Diseases (WTCEID) at Oxford University presented their latest estimates of the numbers of cases in the BSE epidemic from 1996 to 2001, the likely numbers of infected animals entering the food chain, and the

impact of the various culls. The Committee noted that the predictions had been revised upwards from the predictions made in 1996 but had much narrower confidence bands than previous estimates for the same period. However, they still fell within the confidence bands of the earlier analysis. The predictions were higher because the estimated risk from infected feed in the period 1991-1996 did not decline as rapidly as projected in the earlier analysis. This was probably because cattle were exposed to feed which was accidentally cross-contaminated with BSE infected meat and bone meal destined for pigs and poultry.

BSE SURVEILLANCE

40. In February 2000, the Committee noted a proposal by MAFF to survey the brains of 10,000 cattle over 5 years in the Over Thirty Month Scheme in the forthcoming year. Members felt that this work was important as it provided an independent check on models of the progress of the BSE epidemic.

BSE- DIAGNOSTIC TESTS

41. In February 2000, SEAC considered future surveillance work to assess BSE prevalence. Members agreed that the performance of diagnostic tests was critical to the outcome of the surveillance. To that end the Committee welcomed the intention of the Commission to support a study to evaluate if the recently validated diagnostic tests for clinical BSE cases could be used for the detection of PrP in healthy cattle during the incubation period. The study was expected to indicate how long before the onset of clinical signs the test would be reliable to detect PrP which, by inference, would indicate that a positive animal be infected.

BEEF BONES - DORSAL ROOT GANGLIA (DRG) AND BONE MARROW

42. In November 1999, after considering the revised predictions for future BSE cases from the group from Oxford University, Members re-examined previous advice on the risk from DRG and bone marrow. A year earlier in November 1998, SEAC had concluded that although the risks to public health from DRG or bone marrow were difficult to quantify, the risk, if any, from bone marrow tissue and DRG were likely to be very small. SEAC agreed that estimates of the number of animals under 30 months of age slaughtered for human consumption that were infected with BSE and within 12 months of developing clinical disease was key to the Committee's previous advice. The revised estimates were comparable to the figures considered previously and consequently SEAC did not consider it necessary to review their advice from November 1998.

REVIEW OF THE OVER THIRTY MONTH RULE

43. In November 1999, SEAC conducted a full review of the Over Thirty Month (OTM) rule, taking account of the latest predictions of the BSE epidemic from the group from Oxford University. The Committee agreed that although the epidemic was in rapid decline and the estimated risk to humans from animals currently entering the human food chain remained very low, one of the key findings from the latest analysis was that the over thirty month rule had a major impact on reducing the risk to public health by significantly limiting the number of infected animals which might otherwise enter the food chain. On that basis, Members concluded that modifying the rule to increase the age of animals permitted to be slaughtered for human consumption would be premature as this might re-introduce an unacceptable level of risk at the present time. Furthermore, the Committee recommended that the existing controls should continue to be rigorously enforced to ensure that these risk reduction measures remain effective even though the overall risk is declining with the epidemic. SEAC also requested further information to enable them to consider the balance of risk from cattle in the UK compared with the risk from imported beef and beef products.

BSE PATHOGENESIS - FOOD SAFETY

44. In February 1999, the Committee considered preliminary research suggesting that infectivity was detectable in the blood plasma of mice experimentally challenged with a mouse adapted BSE strain. The Committee noted that the pathogenesis of the disease caused by BSE in mice was different to the pathogenesis of BSE in cattle but more similar to that of TSEs in sheep and humans. Given the difference in the pathogenesis of the disease in cattle and this mouse model, and taking account of the results of bioassays of cattle tissues in both mice and cattle, the Committee concluded that there were no implications for the safety of the food chain from these findings.

SPECIFIED RISK MATERIAL (SRM)

45. The Committee considered EU proposals on SRMs. Under the proposals, Member States would be classified according to BSE incidence in cattle. Members noted that to set out SRM controls for sheep and goats on this basis would not be consistent with the likely routes of exposure of sheep to BSE infection. This is because the risk of exposure would vary according to feeding practices, assuming that sheep had in fact been infected from feed. It would also depend on if, and how infection and disease associated with the BSE agent could be propagated in sheep. Members also advised that if the intestines of sheep and goats were to be included in the new EU proposals, the whole intestine from sheep of all ages should be

classified as specified risk material.

SHEEP RESEARCH & SURVEILLANCE

46. In June 1999, SEAC considered preliminary results of an anonymous postal survey of sheep farmers to assess the prevalence of scrapie. Members agreed that the level of response to the questionnaire had been encouraging and noted that a paper is being prepared for publication in a peer reviewed journal (Subsequently published- Vet. Rec. 1999 **145** 405-406). The Committee emphasised the priority of analysing sheep brains for evidence of prion disease as rapidly as possible.

47. In September, Members considered an interim progress report on research work highlighted in the SEAC sub-group's report on research and surveillance for TSEs in sheep published in April 1999. Members noted the complexities associated with some of the recommended research, but continued to accord very high priority to research on the possible presence of BSE in sheep. The Committee requested a position paper to enable them to identify problems and track progress. They also agreed that a subgroup should consider the objectives and options for further surveys of TSEs in sheep.

PATHOGENESIS IN SHEEP

48. In February 2000, Members considered the latest work on studies of experimental BSE pathogenesis in sheep. They agreed that preliminary and interim results to date support the conclusions reached by SEAC in July 1996 and July 1998 that BSE in sheep is likely to behave in a very similar manner to the natural disease of sheep scrapie. The latest work on the pathogenesis of scrapie confirms earlier findings that the disease appears to infect peripheral tissues including the lymph nodes, spleen and parts of the intestine as well as the central nervous system. It also indicates that the spread of the infection is likely to be from the gut via peripheral nerves or via innervations of the lymphatics to the central nervous system. A representative from the Institute of Animal Science and Health, Lelystad, Netherlands presented some of their recent work on the pathogenesis of scrapie. Progress reports on the work at the Institute of Animal Health and Veterinary Laboratories Agency on the pathogenesis of BSE in sheep were also presented to the Committee.

STRAIN TYPING IN SHEEP

49. In February, the Committee was updated on strain typing work to assess if the BSE agent profile exists. Agent strain typing is underway on isolates from over 130 brains of sheep with natural scrapie. Although incomplete (each study takes up

to two years) over 30 isolates are advanced enough to suggest that they do not have the characteristics associated with the BSE agent. Members also noted strain typing of isolates from a pool of brains from scrapie affected sheep which had been collected for a rendering experiment between 1990 and 1992. The Committee agreed that further work needed to be done on screening sheep for evidence of infection with the BSE agent but concluded that at present there was no need for further public health controls.

ANIMAL FEED

50. In June, the Committee considered a number of papers dealing with possible relaxations in the existing controls on farm-animal feeds. Members agreed that, at present, there was no scientific justification for changing the current controls. They were also concerned about the potential enforcement implications which could arise if any changes were made. It therefore recommended that:

- the ban on feeding mammalian meat and bone meal to livestock should not be lifted, in whole or in part;
- UK-derived bones should not be used to produce calcium phosphate for farm animal feed; and
- a recent change to the EU ban on mammalian protein in ruminant feed, which would allow hydrolysed protein to be fed to ruminants should not be adopted, since complete hydrolysis could not be constantly ensured and portions of the prion molecule might still be infectious.

ANIMAL FEED - PIG MBM

51. In November 1999, the Committee were asked to consider further the issues surrounding the possible use of meat and bone meal derived from pigs for inclusion in poultry feeds in the light of a recent Scientific Steering Committee opinion. The Committee considered that a relaxation of the feed ban in the UK to allow the inclusion of pig MBM in poultry feed could not be supported on scientific grounds. The principal concern remained that the recycling of animal-derived proteins within or between species, via feed, represented a potential risk of the development of TSE infection in livestock.

MATERNAL TRANSMISSION

52. In November 1999, the Committee considered a proposal for a study of offspring of BSE cases to measure the rate of maternal transmission of BSE in cattle. Members agreed that the offspring were valuable animals for study but given the revised predictions of the decline of the BSE epidemic and the long term

nature of the experiment, the Committee did not think that the study would yield results within a useful time frame and did not consider it high priority. Members agreed that although maternal transmission would not sustain the BSE epidemic in cattle it was important that further studies exploring this route of transmission were undertaken.

C. Environmental Issues

DISPOSAL OF MEAT AND BONE MEAL

53. In June 1999, SEAC considered disposal options for OTMS meat and bone meal following delays in arranging facilities for the incineration of stored stocks. Members concluded that there was no recent scientific evidence which called into question their earlier view, in 1996, that landfill is an acceptable outlet for MBM of any origin, although their preferred option was that the material was incinerated. The Committee agreed that a further risk assessment on disposal of OTMS MBM in landfill sites should be undertaken.

RENDERING CONDENSATE

54. In June 1999, the Committee clarified its earlier advice from November 1998 by confirming that rendering condensate should no longer be spread on any land, and not just those fields where cattle might graze.

PART III - FUTURE WORK

55. There is a continuing need for independent advice to Government on TSEs. As the BSE epidemic in cattle continues to decline, work is beginning to focus more on the identification and surveillance of vCJD and TSEs in other species, particularly sheep.

56. During 2000/2001 the Committee will continue to review the epidemiology of TSEs and possible routes of transmission of vCJD. They will also review key research findings as they emerge and deal with any specific issues that are raised. These issues are expected to include a study in mice infected with a mouse adapted BSE agent, work to ascertain the sub-clinical prevalence of vCJD in the human population and further work on agent strain typing of sheep brains to determine if the BSE agent profile is present.

Membership of SEAC at 31st March 2000

Acting Chairman: Professor Peter Smith

Head of Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine.

Members:

Professor Adriano Aguzzi

Professor of Neuropathology and Director, Institute of Neuropathology, University of Zurich. Associate Dean of Research, University of Zurich Medical School. Professor Aguzzi specialises in neurodegenerative disease research, including prion diseases.

Professor Roy Anderson FRS

Wellcome Trust Centre for the Epidemiology of Infectious Disease, University of Oxford.

Professor Christopher Bostock

Director of the Institute for Animal Health. Dr Bostock has led the TSE research work at IAH for many years and was an advisor to SEAC in the past.

Mr Ray Bradley CBE

Veterinary Pathologist and BSE co-ordinator for MAFF until his retirement in 1995.

Professor John Collinge

Professor of Molecular Neurogenetics at Imperial College School of Medicine; Honorary Consultant Neurologist at St Mary's Hospital and the National Hospital for Neurology and Neurosurgery, London

Professor Harriet Kimbell MBE

Principal Lecturer at the Guildford College of Law, Deputy Chairman of the

Consumers' Association, member of the Polkinghorne Committee on the ethics of genetic modification and food use and the Banner Committee on the ethics of novel breeding techniques and farm animals. Professor Kimbell is SEAC's public interest representative.

Dr James Ironside

Neuropathologist at the CJD Surveillance Unit, Edinburgh

Dr Michael Painter

Consultant in Communicable Disease Control, City of Manchester

Dr David B Pepper

Private Veterinary Surgeon (retired), with extensive experience in cattle veterinary practice and slaughterhouse work.

Professor I McConnell

Professor of Veterinary Science at the University of Cambridge and Director of Research at the University of Cambridge Veterinary School. Professor McConnell has research expertise in immunology and slow virus diseases of animals.

Professor Colin Masters

Head of the Department of Pathology at the University of Melbourne, Australia

Dr Jiri Safar

Adjunct Associate Professor in the Department of Neurology at the University of California

DEPARTURES FROM SEAC DURING THE YEAR

Three members have left the Spongiform Encephalopathy Advisory Committee in 1999-2000.

Professor Sir John Pattison - Professor of Medical Microbiology and Vice-Provost of University College, London. Sir John chaired his last meeting on 3 June 1999 before taking up his new appointment as Director of Research and

Development at the Department of Health in early September.

One member retired at the end of 1999:-

Professor William Hueston - Veterinary epidemiologist and Professor of Veterinary Medicine

Professor Hueston retired at the end of an extended term of membership. He had served on the Committee since January 1994.

In addition one member resigned during the year:-

Dr Peter Goodfellow geneticist. Dr Goodfellow joined the Committee in February 1998 for a three year term. He resigned his appointment following his appointment to the Human Genetics Commission.

ANNEX II

REGISTER OF MEMBERS' INTERESTS AT 31 MARCH 2000

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Professor P G Smith	None	None	Department of Health	Grant Holder
Prof A Aguzzi	Boehringer Ingelheim	Occasional consultancy	Swiss National Foundation No: 31-36059.92 3100-040827.94	Principal investigator
	Abbott Laboratories (Chicago)	Support of some laboratory costs e.g. care of mice, instrumentation	Cancer League of the Kanton Zürich	Principal investigator
	Immuno A G (Vienna)	Support of some laboratory costs e.g. care of mice, instrumentation	European Union No. BMHI-CT93-1142	Co- investigator
			National Institutes of Health U.S.A. No 1-ROI-NS33377-01	Co-investigator
			Swiss National Research Program NFP38 & NFP38+	Principal investigator
Professor R M Anderson	Decode	Scientific Advisory Board	The Wellcome Trust	Governor
	Abbott Pharmaceuticals	Scientific consultancy	Tropical Health and Education Trust	Trustee
	IBHSC Ltd	Director	London School of Hygiene and Tropical Medicine	Court of Governors
	SKB	Scientific consultancy	Hamburg Institute of Tropical Medicine	Scientific Advisory Board
			Isaac Newton Institute, Cambridge	Scientific Advisory Board
			Maxwell Institute, Edinburgh	Scientific Advisory Board
Professor C J Bostock (Appointed as an expert from the Institute for Animal Health (IAH), a Biotechnology and Biological Sciences Research Council sponsored institute)	Safeway	Share holding	The UK and some overseas Governments	Research contracts with the IAH
			Non-governmental organisations and companies, spanning a wide range of interests including food, agriculture, chemicals and pharmaceuticals. Further details of the customers of IAH can be found on the Institute's Web Site (www.iah.bbsrc.ac.uk)	Research contracts with the IAH

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Mr R Bradley	European Natural Sausage Casings Association	Advisor	Ministry of Agriculture, Fisheries and Food	Advisor
	Meat and Livestock Commission	Advisor	Veterinary Laboratories Agency	Advisor
			World Health Organisation	Advisor
			Office International des Epizooties	Advisor
			Harder Brothers Ltd	Advisor
			European Commission	Advisor
			National Governments and individuals; especially in Africa, Europe and the Americas	Advisor
			International Natural Sausage Casings Assoc (INSCA)	Advisor
			North American Natural Casing Assoc (NANCA).	Advisor
			Natural Sausage Casings Association (NSCA)	Advisor
			Animal Proteins Corporation (APC) Europe SA	Advisor
			Crackwillow Ltd	Advisor
Professor J Collinge	None	None	Wellcome Trust	Research Grant Holder
			Glaxo Wellcome PLC	Research collaboration
			Dept. of Health	Research Grant Holder
			European Commission BIOMED programme	Research Grant Holder
			Medical Research Council	Unit Director and Research Grant holder
			Motor Neurone Disease Association	Chairman, Research Advisory Panel
			World Health Organisation	Ad hoc Advisor
Dr J Ironside	None	None	Baxter Healthcare USA	Research investigator on a Baxter funded project on the transmission of CJD (Principal investigator Dr Paul Brown USA)
			Department of Health	Research grant holder: Surveillance of CJD (neuropathology) DoH 1216469-National retrospective review of CJD and respective disorders DoH 1216982-Immunocytochemical testing for disease associated prion protein in lymphoid tissues Advisor: Decontamination of surgical instruments Assessment of risk of exposure to vCJD: infectivity in blood and blood products
			Medical Research Council	Grant holder: G9708080-Edinburgh HIV brain and tissue resource G9627376-Phenotypic variation in CJD, a clinical pathological and molecular study

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Dr J Ironside (cont.)			BBSRC	Grant holder: 15/BS204814-Neuronal pathology in CJD: an immunocytochemical study with quantitative and microscopic analysis 201/BS410537-The relationship between neuron damage and clinical disease: relating murine and ovine scrapie to BSE and CJD Advisor: BSEP
			European Union	Grant Holder: EC B104-98-6046-Diagnosis of TSE using PrP ^{SC} /PrP ^C EC CT98-6015 - European centralised facility for human transmissible spongiform encephalopathies (prion disease) EC PL97-6003 - Transgenic mice expressing human prion protein. Use for characterisation of human encephalopathies and sensitivity for detection of infectivity EU CT98-6048 - Quantitative analysis of MR scans in CJD (QAMRIC) Advisor
			Committee on safety of medicines	Advisor
			World Health Organisation	Advisor
			UK Xenotransplantation Interim Regulatory Body	Advisor
Prof C Masters	Merck	Consultant	National Health and Medical Research Council of Australia Several research grants	Principle and Associate investigator
	PRANA Biotechnology Plc	Director	World Health Organisation	Occasional consultancies on CJD
			Australian Government	Occasional consultancy on CJD and Director of the National CJD Registry
Professor H Kimbell	Bass plc	Small share holding		
	Tesco's plc	Small share holding		
Dr M J Painter	None	None	None	None
Mr D B Pepper	The Veterinary Defence Society Ltd	Director and Claims Consultant	None	None
	Pfizer Animal Health (Pfizer Ltd)	Advisor		
	Intervet International BV (Netherlands)	Advisor		
	Intervet UK Ltd	Advisor		
Prof I McConnell	Marks & Spencer	Veterinary consultant on occasional basis	Wellcome Trust	Fellowship holder Research grant holder Panel member for Veterinary Interest Group
			BBSRC	Research grant holder

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Dr J Safar		Dr Safar has no commercial interests but according to the intellectual property policies of the University of California (UC) is entitled to a portion of income when UC licences to a commercial entity any patents on which he is named as inventor	National Institute of Health, Grant # AGO- 10770	Co-investigator
			World Health Organisation	Advisor
			Swiss National Research Programme	Advisor
			Medical Research Council	Advisor
			Non-governmental organisations and companies	Research contacts with UCSF

(The interests of those members who departed during the year are listed in last year's Annual Report.)

An [up-to-date table](#) of Members interests can be found on the SEAC Website:

<http://www.maff.gov.uk/animalh/bse/bse-science/level-4-seac.html>

INDEMNITY BY THE MINISTER OF AGRICULTURE, FISHERIES AND FOOD AND THE SECRETARY OF STATE FOR HEALTH TO MEMBERS OF THE SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE AND RELATED COMMITTEES.

1. The Minister and the Secretary of State ("the Ministers") hereby jointly undertake with each of the members of the Spongiform Encephalopathy Advisory Committee and all of its sub-groups covered by the code of practice ("the members") that they will indemnify them, their estates and their heirs against all personal civil liabilities in respect of any action or claim which may be brought, or threatened to be brought, against them either individually or collectively by reason of or in connection with the performance at any time of their duties as members, whether before or after the date of this indemnity, including all costs, charges and expenses which the members or any member may properly and reasonably suffer or incur in disputing any such action or claim.

2. The members or any member shall as soon as reasonably practicable notify the Ministers if any action or claim is brought or threatened to be brought against them or any of them in respect of which indemnity may be sought pursuant to paragraph 1. If any action or claim is brought the Ministers shall be entitled to assume the defence. The Ministers shall notify the members or member as soon as practicable if the Ministers intend to assume the defence and the members or member shall then provide such information as the Ministers reasonably request, subject to the Ministers reimbursing all out of pocket expenses properly and reasonably incurred by members or any of them. The Ministers shall, where reasonable and practicable, consult with and keep the members or any of them informed of the progress of the action or claim. Where Ministers do not assume the defence, members or any of them shall keep the Ministers fully informed on its progress and any consequent legal proceedings and consult with the Ministers as and when reasonably required by them or any of them concerning the action or claim.

3. The indemnity contained in paragraph 1 shall not extend to any losses, claims, damages, costs, charges, expenses or any other liabilities:

a) in respect of which members are indemnified by or through any defence organisation or insurers; or

- b) which may result from bad faith or wilful default or recklessness on the part of the members; or
- c) which may result from any of the following circumstances (without the prior written consent of the Ministers having been obtained such consent not to be unreasonably withheld):
- any settlement made or compromise effected of any action or claim brought, or threatened to be brought, against them; or
 - any admission by the members of any liability or responsibility in respect of any action or claim brought, or threatened to be brought, against them; or
 - members taking action that they were aware, or ought reasonably to have been aware, might prejudice the successful defence of any action or claim, once the members had become aware that such an action or claim had been brought or was likely to be brought.

Signed on behalf of the Minister of Agriculture, Fisheries and Food and the Secretary of State for Health:

Signature:

Name:

Date:

Signed:

Members name:

Date:

ANNEX IV

FINANCE

The cost of running the Committee in 1999/00 was £86,631.00. The breakdown between the departments was as follows:

SEAC Fees and Expenses*	£37,117
Hire of audio equipment	£5,132
Catering (inclusive of VAT)	£1,261
Reimbursement of travel and expenses to Committee guests	£9,014
Advertising for new members	£22,227
Miscellaneous expenditure	£8,132
Total SEAC Expenses	£82,883

SEAC Epidemiology Sub Group expenses(including consultancy fees)	£3,748
Total SEAC and Sub-Group expenses	£86,631

DEPARTMENT OF HEALTH

Contribution to SEAC expenses**	£27,500
Epidemiology Sub-group expenses	£3,748
DH Total	£31,248

MINISTRY OF AGRICULTURE FISHERIES AND FOODS

Balance of SEAC expenses	£55,383
MAFF Total	£55,383

TOTAL COST OF SEAC 1999/00:	£86,631
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* Member fees and entitlements (revised 1.1.98) are as follows

	Chairman	Members
Basic fee per day	£148	£122
Exceptional circumstances allowance (payable currently to SEAC members)	£37	£31
Preparation time allowance		
For up to one day's preparatory work	£33	£33
For up to two days' preparatory work	£66	£66

**For the financial year 1999/00, SEAC expenses were paid by MAFF, with a contribution from DH at the end of the financial year.

MEMBERSHIP OF THE SEAC/ACDP SUB-GROUP AT 31 MARCH 2000

Chairman:

Professor D J Jeffries

Chairman - ACDP

Members:

Dr M Painter

Consultant in Communicable
Disease Control

Professor P G Smith

London School of Hygiene &
Tropical Medicine

Dr J Ironside

National CJD Surveillance Unit

Mr R Bradley

Private BSE Consultant

Mr R Clare

Director
Bob Clare Associates

Dr J Hope

Institute for Animal Health

Dr P Jones

Institute for Animal Health

Mr J Richards

Unison

Dr T Wyatt

Consultant Clinical Scientist

Dr G Ridgway

University College hospital

Ms J McCulloch

Infection Control nurse Wiltshire Health
Authority

Dr R Salmon

PHLS Wales

Dr D M Taylor

Retired - previously at the Institute for
Animal Health Neuropathogenesis Unit

**MEMBERSHIP OF THE SHEEP SURVEILLANCE SUB GROUP AT 31
MARCH 2000**

Chairman:

Professor P G Smith

London School of Hygiene
& Tropical Medicine

Members:

Professor A Aguzzi

Institute of Neuropathology
University Hospital of Zurich

Professor C J Bostock

Director
Institute for Animal Health

Professor I McConnell

Centre for Veterinary Science
University of Cambridge

Professor R Anderson

Department of Zoology
University of Oxford

Professor M Woolhouse

Centre for Tropical Veterinary
Medicine
University of Edinburgh

Dr A McLean

BBSRC
Institute for Animal Health

Dr L Hoinville

Veterinary Laboratories Agency

Mr J W Wilesmith

Head of Epidemiology Department
Central Veterinary Laboratory
Veterinary Laboratories Agency

Mr S Cousens

London School of Hygiene and
Tropical Medicine

**MEMBERSHIP OF THE SEAC EPIDEMIOLOGY SUB-GROUP ON vCJD
AT 31 MARCH 2000**

Chairman:

Professor P G Smith

London School of Hygiene
and Tropical Medicine

Members:

Professor R G Will

National CJD Surveillance Unit
Edinburgh

Professor C J Bostock

Director
Institute for Animal Health

Professor J Collinge

Prion Disease Group
Imperial College School of Medicine
St. Mary's Hospital, London

Professor R Anderson

Department of Zoology
University of Oxford

Professor N Day

Professor of Public Health & Director
of the Institute of Public Health
Service

Professor R N Curnow

Department of Applied Statistics
University of Reading

Dr H Ward

CJDSU

Dr G Medley

Dept. Biological Science
University of Warwick

Dr S Cousens

London School of Hygiene and
Tropical Medicine

Dr C P Farrington

Communicable Disease Surveillance
Centre
Public Health Laboratory

Mr J W Wilesmith

Head of Epidemiology Department
Central Veterinary Laboratory
Veterinary Laboratories Agency

Dr A Hall

London School of Hygiene and
Tropical Medicine

**SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE
EPIDEMIOLOGY SUB-GROUP**

***Report on the work of the Sub-group
to SEAC and Chief Medical Officers***

GENERAL

1. The Epidemiology Sub-group was set up in September 1997. It reports jointly to the Chief Medical Officer and the Spongiform Encephalopathy Advisory Committee. Its terms of reference are: -

"To assess the information about the epidemiology of nvCJD and develop as far as possible advice on trends in the disease".

2. The Sub-group has met on six occasions. Members have sought to identify what information was needed to enable soundly based predictions to be made about the evolution of the epidemic. Members have concluded that prediction of the course of the epidemic would be facilitated if there were more, or better, data on:

- exposure of the UK population to the infective agent;
- infective dose;
- incubation period;
- genetic susceptibility.

3. Members have been provided with a range of information including:

- Leatherhead Food Research Association Audit Report, together with SEAC's comments on it;
- information about the UK CJD Surveillance system;
- details of TSE research strategy;

- work on short term predictions;
- published (and unpublished) papers on predicting the course of the disease.

4. Members have discussed where the gaps in knowledge were and how these might be filled. These issues are covered in more detail below. The Sub-group has also discussed other issues that would be helpful in determining the future course of the disease. These include the development of a diagnostic test for infection and the use of anonymised surveys to assess the prevalence of infection in the population. In terms of incubation period and infective dose it was considered that information about other human TSEs, notably kuru and cases of CJD related to the use of contaminated human growth hormone, should be obtained.

5. It was also decided that an examination of other animal epidemics, for example Feline Spongiform Encephalopathy, might shed light on how the vCJD epidemic might behave. The search for this information has formed the basis for the Sub-group's work. Reports on the various aspects are set out below.

EXPOSURE OF THE UK POPULATION TO BSE INFECTIVITY

6. Although other avenues of exposure to the BSE agent have not been ruled out, the need to obtain better information about the amount of BSE-infected material (particularly tissues likely to have titres of the agent) that entered the human food chain at different times was identified as a priority. The Leatherhead Food Research Association (LFRA) had conducted a survey to try to obtain relevant information retrospectively but their report provided only very limited useful information. It was also noted that risk assessment work subsequently carried out by Det Norske Veritas (DNV) on behalf of SEAC relied heavily on these data.

7. There have been discussions with the meat industry, retailers and others to try and obtain a clearer picture of the products most likely to contain infected tissue. Obtaining any information has proved to be very difficult and the Sub-group has been told that these data is unlikely to be available.

8. In an attempt to obtain better information the Department of Health (DH) commissioned an analysis of data from past National Food Surveys to determine if these could provide such information. The Australian and New Zealand authorities were also approached, on the basis that they were culturally similar to the United Kingdom, to try to obtain data relating to the consumption of bovine brain and other offals in their countries. DH also undertook a postal survey of environmental health officers to see what information they might have on the use of brain and offals. It is disappointing to report that this activity has produced few useful data.

9. The Sub-group has also been in discussion with researchers from the Medical Research Council's Bio-statistics Unit in Cambridge regarding their ongoing investigations into the amount and use of potentially infected material.

10. Although the search for information will continue, it looks increasingly likely that it will not be possible to produce a reliable estimate of the exposure of the population to any contaminated beef products. Furthermore, there is little chance of being able to identify, by brand name, any beef products that might have contained higher levels of infected material – this information would have been particularly valuable to the CJD Surveillance Unit in refining their questionnaire to the relatives of vCJD patients and controls.

DATA ABOUT OTHER HUMAN TSEs

KURU

11. Dr Michael Alpers and Dr Paul Brown attended a meeting of the Sub-group and presented information about the kuru epidemic among the Fore people of Papua New Guinea (PNG).

12. Members were provided with an outline of the history of the Fore people, the region of PNG in which they had lived and their relationship with other tribes.

13. Until about 1954 it had been customary for adult females and children of both sexes to consume the body of their relatives, unless they had been suffering from a disease like leprosy⁷. The women and young children would have been exposed to the infectious agent through ingestion and/or the smearing of infected material on their bodies as part of the ritual associated with these feasts. Adult males were not usually involved in these feasts but would have prepared the bodies. From about the age of six boys were taken away from their mothers and lived with the adult males. It was likely that, on average, they would have been involved in two or three feasts before this event.

14. Epidemiological studies have shown that the majority of adult male kuru victims were likely to have been infected in early childhood. Incubation periods as long as 40 years had been reported. However, firm information about the number of males who might have died from kuru was limited as many died of other causes before the symptoms of kuru developed.

15. Comprehensive data has been collected from about 1957. Between 1957 and 1961 approximately 200 cases per year were recorded, the majority being women and young children. Between 1971 and 1981 the number of deaths from kuru had declined and there

⁷ Although endo-cannibalism officially ceased in 1954 there is evidence that as a ritual continued in some areas for a few more years.

had been no cases in persons born after 1959.

16. It has been proposed that the kuru epidemic had occurred as a result of a person with sporadic CJD having been consumed at a funeral feast (probably around 1900) and that further cases arisen through transmission at the endo-cannibalistic rituals.

17. Information was available about children born to women with kuru after 1959 who could have been breast-fed for up to eighteen months. None of these children (estimated to be in excess of 1000) had developed disease and this suggested there was no maternal transmission of kuru.

18. In terms of comparing kuru with vCJD, it seemed that the route of infection could be either ingestion or smearing with infected material. Kuru had been observed in a large number of pre-adolescent children. This has not, as yet, been observed in vCJD. Data in relation to kuru indicated that the incubation period could, in a very few cases, be as long as 40 years. It was likely that the average incubation period was between ten and fifteen years.

19. Members were informed about some transmission studies that had been carried out using brains and other non-CNS tissue from kuru victims. In animal experiments, where infected brain tissue from nineteen victims had been used, eighteen had transmitted disease to chimpanzees. These results were similar to those observed in experiments using brain from patients with sporadic CJD.

20. Kuru experiments had also shown that a large dose of infected material always transmitted disease, whichever route was used. A smaller dose, given centrally, acted like a large peripheral dose. Smaller doses administered peripherally resulted in either a longer incubation period or no transmission of disease.

21. Genetic typing of kuru patients and controls of Fore and non-Fore people had been performed. There was evidence pointing to a genetic susceptibility to kuru associated with methionine/methionine at codon 129. Following discussion the Sub-group concluded that it was likely that codon 129 played a role in determining susceptibility and incubation period. Results from animal studies using mice with different genotypes were also available. These experiments, that involved mice being administered with the same level of infectivity, had shown that although all of the mice came down with disease in some cases the incubation period was longer. It seemed that codon 129 did show a correlation between susceptibility and incubation period but it was agreed that further work was needed in relation to the size of the infectious dose.

22. The Sub-group concluded that whilst it had been important to see what, if any, implications the kuru epidemic might have for the vCJD epidemic it was unclear how useful kuru was as a model for vCJD.

b) HUMAN GROWTH HORMONE CASES

23. The Sub-group has also assessed information about CJD cases associated with treatment with human growth hormone (HGH). Professor Annick Alperovitch and Jerome Hulliard had provided information about these cases in France. Professor Tony Swerdlow, from the London School of Hygiene and Tropical Medicine, gave information about the studies that he is carrying out involving UK cases.

i) HGH cases in France

24. The study carried out in France had shown a mean incubation period of 8.8 years in Methionine Methionine homozygous cases. This was shorter than had been reported in the UK series. Information about contaminated HGH was difficult to interpret as it seemed likely that there had been a mixing of the lots that were used and, it was reported, between 1983 and 1984 about half the lots had been contaminated. It was suggested that this might have contributed to the relatively high number of HGH cases in France. Analysis of the data on French cases also showed longer incubation periods among those heterozygous at codon 129 of the PrP gene.

ii) LSHTM study

25. In the UK treatment with HGH had first been used in 1959. Its use had been stopped in May 1985 after four cases of CJD had been reported in recipients. The LSHTM study was looking at 1,908 patients who had received treatment with HGH between 1959 and 1985. Good information was available on all but 40 of these cases. Action was being taken to improve the quality of the data, including the examination of recently discovered pharmacy records. It was thought unlikely that any CJD cases linked to treatment with HGH in the UK would be missed. A formal report on this study is expected during 2000.

26. A collaborative project involving the UK, France, USA and perhaps New Zealand was planned. Such a study would give a cohort of about 10,000 treated individuals.

FELINE SPONGIFORM ENCEPHALOPATHY (FSE) EPIDEMIC

27. The Sub-group considered the FSE epidemic to see what it might reveal about the vCJD epidemic in humans. There does not appear to have been an extensive epidemic of FSE in domestic cats and the incidence of disease is in decline. However, it was important to recognise that FSE was not notifiable unless the disease had been pathologically diagnosed. This could mean there had been some under-ascertainment. Several universities were examining archived material to check if any cases of FSE had been misdiagnosed. So far there was no evidence to support this. Internationally there had been single cases of FSE

reported in Liechtenstein and Norway.

28. There had been seven cases of FSE confirmed in cats born after the Specified Bovine Offal (SBO) ban. Of these, one had been confirmed in 1999. It was possible that these cases might be linked to old canned cat food. The pet-food industry was to be contacted about the shelf life of canned products. These cats had lived in a variety of residences and there was no evidence to suggest that more born after the ban FSE cases had lived on farms.

29. Studies in captive wild cats, especially cheetahs and lions, were a high priority. Evidence from studies of lions suggested the incubation period could be up to 12 years. Further studies in wild cats were required to explain why it appeared that more cheetahs than lions had been affected.

30. In many respects the FSE epidemic seemed to mirror the early stages of the vCJD epidemic. In relation to improving understanding about the vCJD epidemic it was possible that these studies could provide an indicator of when and where exposure was greatest. How valuable that information would be in the long-term remained difficult to judge. Analyses of the FSE and vCJD epidemics have not revealed any evidence of a geographical correlation between the incidence of FSE in cats and vCJD in humans.

DIAGNOSTIC TESTING/FEASIBILITY STUDIES FOR ASSESSING PREVALENCE

31. The Sub-group received a presentation on the progress being made towards the development of a diagnostic test for infection. The Sub-group had strongly recommended that consideration be given to carrying out anonymised unlinked prevalence studies when a suitable test became available.

32. The detection of the abnormal prion in the appendix removed from a patient eight months before the appearance of clinical symptoms who subsequently died of the vCJD had led to this issue being taken forward more speedily than originally envisaged. As a result feasibility studies of surveys of appendix and tonsil tissue are underway. It is recognised that there are likely to be many uncertainties surrounding the interpretation of the results from such studies. However, the sub-group believe they have the potential to provide information that will eventually aid prediction of the evolution of the epidemic.

33. The Sub-group reviewed discussions at the DH/MRC Steering Group for studies of detectable PrP^{Sc}, on the issue of whether larger scale surveys would be necessary in the light of results from the feasibility studies.

34. The Sub-group recognised the need for a blood or saliva test that would detect infection early in the incubation period. They noted that Mary Jo Schmerr's developmental

work on a possible blood test is currently in the process of being validated by the CJD Surveillance Unit and Institute of Animal Health.

INFECTIOUS DOSE

35. The Sub-group has received information from the ongoing attack rate study in cattle that suggests that the infective dose could be less than one gram. Based on work carried out by DNV it has been estimated that each carcass from an infected animal could contain some 800 infective doses. Although many uncertainties surround this issue, most infective material should have been prevented from entering the food chain through the controls which have been in place since 1989.

36. The Sub-group has also considered the question of cumulative exposure and suggested that experimental work, to see if low level exposure over a prolonged period could result in disease, should be undertaken. It was recognised that this would not be an easy experiment to carry out. However the Sub-group noted that recent work by Professor Coleman at the LSHTM has found no evidence of occupational exposure.

GENETIC SUSCEPTIBILITY

37. The Sub-group has received information relating to the genotype of vCJD cases. Of the cases analysed so far, all have been homozygous for methionine at codon 129 of the PrP gene. It is estimated that about 40 per cent of the population were homozygotes for methionine at codon 129 of the PrP gene.

38. In France the study of HGH cases had shown that the first cases, reported in 1989, had been methionine methionine homozygous at codon 129. The first heterozygote case had appeared six years later, in 1995. From these results it appeared that genetic make-up might influence susceptibility to the disease and for the incubation period.

APPROACHES TO MODELLING THE FUTURE COURSE OF THE DISEASE

39. The Sub-group convened a one-day meeting to consider what approaches to modelling the epidemic might be adopted to assist in providing advice on the future trend of the disease. The Sub-group decided that discussion of this issue should include a range of people with an interest and expertise in this area. A seminar to discuss this topic was held in October 1998.

40. The main conclusions arising from this seminar were that the lack of knowledge about key elements of the disease and exposure of the human population meant that making an

early, soundly based, prediction about the future course of the disease was impossible. Any predictions made at this stage would, of necessity, have many associated uncertainties. Consequently predictions of the possible epidemic size range from less than one hundred to many thousands.

41. The consensus view was that it was likely to be some 3-4 years before any soundly based prediction could be made, even then there would be considerable uncertainty. However, this might change as further scientific evidence emerged, particularly if a sensitive and specific test for infection were developed which could be used in large population surveys. In the meantime the approach adopted to monitor the short-term trend of the disease should continue as this was likely to identify, at an early stage, any increase in the incidence rate of disease.

42. The CJDSU reported an increase in cases in the last quarter of 1998. This observation has been monitored during 1999 but it appears that this increased rate in mortality has not been sustained.

43. The Sub-group considers that it is important that detailed information about the BSE and vCJD epidemics is made available to as wide a group of researchers as possible. The Sub-group has noted that applications for research in this area would be welcome.

CONCLUSIONS

44. As anticipated when the Sub-group was formed, fulfilling its remit has proved difficult. There remains much that we do not know about the disease. Of the four parameters initially identified by the Sub-group it seems increasingly unlikely that accurate information about the level of exposure of the UK population to the infective agent will become available. However, better information on the relative levels of exposure at different times is available, and it is this that is critical to epidemic prediction in the absence of information on the dose of the agent required to induce vCJD in humans. Examination of incubation periods in other human and animal TSEs have confirmed this can vary and may also be dose dependent. However, it cannot be assumed that vCJD will behave in the same way as other TSEs. All of the cases of vCJD to date for which analyses are available have been shown to be of the same genotype. However, the examination of HGH cases has shown that although one genotype was affected initially, other genotypes succumbed later, suggesting that all genotypes might be susceptible to infection but that incubation period could vary.

45. The Sub-group has identified ways in which qualitative information might be obtained. Action has been taken on many of these including the ongoing feasibility studies of tonsil and appendix tissue. The Sub-group has identified the need to develop a diagnostic test as soon as possible and that work is necessary to assess the possible impact of secondary transmission of disease.

46. Amongst the issues that the Sub-group has identified for its future work plan are:

- ◆ the need to continue to explore methodologies for predicting the evolution of the human epidemic;
- ◆ the need to continue to try and ascertain the exposure of the human population to potentially contaminated foods. This will include further discussion with the Cambridge Group;
- ◆ the need to make data on BSE and vCJD available to a wider scientific audience; to encourage collaborative activity on modelling the vCJD epidemic as further data become available and to encourage an increase in the number of groups working on the modelling of the epidemic;
- ◆ further development, deployment and the use of tests for infection, as they become available;
- ◆ the design of epidemiological studies to monitor possible secondary transmission of vCJD;
- ◆ to continue critically to review ongoing and published work.

47. In the meantime, the Sub-group's view is that it remains too soon to be able to make soundly based predictions about the future evolution of the epidemic.

CMO/SEAC Secretariat Sub-group

July 2000

**Complete Texts of SEAC Statements and Summaries
(1999/2000)**

**SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE
MEETING: 3 JUNE 1999**

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth on 3 June 1999. This was Sir John Pattison's last meeting as Chairman before taking up his new appointment as Director of Research and Development at the Department of Health in early September. Dr James Ironside of the CJD Surveillance Unit in Edinburgh also attended his first meeting as a full member following his recent appointment to the Committee.

SEAC conducted its regular review of research findings and epidemiological information on BSE and vCJD. It noted that the total number of vCJD cases in the UK was 40 (since the meeting a further case has been confirmed). Although, at the time of the meeting, there had been only one confirmed case in 1999, a number of suspect cases were being investigated. It was too early to draw any conclusions as to whether or not the increase seen in the last quarter of 1998 would be sustained.

The Committee was also informed that in view of recent press speculation about the possible link of vCJD to childhood vaccines, the CJD Surveillance Unit had undertaken an analysis of cases by year of birth. The Committee noted the conclusion that it is unlikely that the cases of vCJD to date would have been exposed to BSE infectivity through the vaccines needed to immunise them as young children, since the vaccines would have been produced well before the BSE epidemic.

A report was also received on work being undertaken by the CJD Surveillance Unit and workers in other European countries to develop clinical criteria for the diagnosis of probable cases of vCJD. Once these had been agreed they would form the basis of published statistics on the number of probable cases. Some suggestions for additions to the criteria were made, including the possible use of tonsil biopsy.

The number of cases of BSE continues to decline, albeit at a lesser rate than in

previous years. The likely explanation is that the decline in 1996 and 1997 was more pronounced as a result of the culling of certain birth cohorts. A progress report was given on the preparation of revised predictions on the future of the epidemic and on the preparation of other information required for a review of the over-thirty-month scheme. These were expected to be available in time for a substantive discussion of the issues at the Committee's next meeting in September.

Preliminary results of the scrapie postal survey, and possible follow up action, were considered. The level of response to the questionnaire had been encouraging and a paper is being prepared for publication in a peer reviewed journal. The Committee then went on to emphasise the priority of analysing sheep brains for evidence of prion disease as rapidly as possible.

The Committee had been asked to consider a number of papers dealing with possible relaxations in the existing controls on farm-animal feeds. It could not at present see any scientific justification for change in the current controls, and was concerned about the potential enforcement implications which could arise if any changes were made. It therefore recommended that:

- the ban on feeding mammalian meat and bone meal to livestock should not be lifted, in whole or in part;
- UK-derived bones should not be used to produce calcium phosphate for farm animal feed; and
- a recent change to the EU ban on mammalian protein in ruminant feed, which would allow hydrolysed protein to be fed to ruminants, should not be adopted, since complete hydrolysis could not be constantly ensured and portions of the prion molecule might still be infectious.

The Committee also clarified its earlier advice (November 1998) by confirming that rendering condensate should no longer be spread on any land, and not just those fields where cattle might graze.

Following delays in arranging facilities for the incineration of stored stocks of OTMS meat and bone meal, SEAC's advice had been sought on the suitability of landfill as a possible supplementary disposal option. SEAC concluded that there was no recent scientific evidence which called into question their earlier view, in 1996, that landfill is an acceptable outlet for MBM of any origin, although SEAC's preference for incineration remains. The Committee recalled that it had given its opinion on the range of assumptions to be included in risk

assessments commissioned by the Environment Agency in 1997, one of which led to the conclusion that landfill had been a suitable option for the past practice of disposing of some BSE suspects by this method. The Committee agreed that a further risk assessment on disposal of OTMS MBM in landfill sites should be undertaken.

At the request of the Department of Health, the Committee considered the possible risk of transmission of vCJD through the re-use of trial contact lenses on subsequent patients. Scientific data relevant to the issue are limited. Any potential risk is probably very low, but the Committee felt strongly that the Department of Health should encourage opticians to adopt, as a matter of best practice, the single use of trial lenses followed by safe disposal.

An update was also given on work to follow up the recommendations made at previous meetings aimed at reducing the potential risk of vCJD transmission associated with surgery. The Committee noted that various aspects of the issue are under consideration and requested for its next meeting, a full report on what had been achieved, with the identification of any constraints on progress.

SEAC
June 1999

LIST OF SCIENTIFIC PAPERS SUPPLIED TO SEAC MEMBERS BY THE SECRETARIAT BETWEEN 18 MARCH AND 3 JUNE 1999

Paper by A.Giese, D.R.Brown, M.H.Groschup, C.Feldmann, I Haist and H.A.Kretzschmar, 'Role of microglia in neuronal cell death in prion disease', published in Brain Pathology, volume 8, 1998, pages 449-457;

Paper by C.A.McLean, J.W.Ironside, M.P.Alpers, P.W.Brown, L.Cervenakova, RMcD Anderson and C.L.Masters, 'Comparative neuropathology of kuru with the new variant of CJD: Evidence for strain of agent predominating over genotype of host', published in Brain Pathology, volume 8, 1998, pages 429-437;

Paper by P.Brown, R.G.Rohwer, B.C.Dunstan, C.MacAuley, D.C.Gajdusek and W.N.Drohan, 'The distribution of infectivity in blood components and plasma derivatives in experimental models of transmissible spongiform encephalopathy', published in Transfusion, volume 38, September 1998, pages 810-816;

Paper by B Evatt, H Austin, E Barnhart, L.Schonberger, L.Sharer, R.Jones and S.DeArmond, 'Surveillance for CJD among persons with hemophilia', published in

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Paper by A.C.Ghani, N.M.Ferguson, C.A.Donnely, T.J.Hagenaars and R.M.Anderson, 'Estimation of the number of people incubating variant CJD', published in the Lancet, volume 352, October 24, 1998, pages 1353-1354;

Paper by S.Betmouni and V.H.Perry, 'The acute inflammatory response in CNS following injection of prion brain homogenate or normal brain homogenate', published in Neuropathology and Applied Neurobiology, 1999, volume 25, pages 20-28;

Paper by H.K.Edskes, V.T.Gray and R.B.Wickner, 'The [URE3] prion is an aggregated form of Ure2p that can be cured by overexpression of Ure2p fragments', published in Proceedings of the National Academy of Sciences USA, 1999, volume 96, pages 1498-1503;

Paper by J.H.Viles, F.E.Cohen, S.B.Prusiner, D.B.Goodin, P.E.Wright and H.Jane Dyson, 'Copper binding to the prion protein: Structural implications of four identical cooperative bindingsites', published in Proceeding of the National Academy of Sciences USA, 1999, volume 96, pages 2042-2047;

Paper by U.Agrimi, G.Ru, F.Cardone, M.Pocchiari and M.Caramelli, 'Epidemic of transmissible spongiform encephalopathy in sheep and goats in Italy, published in the Lancet, 1999, volume 353, pages 560-561;

Paper by D.Heim and U.Kihm, 'BSE in Switzerland- the past and the present', published in Revue Scientifique et Technique de l'Office International des Epizotes, 1999, volume 18, pages 135-144;

Paper by A.Aguzzi and C.Weissmann, 'Prion diseases', published in Haemophilia, 1998, volume 4, pages 619-627;

Paper by P.Demaerel, L.Heiner, W.Robberecht, R.Sciot and G.Wilms, 'Diffusion-weighted MRI in sporadic CJD', published in Neurology, 1999, volume 52, January, (1 of 2), pages 205-208;

Paper by J.Foster, C.Farquhar, J Fraser and R Somerville, 'Immunolocalization of the prion protein in scrapie affected rodent retinas', published in Neuroscience Letters, 1999, volume 260, pages 1-4;

Abstract by J.W.Herms, T.Tings, S.Dunker and H.A.Kretzschmar, 'Prion protein modulates CA2+-activated K+-currents in cerebellar Purkinje cells', published in

Society for Neuroscience, 1998, volume 24, page 516, item 206.10;

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Paper by I.Vorberg, A.Buschmann, S.Harmeyer, A.Saalmuller, E.Pfaff and M.Groschup, 'A novel epitope for the specific detection of exogenous prion proteins in transgenic mice and transfected murine cell lines', published in Virology, 1999, volume 255, pages 26-31;

Paper by P.M.Harrison, H.S.Chan and S.B.Prusiner, 'Thermodynamics of model prions and its implications for the problem of prion protein folding', published in the Journal of Molecular Biology, 1999, volume 286, pages 593-606.;

Paper by G.A.Ascoli, P.Pergami, K.X.Luu, D L.Alkon, E.Bramanti, C.Bertucci, L Di Bari and P.Salvadori, 'Use of CD and FT-IR to determine the secondary structure of purified proteins in the low-microgram range', published in Enantiomer, 1998, volume 3, pages 371-381;

Paper by K.T.Adjou, R Demaimay, J-P Deslys, C.I.Lasmezas, V.Beringue, S.Demart, F.Lamoury, M.Seman and D.Dormont, 'MS-8209, a water-soluble amphotericin B derivative, affects both scrapie agent replication and PrPres accumulation in Syrian hamster scrapie', published in Journal of General Virology, 1999, volume 80, pages 1079-1085;

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Paper by R.G.Will, S.N.Cousens, C.P.Farrington, P.G.Smith, R.S.G.Knight and J.W.Ironside, 'Deaths from variant CJD', published in the Lancet, March 20 1999, volume 353, page 979;

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gene polymorphisms in sheep with natural scrapie and healthy controls in Norway', published in *Journal of General Virology*, 1999, volume 80, pages 1073-1077;

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Paper by S.Supattapone, P.Bosque, T.Muramoto, H.Wille, C.Aagaard, D.Peretz, H.B.Nguyen, C.Heinrich, M.Torchia, J.Safar, F.E.Cohen, S.J.DeArmond, S.B.Prusiner and M.Scott, 'Prion Protein of 106 residues creates an artificial transmission barrier for prion replication in transgenic mice', published in *Cell*, 19 March 1999, volume 96, pages 869-878;

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Paper by A.Aguzzi and A.J.Raeber, 'Neurodegeneration: Of (transgenic) Mice and Men', published in *Brain Pathology*, 1998, volume 8, pages 695-697;

Paper by R.Cappai, L.Stewart, M.F.Jobling, J.M.Thyer, A.R.White, K.Beyreuther, S.J.Collins, C.L.Masters and C.J.Barrow, 'Familial Prion Disease Mutation alters the secondary structure of recombinant mouse Prion Protein: implications for the mechanism of Prion formation', published in *Biochemistry*, 1999, volume 38, pages 3280-3284;

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Paper by P.R.Foster, 'Assessment of the potential of plasma fractionation processes to remove causative agents of transmissible spongiform encephalopathy', published in *Transfusion Medicine*, 1999, volume 9, pages 3-14;

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Paper by K.Kawai, S.Watarai, H.Takahashi, H.Ishizu, K.Fukai, Y.Tanabe, O.Yokota and S.Kuroda, 'Demonstration of ganglioside GD3 in human reactive astrocytes', published in Psychiatry and Clinical Neurosciences, 1999, volume 53, pages 79-82;

Paper by S.Liemann and R.Glockshuber, 'Influence of amino acid substitutions related to inherited human prion diseases on the Thermodynamic stability of the cellular prion protein', published in Biochemistry, 1999, volume 38, pages 3258-3267;

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Paper by D.Verjat, P.Prognon and J.C.Darbord, 'Fluorescence-assay on traces of protein on re-usable medical devices: cleaning efficiency', published in International Journal of Pharmaceutics, 1999, volume 179, pages 267-271;

Paper by J.M.Peyrin, C.I.Lasmezas, S.Haik, F.Tagliavani, M.Salmona, A.Williams, D.Richie, J-P.Deslys, and D.Dormont, 'Microglial cells respond to amyloidogenic PrP peptide by the production of inflammatory cytokines', published in Neuroreport, 1999, volume 10, pages 723-729;

Abstract by E.Stimson, J Hope and A.L.Burlingame, 'Structures of the N-linked glycans of the prion protein isolated from murine models of scrapie', published in FASEB Journal, 1998, volume 12 part 8, A1349;

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SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING: 20 SEPTEMBER 1999

The Spongiform Encephalopathy Advisory Committee met at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth on the 20th September 1999. This was Professor Peter Smith's first meeting as Acting Chairman of the Committee and Professor Ian McConnell's first meeting following his recent appointment to the Committee.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD.

The Committee noted that the total number of confirmed vCJD cases in the UK had risen to 44 (since the meeting a further three cases have been confirmed). The Committee was informed that the CJD Surveillance Unit had undertaken a further analysis of the geographical distribution of vCJD cases the results of which had confirmed earlier analyses that there was no evidence of any geographical clustering of cases.

At the request of the Department of Health (DH) the Committee considered whether the advice it had given in June with regard to contact lenses should also apply to trial or diagnostic contact lens fitting sets and ophthalmic devices that come into contact with the eye. After careful consideration the Committee provided advice to Ministers.

The Committee reviewed the action being taken in the UK to reduce the theoretical risk of transmitting vCJD through blood and blood products. This review was undertaken following the recent decision of the USA and Canadian authorities not to accept blood and plasma donations from people who had spent six months or more cumulatively in the UK between 1980 and 1996 and the results of recently published research. The Committee were pleased to note that following their earlier advice and that of the Committee on Safety of Medicines, all licensed blood products are now manufactured using non-UK plasma, and all blood collected in the UK will be leucodepleted from 1 November 1999. Having considered the available evidence, the Committee concluded that no further steps were currently necessary to ensure the safety of UK blood.

The Committee considered a report on action being taken by the DH to reduce the risks of iatrogenic transmission of vCJD through surgical procedures. The Committee confirmed its earlier view that rigorous implementation of washing, decontamination and general hygiene procedures were key measures in

minimising the risk of infection. They noted the comprehensive package of guidance recently issued by DH to the NHS and independent sector reminding them of the action they should be taking with regard to the cleaning and decontamination of instruments and that an audit was planned to verify compliance with this guidance.

The Committee was provided with updated information from mathematical risk assessment models for assessing the possible risk of transmission of vCJD from contaminated instruments. They noted that the huge uncertainty about the possible number of people who might be incubating vCJD remained a key factor in determining conclusions. The Committee recommended that a group of experts be convened to review the model and report back to the Committee.

The Committee concluded that although the theoretical risk of iatrogenic transmission could depend on a number of factors, it was likely to be greatest from operations involving central nervous system and ophthalmic tissue, followed by lymphoid tissue. The Committee considered that, wherever practicable, the use of disposable instruments for such surgery was to be encouraged. Tonsillectomies were identified as a discrete operation where specific practical steps might readily be taken and the Committee noted that DH was examining the feasibility of the use of disposable tonsillectomy instruments. The results of this assessment were expected shortly.

On research being undertaken into vCJD, the Committee accepted that most of the major areas were being addressed. The Committee recognised that it would be some time before many of these projects produced results but that these research findings would increase considerably understanding and knowledge of the disease. The Committee did however reiterate its view that the search for a diagnostic test using blood should be a key priority and recommended that the DH explore with urgency all possible means of securing such a test.

The Committee conducted their usual review of BSE research and epidemiology. The BSE epidemic in cattle continues to decline although the rate of decline has slowed as the tail of the epidemic is reached. The Committee noted that it was expected that updated epidemiological analyses of the epidemic would be available for its meeting in November. The Committee agreed to postpone discussion of the Over Thirty Month rule until that meeting so that it could take these analyses into account.

In April 1999 the Committee published a report from its subgroup on research and surveillance for TSEs in sheep. Members considered an interim report on progress and noted the complexities associated with some of the recommended

research. The Committee continued to accord very high priority to research on the possible presence of BSE in sheep. They requested a position paper to enable them to identify problems and track progress. They also agreed that a subgroup should consider the objectives and options for further surveys of TSEs in sheep.

Members noted a proposal for a further study of maternal transmission of BSE in cattle. They deferred making a recommendation on the proposal until the November meeting when it could be considered in the light of fresh epidemiological analysis.

SEAC
October 1999

LIST OF SCIENTIFIC PAPERS SUPPLIED TO SEAC MEMBERS BY THE SECRETARIAT BETWEEN 4 JUNE AND 20 SEPTEMBER 1999

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Paper by T.Nemoto, M Horiuchi, N.Ishiguro and M.Shinagawa, 'Detection methods of possible prion contaminants in collagen and gelatin', published in Archives of Virology, 1999, volume 144, pages 177-184;

Paper by G.Forloni, N.Angeretti, P.Malesani, E.Peressini, T.Rodriguez Martin, P.Della Torre and M.Salmona, 'Influence of mutations associated with familial prion-related encephalopathies on biological activity of prion protein peptides', published in Annals of Neurology, April 1999, volume 45, part 4, pages 489-494;

Paper by M.E.Bruce, 'Pathogenesis and pathology in animal TSE models', published in Transfusion Clin. Biol., 1999, volume 6, pages 29-30;

Paper by S.Betmouni, R.M.J.Deacon, J.N.P.Rawlins, and V.H.Perry, 'Behavioral consequences of prion disease targeted to the hippocampus in a mouse model of scrapie', published in Psychobiology, 1999, volume 27 (1), pages 63-71;

Paper by F.Schelcher, N.Picard-Hagen, V.Laroute, V.Gayrard, M.A.Popot, O.Andreoletti and P.L.Toutain, 'Corticoid concentrations are increased in the plasma and urine of ewes with naturally occurring scrapie', published in

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Paper by Michael F.Murphy, 'New variant CJD (nvCJD): The risk of transmission by blood transfusion and the potential benefit of leukocyte-reduction of blood components, published in Transfusion Medicine Reviews, April 1999, Volume 13 No 2, pages 75-83;

Paper by R.Will, 'New variant CJD, published in Biomed & Pharmacother, 1999, volume 53, pages 9-13;

Paper by F.Gray, F.Chretien, H.Adle-Biassette, A.Dorandeu, T.Ereau, M-B.Delisle, N.Kopp, J.W.Ironside and C Vital, 'Neuronal apoptosis in CJD', published in Journal of Neuropathology and Experimental Neurology, 1999, volume 58 (4), pages 321-328;

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Paper by P.Beauvais and T.Billette de Villemeur, 'Maladies a prion transfusion sanguine (Prion diseases and blood transfusion)', published in *Transfus.Clin.Biol*. 1999, volume 6, pages 24-28; (only summary in English)

Paper by S.Laperche, 'Maladie de Creutzfeldt-Jakob et risque transfusionnel: le point en 1998(CJD and blood transfusion-related risk in 1998), published in *Transfus.Clin.Biol*. 1998, volume 6, pages 67-71; (only summary in English)

Paper by M.Russelakis-Carneiro, S.Betmouti and V.H.Perry, 'Inflammatory response and retinal ganglion cell degeneration following intraocular injection of ME7' published in *Neuropathology and Applied Neurobiology*, 1999, volume 25, pages 196-206.

ADVICE TO MINISTERS ON THE USE OF OPHTHALMIC FITTING SETS AND OTHER OPHTHALMIC DEVICES

In June this year, SEAC advised Ministers that eye practitioners should adopt, as a matter of best practice, the single patient use of trial contact lenses. After further consideration the Committee has confirmed that advice and, in addition, recommends that trial or diagnostic lens fitting sets should also be confined to single patient use.

It is theoretically possible that objects that come into contact with the cornea of the eye might transfer infectivity. The Committee further recommends that, as a precautionary step to limit such transfer, those components of ophthalmic devices that touch the cornea should be for single patient use, wherever practicable. We recommend that research into the binding of abnormal prion protein to glass and plastic surfaces be undertaken, and that research is carried out into the possibility of reducing the risk of infectivity by using disposable films with components that touch the cornea.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING: 29 NOVEMBER 1999

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture Fisheries and Food, Tolworth on 29 November. This was Professor Colin Masters' and Dr Jiri Safar's first meeting following their recent appointment to the Committee. Professor Will Hueston was attending his last meeting before retiring from the Committee. Professor Hueston was thanked for his valuable contribution to the Committee's work during his 6 years of service.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD. The total number of people who had died of vCJD now stood at 48. It remained too soon to make predictions with any confidence about the likely total number of deaths in the coming years.

The Committee noted the continuing work to prevent the potential transmission of vCJD through use of surgical instruments.

The Committee received an update from the Advisory Committee on Dangerous Pathogens (ACDP) / SEAC Joint Working Group (JWG) on the work that it had been taking forward on the safe working with TSE agents. The JWG had also considered the categories of patient risk groups set out in guidance issued by ACDP/SEAC. The JWG had recommended that recipients of corneal transplants should be added to the list within the guidance of those patients for whom special precautionary measures would be necessary in a health care setting, to prevent any risk of person to person transmission of TSE infection. SEAC endorsed the JWG's recommendation.

Scientists from the Wellcome Trust Centre for Epidemiology of Infectious Diseases (WTCEID) at Oxford University presented their latest estimates of the numbers of cases in the BSE epidemic from 1996 to 2001 ([Table 1](#)), the likely numbers of infected animals entering the food chain ([Table 2](#)) and the impact of the offspring cull and the Over Thirty Month Scheme (OTMS) on the latter estimates. The revised estimates were based on the most recent data from the BSE epidemic, and take account of the estimated effects of demographic changes and the selective and offspring culls.

The epidemic is still in rapid decline but will have a long tail. The Committee noted that the predictions had been revised upwards from the predictions made in 1996 but had much narrower confidence bands than previous estimates for the same period. However, they still fell within the confidence bands of the earlier analysis. The predictions are higher because the estimated risk from exposure to

infected feed in the period 1991-1996 did not decline as rapidly as projected in the earlier analysis. The likely explanation for this is that cattle were exposed to feed which was accidentally cross-contaminated with BSE infected meat and bone meal destined for pigs and poultry.

The estimate of the number of animals under 30 months of age slaughtered for human consumption that were infected with BSE and within 12 months of developing clinical disease was key to the Committee's previous advice on the risk from dorsal root ganglia and bone marrow. The revised estimates were comparable to the figures considered previously and consequently SEAC did not consider it necessary to review their previous advice of November 1998.

The Committee reviewed the Over Thirty Month (OTM) rule, taking account of the latest predictions of the BSE epidemic. The Committee agreed that the OTM rule had been the key measure put in place to protect public health in 1996. The Committee has provided formal advice to Ministers on their interim conclusions after reviewing the OTM rule and a copy is attached. SEAC requested further information to enable them to consider the balance of risk from cattle in the UK compared with the risk from imported beef and beef products.

The Committee had been asked to consider further the issues surrounding the possible use of meat and bone meal derived from pigs for inclusion in poultry feeds and whether the Committee should reconsider its previous advice in the light of a recent Scientific Steering Committee opinion. The Committee considered that a relaxation of the feed ban in the UK to allow the inclusion of pig MBM in poultry feed could not be supported on scientific grounds. The comprehensive feed ban in place in the UK had been a critical factor in breaking the cycle of infection in the BSE epidemic and SEAC's previous position on this issue had not changed. The principal concern remained that the recycling of animal-derived proteins within or between species, via feed, represented a potential risk of the development of TSE infection in livestock.

The Committee considered a proposal for a study of offspring of BSE cases to measure the rate of maternal transmission of BSE in cattle. They agreed that the offspring were valuable animals for study but given the revised predictions of the decline of the BSE epidemic and the long term nature of the experiment, the Committee did not think that the study would yield results within a useful time frame and did not consider it high priority. Members agreed that although maternal transmission would not sustain the BSE epidemic in cattle it was important that further studies exploring this route of transmission were undertaken.

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The following data are provided courtesy of the Wellcome Trust Centre for Epidemiology of Infectious Diseases, University of Oxford. All data assume 10% maternal transmission occurs where calves are born to infected dams within 6 months of clinical onset. Data take account of the estimated effects of the offspring and selective culls and assume that there was no residual feed risk after 1 August 1996.

Table 1: Predicted BSE case incidence to 2001 (95% prediction intervals shown in parenthesis) including those cases in animals born after mid 1996 from the revised model, compared with actual confirmed cases to date.

Year	Predicted Cases	Predicted cases in animals born after mid 1996 (1)	Actual Confirmed Cases (2)
1996	7576 (7315,7854)	0	7426
1997	4288 (4113,4509)	0	4241
1998	3074 (2916,3283)	0.2 (0,1)	3096
1999	2578 (2394,2798)	4 (1,11)	1720 (3)
2000	1753 (1527,2202)	15 (8,40)	-
2001	866 (733,1283)	23 (13,56) ⁸	-

(1) Note: There are currently no confirmed cases in animals born in 1996.

(2) All cases presented according to year of clinical onset, not by year of restriction or year of confirmation. These figures will therefore differ from some official statistics.

(3) Confirmed cases at 10/12/99. There are approximately another 250 cases slaughtered for which results are pending.

⁸ The Committee has since noted that a correction needed to be made to the figures presented in Table 1. The figures presented did not take account of the estimated effects of the offspring and selective culls. This did not have a significant impact on the majority of the data presented in the table, however, for column 3 - 'Predicted cases in animals born after mid 1996' - the predicted numbers of cases for 1999-2001 should be reduced to the following:

Year	Predicted cases in animals born after mid 1996 (95% prediction interval)
1999	2 (0,5)
2000	6 (3,16)
2001	9 (5,23)

Table 2: Revised model: Predicted number of BSE infected cattle entering the human food chain under 30 months of age in the last year of BSE incubation period (95% prediction intervals shown in parenthesis).

Year	1998	1999	2000	2001
Number of animals	6.2 (2,17)	3.1 (0,7)	1.2 (0,4)	0.8 (0,3)

INTERIM REPORT TO MINISTERS ON THE OTM RULE REVIEW BY SEAC

The Committee has identified the factors which must be taken into consideration when determining whether any change to the rule on slaughter of cattle over thirty months of age could take place. These factors, set out below, have been reviewed by the Committee in discussions held between November 1998 and November 1999:

- forecasts of the future incidence of BSE cases and of infected animals entering the food chain;
- the age distribution of cases;
- the results of examination of brains of cattle slaughtered in the over thirty month scheme (OTMS);
- the robustness of the cattle identification systems;
- the robustness of feed controls;
- the robustness of specified risk material controls;
- the relative risk from imported beef and beef products.

Not all of the Committees deliberations are complete but, following study of a recent analysis of the BSE epidemic¹, it is now possible to provide the following summary and interim conclusion.

The number of BSE infected cattle which might be slaughtered for human consumption in the future is the key factor which will determine the risk to public health from the BSE agent. This risk is reduced by the controls in place. These are:

¹ Data provided by the Wellcome Trust Centre for the Epidemiology of Infectious Disease

- Compulsory slaughter, destruction and regulated safe disposal of any animal showing signs of clinical TSE disease;
- the prohibition of the use of mammalian meat and bone meal in any farm animal feed;
- the removal from the food chain and regulated disposal of specified risk materials (any tissue thought to have a significant risk of carrying TSE infectivity);
- the slaughter and regulated disposal of animals over the age of thirty months with the exception of animals from the beef assurance scheme (where different age limits apply)
- the slaughter and regulated disposal of all offspring of BSE affected dams born after 1 August 1996.

Current predictions show that the epidemic is still in rapid decline but will have a long tail. The estimated risk from contaminated cattle feed does not appear to have declined as rapidly in the period 1991-1996 as had been estimated previously. However, the estimated risk to humans from animals currently entering the human food chain remains **very low**. The number of animals entering the food chain which are infected and within 12 months of developing clinical disease is predicted to be between 0 and 4 in the year 2000. As set out in previous advice² the Committee believes that, given the controls currently in place to remove specified risk materials and continuing high compliance levels, the risk to public health from these animals is **extremely small**.

One of the key findings from the latest analysis of the BSE epidemic is that the over thirty month rule has had a major impact on reducing the risk to public health by significantly limiting the number of infected animals which might otherwise enter the food chain. From its introduction in April 1996 to the current time, it has reduced the volume of infected cattle in the last year of the BSE incubation period entering the human food supply by over 99%, and is projected to continue at this level of effectiveness for at least the next 2 years. In part this effectiveness is due to the lower incidence of infection in younger animals, and in part to the fact that the great majority of infected animals only show clinical signs of BSE at 4 years of age or later. This means that it is highly unlikely that an animal under thirty months of age would be in the last 12 months of its incubation period.

On this basis, we conclude that modifying the rule to increase the age of animals permitted to be slaughtered for human consumption would be premature as this may re-introduce an unacceptable level of risk at this time. Furthermore, we recommend that the controls set out above should continue to be rigorously enforced to ensure that these risk reduction measures remain effective even though the overall risk is declining with the epidemic.

This represents our interim conclusions. We will continue to keep the over thirty month rule under review in the light of further estimates of the progress of the epidemic, data from surveys of the brains of OTMS cattle, and reports on the monitoring of control measures. We have also asked for further information to enable us to consider the balance of risk from cattle in the UK compared with that from imported beef and beef products.

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LIST OF SCIENTIFIC PAPERS SUPPLIED TO SEAC MEMBERS BY THE SECRETARIAT BETWEEN 21 SEPTEMBER AND 29 NOVEMBER 1999

Paper by Michael Beekes, Markus Otto, Jens Wiltfang, Erik Bahn, Sigrid Poser, and Michael Baier, "Late increase of serum S100 (protein levels in hamsters after oral or intraperitoneal infection with scrapie", published in The Journal of Infectious Diseases, 1999 volume 180, pages 518-520;

Paper by Joelle Charby, Suzette A.Priola, Kathy Wehrly, Jane Nishio, James Hope and Bruce Chesebro, "Species-independent inhibition of abnormal prion protein (PrP) formation by a peptide containing a conserved PrP sequence", published in Journal of Virology, 1999 volume 73 No.8, pages 6245-6250;

Paper by Adriano Aguzzi and Sebastian Brandner, "The genetics of prions - a contradiction in terms?", published in The Lancet 1999, volume 354, pages 22-25;

Paper by Nora Hunter, "Prion diseases and the central dogma of molecular biology", published in Trends In Microbiology 1999, volume 7, No.7, pages 265-266;

Paper by Jia-Jia-Liu and Susan Lindquist, "Oligopeptide-repeat expansions modulate 'protein-only' inheritance in yeast". published in Nature 1999, volume 400, pages 573-576;

Paper by S.McHattie, G.A.H. Wells, J.Bee and N.Edington, "Clusterin in Bovine Spongiform Encephalopathy (BSE)", published in Journal of Comparative Pathology 1999, volume 121, pages 159-171;

Paper by L.J.M.van Keulen, B.E.C.Schreuder, M.E.W. Vromans, J.P.M.Langeveld and M.A.Smits, "Scrapie-associated prion protein in the gastro-intestinal tract of sheep with natural scrapie", published in Journal of Comparative Pathology 1999, volume 121, pages 55-63;

Paper by Jozef Orpiszewski and Merrill D. Benson, "Induction of β -sheet structure in amyloidogenic peptides by neutralization of aspartate: A model for amyloid nucleation", published in Journal of Molecular Biology 1999, volume 289, pages 413-428;

Paper by Naava Naslavsky, Hilary Shmeeda, Gilgi Friedlander, Anat Yanai, Anthony H. Futerman, Yechezkel Barenholz, and Albert Taraboulos, "Sphingolipid depletion increases formation of the scrapie prion protein in neuroblastoma cells infected with prions", published in The Journal of Biological Chemistry 1999, volume 274, No.30, pages 20763-20771;

Paper by Remy Narwa and David A.Harris, "Prion proteins carrying pathogenic mutations are resistant to phospholipase cleavage of their glycolipid anchors", published in Biochemistry 1999, volume 38, pages 8770-8777;

Published abstract by Hans. A. Kretzchmar and Jochen W. Herms, "Cellular localization and possible function of the prion protein", published in European J Cell Biology 1999, volume 78, No.49, page 7;

Paper by Laszlo L. P. Hosszu, Nicola J. Baxter, Graham S. Jackson, Aisling Power, Anthony R. Clarke, Jonathan P. Waltho, C Jeremy Craven and John Collinge, "Structural mobility of the human prion protein probed by backbone hydrogen exchange", published in Nature Structural Biology 1999, volume 6, No.8, pages 740-743;

Published abstract by David Peretz, Anthony R Williamson, Michael R Scott, Darlene Groth, Dennis R Burton, Fred E Cohen and Stanley B Prusiner, "Four distinct prion protein structures seem to dictate protease resistance of prion strains replicated in syrian hamsters", published in Protein Structure volume II (1312-1317);

Paper by C.V. Prowse, V.S. Hornsey, O. Drummond, I. R. MacGregor, D. S. Pepper, G. R. Barclay, H. Bethel, B. Walker, G Barnard, L. Kirby and J. Hope,

"Preliminary assessment of whole-blood, red-cell and platelet-leucodepleting filters for possible induction of prion release by leucocyte fragmentation during room temperature processing", published in British Journal of Haematology 1999, volume 106, pages 240-247;

Published abstract by Patrick Tremblay, Zeev Meiner, Hermann Bujard, Stephen J DeArmond and Stanley B Prusiner, "Doxycycline control of prion protein transgene expression modulates prion disease in mice", published in Gene Regulation I (246-251);

Published abstract by J H Wissler, "Prion modeling: potential of copper - mediated ribokine formation and relation of molecular mechanisms in bioinformation transfer of prion "infectivity" and (transfer factors of delayed) cell-mediated immunity", published in Signal Transduction I (1027-1032);

Paper by Gudrun Wildegger, Susanne Liemann and Rudi Glockshuber, "Extremely rapid folding of the C-terminal domain of the prion protein without kinetic intermediates", published in Nature Structural Biology, 1999, volume 6 No.6, pages 550-555;

Paper L Hoinville, A.R. McLean, A. Hoek, M.B.Gravenor and J Wilesmith, "Scrapie occurrence in Great Britain", published in the Veterinary Record, October 2 1999, pages 405-406;

Paper by W Goldman, G O'Neill, F Cheung, F Charleson, P Ford and N Hunter, "PrP (prion) gene expression in sheep may be modulated by alternative polyadenylation of its messenger RNA", published in the Journal of General Virology, 1999, volume 80, pages 2275-2283;

Paper by D Miller, "Risk science and policy: definitional struggles, information management, the media and BSE", published in the Social Science & Medicine, 1999, volume 49, pages 1239-1255;

Paper by T Kuczus and M H Groschup, "Differences in proteinase K resistance and neuronal deposition of abnormal prion proteins characterize bovine spongiform encephalopathy (BSE) and scrapie strains", published in the Molecular Medicine, 1999, volume 5, pages 406-418;

Paper by H A Kretschmar, A Giese, J W Herms and D R Brown, "Neuronal degeneration and cell death in prion disease", published in the Prions and Brain Diseases in Animals and Humans;

Paper by D R Brown, "Prion protein peptide neurotoxicity can be mediated by astrocytes", published in the Journal of Neurochemistry, 1999, volume 73, pages 1105-1113;

Paper by D J Waggoner, T B Bartnikas and J D Gitlin, "The role of copper in neurodegenerative disease", published in the Neurobiology of Disease, 1999, volume 6, pages 221-230;

Paper by R Rubenstein, R J Kascsak, M Papini, R Kascsak, R I Carp, G LaFauci, R Melen and J Langeveld, "Immune surveillance and antigen conformation determines humoral immune response to the prion protein immunogen", published in the Journal of Neuro Virology, 1999, volume 5, pages 401-413;

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Paper by M H Anil, S Love, S Williams, A Shand, J L McKinstry, C R Helps, A Waterman-Pearson, J Seghatchian and D A Harbour, "Potential contamination of beef carcasses with brain tissue at slaughter", published in the Veterinary Record, October 16 1999, volume 145, pages 460-462;

Paper by M Salmona, P Malesani, L De Gioia, S Gorla, M Bruschi, A Molinari, F Della Vedova, B Pedrotti, M A Marrari, T Awans, O Bugiani, G Forlini and F Tagliavini, 'Molecular determinants of the physicochemical properties of a critical prion protein region comprising residues', published in the Biochemical Journal, 1999, volume 342, pages 207-214;

Paper by T G M Baron, J-Yves Madec and D Calavas, 'Similar Signature of the Prion Protein in Natural Sheep Scrapie and Bovine Spongiform Encephalopathy-Linked Diseases', published in the Journal of Clinical Microbiology, volume 37, pages 3701-3704;

Paper by D Dormont, 'Transmissible Spongiform Encephalopathy Agents and Animal Sera', published in Developments in Biological Standardization, 1999, volume 99, pages 25-34;

Paper by R Bradley, 'BSE Transmission Studies with Particular Reference to Blood', published in Developments in Biological Standardization, 1999, volume 99, pages 35-40;

Paper by D M Asher, 'Bovine Sera Used in the manufacture of Biologicals: Current Concerns and Policies of the U.S Food and Drug Administration Regarding the Transmissible Spongiform Encephalopathies', published in *Developments in Biological Standardization*, 1999, volume 99, pages 41-44;

Paper by J H d'Aignaux, D Costagliola, J Maccario, T Billette de Villemeur, J P Brandel, J P Deslys, J J Hauw, J L Chaussain, Y Agid, D Dormont and A Alperovitch, 'Incubation period of Creutzfeldt-Jacob disease in human growth hormone recipients in France', published in *Neurology*, 1999, volume 53, pages 1197-1201;

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Paper by B Kunz, E Sandmeier and P Christen, 'Neurotoxicity of prion peptide 106-126 not confirmed' published in the *Federation of European Biochemical Societies*, 1999, volume 458, pages 65-68;

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Paper by G R Schmidt, K L Hossner, R S Yemm, D H Gould and J P O'Callaghan, 'An Enzyme-Linked Immunosorbent Assay for Glial Fibrillary Acidic Protein as an Indicator of the Presence of Brain or Spinal Cord in Meat' published in the *Journal of Food Protection*, 1999, volume 62, number 4, pages 394-397;

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SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING: 15 FEBRUARY 2000

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture, Fisheries and Food (MAFF), Page Street, London on 15 February. The Committee thanked outgoing member Dr Peter Goodfellow who had retired from the Committee to take up other duties in relation to human genetics.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD. It considered the recent publication in "Transfusion"¹ suggesting that infectivity was detectable after disease onset in the plasma of mice experimentally challenged with a mouse adapted human TSE. It also considered preliminary evidence which appeared to demonstrate that blood plasma, taken from mice with clinical disease caused by a mouse adapted BSE agent and inoculated into the brains of disease-free mice, gave rise to clinical disease in some of the recipient mice. The Committee concluded that priority should be given to carrying out a study on mice infected with a mouse adapted BSE agent at various stages before development of disease. However, the Committee did not recommend any measures in addition to those already in place to reduce any potential risk to public health from human blood and blood products.

The Committee noted that the pathogenesis of the disease caused by BSE in mice was different to the pathogenesis of BSE in cattle but more similar to that of TSEs in sheep and humans. Given the difference in the pathogenesis of the disease in cattle and this mouse model, and taking account of the results of bioassays of cattle tissues in both mice and cattle, the Committee concluded that there were no implications for the safety of the food chain from these findings.

The Committee recommended that work to ascertain the sub-clinical prevalence of vCJD in the human population should be taken forward with all possible speed. This might, for example, include large scale surveys testing tonsil and appendix tissue for evidence of infection.

The Committee was informed that the total number of people who had died of vCJD stood at 52. Although the final number of deaths from vCJD during 1999 once all confirmations were complete was expected to show a fall from the number who had died in 1998, it remained too soon to make predictions with any confidence about the likely number of deaths in the coming years.

The Committee noted the outcome of the meeting of its Epidemiology Sub-Group on 9 February. On the definitions used for 'confirmed' and 'probable' vCJD, the Committee endorsed the view of the Sub-Group that robust scientific criteria now existed. These definitions would enable live 'probable' cases to be separately identified for the first time. The number of cases meeting these criteria could then be included within the data on vCJD published by the Department of Health.

The Committee conducted a review of key research related to scrapie and BSE in sheep. A representative from the Institute of Animal Science and Health, Lelystad, Netherlands presented some of their recent work on the pathogenesis of scrapie. Progress reports on the work at the Institute of Animal Health and Veterinary Laboratories Agency on the pathogenesis of BSE in sheep and screening brains from sheep with spongiform encephalopathy for the presence of BSE were also presented to the Committee.

Members noted that the preliminary and interim results of the studies of experimental BSE pathogenesis in sheep tend to support the conclusions reached by SEAC in July 1996 and July 1998 that BSE in sheep is likely to behave in a very similar manner to the natural disease of sheep scrapie. The latest work on the pathogenesis of scrapie confirms earlier findings that the disease appears to infect peripheral tissues including the lymph nodes, spleen and parts of the intestine as well as the central nervous system. It also indicates that the spread of the infection is likely to be from the gut via peripheral nerves or via innervations of the lymphatics to the central nervous system.

Agent strain typing is underway on isolates from over 130 brains of sheep with natural scrapie in order to determine if the BSE agent profile exists. Although incomplete (each study takes up to two years) over 30 isolates are advanced enough to suggest that they do not have the characteristics associated with the BSE agent. Members also noted strain typing of isolates from a pool of brains from scrapie affected sheep which had been collected for a rendering experiment between 1990 and 1992. The Committee agreed that further work needed to be done on screening sheep for evidence of infection with the BSE agent but concluded that at present there was no need for further public health controls.

The Committee further noted the existence of an EU proposal on specified risk materials. The proposal would classify individual Member States according to the incidence of BSE in cattle. Members noted that to set out SRM controls for sheep and goats on this basis would not be consistent with the likely routes of exposure of sheep to BSE infection. This is because the risk of exposure would

vary according to feeding practices assuming that sheep had in fact been infected from feed. It would also depend on if, and how infection and disease associated with the BSE agent could be propagated in sheep.

Members further agreed that, in the event that the EU proposal to add intestine to the list of specified risk materials from sheep or goats were adopted by Member States, they would not advise against this but would advise that the whole intestine from sheep of all ages should be classified as specified risk material.

The Committee noted a proposal by MAFF to extend the survey of the brains of cattle in the Over Thirty Month Scheme in the next year. They felt it was important to continue this work as it provided an independent check on models of the progress of the BSE epidemic. The performance of diagnostic tests was seen as critical to the outcome of such surveys. To that end the Committee welcomed the intention of the Commission to support a study to evaluate the usefulness of the recently validated tests that can efficiently detect prion protein (PrP) in the central nervous system (CNS) of clinically affected animals, for the detection of PrP in healthy cattle during the incubation period. This study will use CNS tissues from cattle in the study of pathogenesis of experimental BSE in cattle using the tests previously evaluated for sensitivity and specificity compared with conventional diagnostic methods. The study is expected to indicate how long before the onset of clinical signs the test would be reliable to detect PrP which, by inference, would indicate that a positive animal be infected. Members thought this was a key factor which must be taken into account when designing the surveys.

¹Brown et al 1999, Further studies of blood infectivity in an experimental model of transmissible spongiform encephalopathy, with an explanation of why blood components do not transmit Creutzfeldt - Jakob disease in humans. Transfusion Vol. 39, November/December 1169 - 1178.

SEAC
March 2000

LIST OF SCIENTIFIC PAPERS SUPPLIED TO SEAC MEMBERS BY THE SECRETARIAT BETWEEN 30 NOVEMBER AND 15 FEBRUARY 2000

Paper by S Dearmond, Y Qiu, H Sanchez, P Spilman, A Ninchak-Casey, D Alonso and V Daggett, 'PrP Glycoform Heterogeneity as a Function of Brain Region:

Implications for Selective Targeting of Neurons by Prion Strains', published in the Journal of Neuropathology and Experimental Neurology, 1999, volume 58, number 9, pages 1000-1009;

Paper by John Hardy, 'Pathways to Primary Neurodegenerative Disease', published by the Mayo Foundation for Medical Education and Research, 1999, volume 74, pages 835-837;

Abstract by Chris Bostock, 'Infectious and Genetic Basis of TSEs, Prospects for Control', published in the Journal of Antimicrobial Chemistry, 1999, volume 44, page 15;

Paper by S A Priola, 'Prion protein and species barriers in the transmissible spongiform encephalopathies', published in Biomedicine and Pharmacotherapy, 1999, volume 53, pages 27-33;

Paper by S Lehmann, O Milhavet and A Mange, 'Trafficking of the cellular isoform of the prion protein', published in Biomedicine and Pharmacotherapy, 1999, volume 53, pages 39-46;

Paper by J C Darbord, 'Inactivation of prions in daily medical practice', published in Biomedicine and Pharmacotherapy, 1999, volume 53, pages 34-38;

Paper by T Maignien, C I Lasmezas, V Beringue, D Dormont and J-F Deslys, 'Pathogenesis of the oral route of infection of mice with scrapie and bovine spongiform encephalopathy agents', published in the Journal of General Virology, 1999, volume 80, pages 3035-3042;

Paper by L Ingrosso, F Pisani and M Pocchiari, 'Transmission of the 263K scrapie strain by the dental route', published in the Journal of General Virology, 1999, volume 80, pages 3043-3047;

Paper by R Frigg, M A Klein, I Hegyi, R M Zinkernagel and A Aguzzi, 'Scrapie Pathogenesis in Subclinically Infected B-Cell- Deficient Mice', published in the Journal of Virology, 1999, volume 73, pages 9584-9588;

Paper by R K Meyer, B Oesch, R Fatzer, A Zurbriggen and M Vandeveldel, 'Detection of Bovine Spongiform Encephalopathy-Specific PrP by Treatment with Heat and Guanidine Thiocyanate', published in the Journal of Virology, 1999, volume 73, pages 9386-9392;

Paper by J A Hainfellner and H Budka, 'Disease associated prion protein may

deposit in the peripheral nervous system in human transmissible spongiform encephalopathies', published in *Acta-Neuropathologica*, 1999, volume 98, pages 458-460;

Paper by M H Groschup, M Beekes, P A McBride, M Hardt, J A Hainfellner and H Budka, 'Deposition of disease-associated prion protein involves the peripheral nervous system in experimental scrapie', published in *Acta-Neuropathologica*, 1999, volume 98, pages 453-457;

Paper by O Schaller, R Fatzer, M Stack, J Clark, W Cooley, K Biffiger, S Egli, M Doherr, M Vandeveld, D Heim, B Oesch and M Moser, 'Validation of a Western immunoblotting procedure for bovine PrP detection and its use as a rapid surveillance method for the diagnosis of bovine spongiform encephalopathy (BSE)', published in *Acta-Neuropathologica*, 1999, volume 98, pages 437-443;

Paper by A R White, G Multhaup, F Maher, S Bellingham, J Camakaris, H Zheng, A I Bush, K Beyreuther, C L Masters and R Cappai, 'The Alzheimer's Disease Amyloid Precursor Protein Modulates Copper-Induced Toxicity and Oxidative Stress in Primary Neuronal Cultures', published in the *Journal of Neuroscience*, 1999, 19(21), pages 9170-9179;

Paper by J Herms, T Tings, S Gall, A Madlung, A Giese, H Siebert, P Schurmann, O Windl, N Brose and H Kretschmar, 'Evidence of Presynaptic Location and Function of the Prion Protein', published in the *Journal of Neuroscience*, 1999, 19(20), pages 8866-8875.

Abstract by W F Butt, C Soto, S R Plotkin and W A Banks, 'Blood-Brain Barrier Transport of Prion Protein', published in the *Journal of Investigative Medicine*, 1999, volume 47, N7, page 254A;

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Abstract by B Oesch, M Moser and O Schaller, 'Prionics-check: A fast and reliable diagnostic test for prion disease', published in Clinical Chemistry and Laboratory Medicine, 1999, volume 37, page S524;

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Paper by K Brown, K Stewart, D Ritchie, N Mabbott, A Williams, H Fraser, W Morrison and M Bruce, 'Scrapie replication in lymphoid tissues depends on prion protein-expressing follicular dendritic cells', published in Nature Medicine, 1999, volume 5, number 11, pages 1308-1312;

Paper by R Hegde, P Tremblay, D Groth, S DeArmond, S Prusiner and V Lingappa, 'Transmissible and genetic prion diseases share a common pathway of neurodegeneration', published in Nature, 1999, volume 402, pages 822-826.

Note: Copies of SEAC's complete monthly bibliography updates from the secretariat (references only and without abstracts) are published regularly on the MAFF website (<http://www.maff.gov.uk/animalh/bse/bse-science/level-3-research.html>)

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DoH homepage:

<http://www.open.gov.uk/doh/dhhome.htm>