



SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE
Draft minutes of the open session of the 85th meeting held on 30th
November 2004

At

The Hilton Hotel
Kingsway
Cardiff
CF10 3HH

Members:

Professor C. Higgins (Chair)
Mr. J. Bassett
Dr. D. Brown
Dr. J. Chambers
Professor N. Hooper
Professor J. Ironside (Deputy Chair)
Mr. P. Jinman
Dr. C. Lasmezas
Professor J. Manson
Professor I. McConnell
Ms. D. McCrea
Professor G. Medley
Dr. P. Rudge

Assessors:

Mr. A. Harvey (FSA)
Mrs. E. Lawrence (DH)

DA Assessors:

Dr. M. Simmons (NAW)
Dr. P. Christie (SEHD)
Dr. A. Douglas (DARDNI)

Technical Advisors:

Dr. P. Barrowman (Defra)
Dr. S. Dixon (FSA)
Dr. D. Matthews (VLA)
Dr. J. Stephenson (DH)

SEAC Secretary: Miss. K. Richards

Secretariat: Dr. T. Barlow
Mr. M. Pemberton
Dr. P. Keep
Dr. C. Ravirajan
Ms. T. Dale

Also in attendance: Dr. I. Hill (FSA) **(Paper 85/2)**
Dr. D. Bourne (Wildlife Information Network)
(Paper 85/2)

DRAFT

ITEM 1 - CHAIR'S INTRODUCTION

1. The Chair welcomed members of the public to the ninth open meeting of SEAC and thanked the Welsh Assembly Government for hosting the first open SEAC meeting to be held outside London.
2. The Chair explained that this was the second live broadcast of a SEAC meeting over the internet, which is part of a one year trial to assess the potential benefits and likely uptake of viewing via this medium. To view the live broadcast, members must register, via the SEAC web site, at least 24 hours in advance to ensure technical compatibility. An archive of meetings would also be available via the SEAC website for which registration was also required.
3. The Chair informed members that this would be Mr Colin Browne's last meeting as a member of SEAC. The Chair thanked Mr Browne, who could not attend the meeting, for his contribution to SEAC. Apologies for absence had also been received from Professors Bulfield and Stanley. The Chair also informed members that Dr Mandy Bailey (Defra's assessor) and Mr Peter Soul (Defra's technical adviser), both of whom could not attend the meeting, would be retiring from Defra in the very near future and recorded his thanks for their valued contribution to SEAC discussions.
4. The Chair welcomed Kate Richards, who had recently taken over from Catherine Boyle as SEAC Secretary, to her first meeting. The Chair also welcomed Dr Debra Bourne (Wildlife Information Network), Dr Irene Hill (FSA), Mrs Eileen Lawrence (DH), Mr Alan Harvey (FSA) and Dr Peter Barrowman (Defra) who were presenting items to the committee.
5. The Chair thanked those members who had responded to the secretariat regarding media training; this would be organised in due course. Members were reminded of their obligation to declare conflicts of interests at the start of each agenda item and were informed that the next meeting would be held on 3rd March 2005 in London.

ITEM 2 – APPROVAL OF DRAFT MINUTES FROM SEAC 84 (SEAC 85/1)

6. The minutes of the open session of the 28th September meeting were agreed as a correct record subject to the following amendments:

- change paragraph 23 first sentence from “...in July 20004...” to read “...in July 2004...”,
 - change paragraph 25 first bullet point from “...these would not reduce scrapie in ARQ sheep, which may be more important than to assumed in the modelling...” to read “...these would not reduce scrapie in ARQ sheep, which may be more important than assumed in the modelling...”,
 - change paragraph 45 first sentence from “Professor Ferguson noted that the 10-fold reduction in the quantity of duodenum and jejunum entering the food supply...” to read “Professor Ferguson noted that the 10-fold reduction in the infectivity from duodenum and jejunum entering the food supply...”, and
 - change paragraph 47 line 2 from “...it was only necessary to consider large animal epidemics in a small number of flocks and suggested that that a model...” to read “...it was only necessary to consider large animal epidemics in a small number of flocks and suggested that a model...”.
7. Under matters arising, the Chair informed members that he had presented the outcome of SEAC’s discussion at the meeting on 28th September 2004 relating to BSE and sheep to the FSA Board, who are considering their contingency arrangements should BSE ever be found in sheep.
 8. At the meeting on 28th September 2004, members noted that there had been a number of cases of animals with clinical signs consistent with BSE that were not confirmed as BSE using diagnostic tests. In view of these cases and the phenotypic differences of TSE infection in sheep and humans, members had suggested that research on methods to allow differential diagnosis of clinical cases of BSE was important. One member asked whether any progress had been made relating to this issue. The Chair agreed to pursue the matter with Defra.

ITEM 3 - CURRENT ISSUES

9. The Chair explained that this would be a regular agenda item to update members of the committee on current TSE issues that had arisen since the previous meeting.

FSA / SEAC Milk Working Group

10. A joint FSA / SEAC milk working group had been established to provide advice to the FSA on research to develop diagnostic tests to detect abnormal PrP in milk from cattle. The Chair informed members that he had discussed this work with Professor Chris Bostock, Chair of the milk working group, who had explained that the assessment of results from tests of experimental samples was currently incomplete and that a discussion at SEAC would have been premature. It is anticipated that a report from the group will be provided at the next SEAC meeting on 3rd March 2005.

Wadsworth *et al* (2004) paper

11. The Chair informed members that a very recent paper by Wadsworth *et al* (2004)¹ suggested that the phenotype and transmission of vCJD and BSE in transgenic mice expressing human PrP were profoundly influenced by polymorphisms at codon 129 of the PrP gene. Animals with homozygous valine at codon 129 were associated with i) altered molecular and neuropathological phenotypes of vCJD infection, ii) a partial barrier to primary infection, and iii) a large barrier to secondary infection compared with methionine homozygous animals. Given the potential implications for human health, consideration would be given on how best to take this forward at the next SEAC meeting.

Possible BSE in a French goat

12. The Chair provided members with the background to this particular case. In 2002, a single healthy goat, from a flock of 300, tested positive for a TSE as part of a French surveillance programme. The results appeared different from normal scrapie strains. All the goats from the flock were destroyed and no product from the flock entered the human food supply. Studies to investigate the type TSE are almost complete and have led to the suspicion of BSE. The results had been passed to the Community Reference Laboratory expert group who concluded that, although the data available are consistent with BSE, a definitive interpretation could not be provided until further data from mouse bioassays were available in approximately two months. The European Food Safety Authority (EFSA) was now considering the implications of these findings.

¹ Wadsworth *et al*. Human prion protein with valine 129 prevents expression of variant CJD phenotype. *Science*. (2004) 306, 1793-1796.

13. In response to members questions, Dr Danny Matthews (VLA) confirmed that the goat was a mature milking goat, although there remained some confusion over its exact age, which the French authorities were trying to clarify. The Chair explained that it was possible the goat could have been exposed to infected mammalian meat and bone meal (MMBM) before the EU wide feeding ban.
14. Members asked what was likely to happen once the further results were known and should BSE be confirmed. Mr Alan Harvey (FSA) explained that decisions regarding risk management measures would be taken at EU level following consideration by the Standing Committee on Food Chain and Animal Health. Dr Matthews added that a TSE working group was being held in Brussels on 30th November 2004 to consider the implications of the findings. It was expected that the working group would make recommendations on increased surveillance and further SRM controls. The committee considered it important that, in the event of confirmation of BSE in the goat, possible risk management measures were identified in advance.

ITEM 4 – CHRONIC WASTING DISEASE IN UK DEER

15. The Chair informed the committee that the FSA had asked SEAC to advise on the potential public and animal health risks of chronic wasting disease (CWD). As SEAC had not considered CWD previously, a position statement would be drafted on the basis of the discussion and, if it was considered necessary, the committee could discuss the issue further at the next meeting. There may also be an opportunity to invite an external expert for that discussion. The Chair reminded members of the advice sought from the committee.
16. Dr Irene Hill (FSA) provided a background to the FSA request. The FSA recognised the potential risks to human health should BSE be found in deer. However, the human health risks of CWD in deer are unknown. Therefore, the FSA has asked the committee to consider the possible human health risks should CWD be found in UK deer. Although no TSEs have been found in deer in the UK to date, surveillance is limited and given the origins of the disease are unknown, the presence of CWD in deer cannot be ruled out. A recent EFSA opinion made recommendations on the scope of TSE surveillance in deer. As a result, it is likely deer surveillance will increase in the future. Should a positive result be found from such surveillance, the FSA will need to consider what action it could take to reduce the possible risks to consumers of venison. With this in mind, the FSA is seeking advice from SEAC on whether CWD

should be considered a risk to human health should it be found in UK deer. However, it was acknowledged that most of the information on CWD is derived from research on North American deer and there are few data on UK species or human health aspects.

17. Dr Debra Bourne (Wildlife Information Network) summarised the current knowledge of CWD. CWD is present in certain North American species of cervid (deer). It is the only prion disease known in free-living animals. In North America, there are concerns about the negative impact that CWD may have on free-ranging cervid populations and on the deer hunting and farming industries. Concerns have also been expressed about the possibility of CWD transmission to other types of livestock and to humans from consumption of infected meat. The disease was first evident in mule deer in a Colorado research facility in the early 1960s but it has since been found in other types of free-living and captive cervids (mule, white-tailed and black-tailed deer, and Rocky Mountain elk) in other areas of the USA and Canada. A small number of cases have occurred in farmed elk imported to South Korea from Canada. CWD has not been found in cervids in Europe but surveillance has been limited.
18. Dr Bourne explained that the origins of CWD are unknown. However, it may have arisen from a spontaneous change of PrP to a disease-associated form, from scrapie, or from an unknown source, but data on these possible origins are either absent or equivocal. Feed-borne or familial origins for CWD appear highly unlikely. CWD has been successfully transmitted to a range of non-cervid species by intracerebral inoculation. However, via the oral route, it has only been transmitted to cervids. The incubation period is generally more than one year. Following oral challenge, PrP^{CWD} is detectable in the gut associated lymphoid tissues before other lymphoid tissues or wide-spread accumulation in the central nervous system, although in many elk it is not found in the retropharyngeal lymph nodes and tonsils. Clinically, CWD is characterised by weight loss and behavioural changes, usually over a period of weeks or months. At the microscopic level, the nature and distribution of tissue lesions are similar to those found in scrapie. Definitive diagnosis of CWD is usually made on the basis of detection of abnormal PrP in brain or lymphoid tissues by IHC but western blot, ELISA and conformation-dependent immunoassay (CDI) tests have also been used.
19. Dr Bourne explained that CWD is transmitted laterally between animals, possibly via environments that become contaminated with

infectious agent. The agent might be shed from animals in the saliva, faeces or urine or as a result of decomposing carcasses. The possibility of some maternal transmission has not been ruled out. Although polymorphisms in the cervid PrP gene have been identified, the influence of these polymorphisms on susceptibility to CWD is unclear. It is possible that European cervid species may be relatively resistant to CWD, although red deer, which are closely related to elk, are more likely to be susceptible. There is no evidence for natural transmission to cattle or sheep co-habiting with CWD infected cervids. Inefficient transmission to cattle, sheep and goats following intracerebral inoculation, as well as the results of *in vitro* PrP conversion experiments, suggest a significant species barrier. In humans, there is no evidence of transmission from studies that examined possible links between consumption or handling of cervid tissues and human cases of prion disease. Additionally, the incidence of CJD in areas of the USA affected by CWD is similar to areas from which CWD is absent. Although, the results from *in vitro* PrP conversion experiments are equivocal, experiments in transgenic mice expressing human PrP, whilst incomplete, suggest some species barrier to infection of humans.

20. Members considered the possibility that CWD is present in UK deer. Surveillance of CWD in Europe is very limited with the most extensive European surveillance programme, in Germany, capable of detecting a one percent incidence of CWD. Thus, members agreed that, although it has not yet been found, it is not possible to conclude that CWD is absent in the European deer population. It was considered that some UK deer species may be susceptible to CWD, particularly red deer, which are a subspecies of elk. There are currently no data from transmission studies of CWD to European cervid species.
21. In response to a suggestion that all slaughtered deer could be tested in the UK, Dr Matthews noted that, although the number of deer slaughtered in the UK was small, it would be very difficult to test each slaughtered animal because of the practical difficulties in obtaining samples from all the animals killed in remote geographical locations. Members suggested that surveys of farmed red deer may be the most practicable way of determining whether CWD is present in UK deer because of the relatively high concentration of animals, the putative susceptibility of red deer to CWD, and the opportunity to observe these animals closely. Members also suggested that, given the experience of cross infection between farmed and wild cervids in the USA, it would be unlikely that CWD would be present in wild deer but absent in farmed deer. SEAC noted that EFSA had issued an opinion on

TSE surveillance in deer and members endorsed the EFSA opinion.

22. One member, who had worked with researchers in Colorado investigating CWD, explained that most cervid samples tested in Colorado were derived from hunter-killed animals and the incidence of CWD infection in these animals was very low with most infected animals being asymptomatic. Thus, it was suggested that in wild populations the apparent increased prevalence of CWD may reflect increased surveillance rather than a real increase in the prevalence of the disease. Dr Bourne agreed but pointed out that some American researchers were of the opinion that the incidence of CWD was increasing and the disease was becoming more widespread. Additionally, in enclosed populations of deer, the prevalence of CWD was much higher due to the relatively high concentration of animals facilitating greater exposure to the infectious agent. It was noted that deer are susceptible to stress and that this may influence the disease in farmed animals.
23. One member explained that some researchers in the USA had suggested that the prevalence of CWD could be modified by levels of trace elements in the environment, such as copper and manganese, which when absorbed could influence PrP conversion. The Chair asked whether the member considered that this theory might provide an alternative to lateral transmission as a mechanism of propagation of the disease. In response, the member explained that in a feeding study in elk, dietary copper had reduced the incidence of CWD in an experimental herd compared with a control herd. Thus, it is possible that trace elements could either reduce the severity of the symptoms or prevent infection. The committee noted that there was strong evidence for lateral transmission of CWD via the environment, from studies of cervids inhabiting paddocks previously inhabited by infected animals or contaminated with infected carcasses.
24. Members considered the possibility that CWD could have originated from scrapie. However, the differing properties of these prion diseases in strain typing bioassays, whilst limited in scope, do not support this hypothesis. It seems most likely that CWD arose from a spontaneous mutation of the endogenous PrP gene resulting in a disease-associated and horizontally-transmissible form of PrP.
25. Members noted that the pathogenesis of CWD is similar to scrapie. Abnormal PrP is found initially in the gut associated lymphoid tissue before spreading more widely within lymphoid tissues and then to

the brain. However, in some naturally and experimentally infected elk, an absence of abnormal PrP in the retropharyngeal lymph nodes and tonsils has been observed despite it being found in the brain.

26. Members asked whether there is evidence for multiple strains of CWD. Dr Bourne explained that a recent report had shown that samples from mule deer and elk had similar properties when inoculated into transgenic mice expressing cervid PrP although a further sample from a different mule deer had behaved differently. Thus, it is unclear whether multiple strains of CWD exist. Further studies to investigate this possibility were underway. Dr Matthews (VLA) indicated that there was some evidence of different CWD strains from CDI experiments.
27. The Chair asked whether diagnostic tests could distinguish CWD from other prion diseases both in the natural hosts and other species. Dr Bourne explained that strain typing bioassays and glycoform patterns in western blots had shown distinct differences between samples of CWD and other TSEs. However, because the number of scrapie strains which have been tested is relatively small, it is possible that CWD is indistinguishable from other prion strains. Additionally, because of a lack of samples, comparative experiments of CWD in non-cervid species have not been conducted. However, it was noted that certain antibodies against abnormal PrP appeared to be effective in analysis of samples from a range of ungulate species, including cervids. Members expressed caution on relying on glycoform patterns in western blots for strain typing analysis and considered that bioassays enhanced the reliability of strain typing TSEs.
28. In response to questions about the possible transmission of CWD to cows and sheep, Dr Bourne explained that transmission of CWD by intracerebral inoculation of cows and sheep was inefficient. In addition, an oral transmission experiment of CWD to cows, whilst incomplete, had not shown transmission of the disease after six years. Additionally, no signs of infection were found from surveillance of cows living in a CWD endemic area for a number of years.
29. In response to questions about the human epidemiological data, Dr Bourne explained that studies of young people with CJD had found no evidence of a link between CJD and consumption of venison from known CWD endemic areas and that there had been no unusual clinical or biochemical features in the analysis of these cases. One member added that a review of these cases by the

NCJDSU had concluded that they were indistinguishable from sCJD. However, it is not known what the clinical symptoms of a CWD infection of humans would be. Dr Bourne also noted that a study of three older men with neurological illnesses who were known to partake in “wild game feasts”, showed that only one of the subjects had CJD and that this was indistinguishable from sCJD.

30. Dr Bourne explained that the age adjusted death rates of CJD in the CWD endemic areas of Wyoming and Colorado were 0.8 and 1.2 cases per million people, respectively. Whilst members were reassured that there was no noticeable difference between the prevalence of CJD in these areas and other areas of the world, they expressed caution about drawing firm conclusions about the apparent lack of transmission to humans because of the possible long incubation period of the disease and the difficulty in detecting a low level of increase in such a rare disease. In addition, because comprehensive CJD surveillance in the USA had started relatively recently, it was considered possible that not all CJD cases had been identified. Members noted that UK surveillance of prion diseases incorporated an assessment of venison consumption and handling of deer.
31. Members asked what form of human PrP was expressed in the transgenic mice used in transmission experiments and whether preclinical signs of infection had been noted in the mice. Dr Bourne explained that this information was not yet available but understood that none of the mice had yet developed clinical disease. The Chair asked the Secretariat to contact the researchers to ask for further information. Members expressed caution about the interpretation of the findings from transgenic mice experiments as the results may be influenced by the expression level of PrP and therefore, may not accurately predict the human situation. Additionally, members noted that the results of *in vitro* experiments examining the conversion of human PrP by abnormal forms of PrP including PrP^{CWD} were equivocal and were difficult to directly extrapolate to the *in vivo* situation.
32. The committee noted that most of the imports of venison into the UK were from New Zealand, which had no reported cases of CWD. The UK imported very little venison from North America. It was noted that there are no specified risk material controls for venison but that tissues other than muscle are not normally consumed.
33. The committee noted that there are no known imports of cervids from North America to Europe that could act as a source of CWD infection to European deer. For this reason, members considered

that the TSE risk in European cervids is more likely to arise as a result of BSE in cervids from feed contaminated with MMBM prior to the MMBM ban followed by lateral transmission of the disease. The committee noted that a study to look at the potential susceptibility of red deer to BSE after ic or oral challenge had shown no signs of transmission of the disease but the study was at a very preliminary stage.

34. In conclusion, it was agreed by the Committee that, given the scope of the discussion and the limited data available, it would not be necessary for the committee to consider the issue at the next meeting. A draft position paper would be prepared and circulated for approval. The Committee noted that:

- the prevalence and geographical distribution of CWD appears to be increasing in North America.
- there is no evidence to suggest CWD is present in UK deer but surveillance data are limited.
- diagnostic tests are available which appear to distinguish CWD from other prion diseases, but are limited by the paucity of reference materials.
- it is possible that many UK deer species are relatively resistant to CWD, although the red deer, which is closely related to elk, is the species most likely to be susceptible. It is possible that trace metals or other environmental factors may affect the susceptibility of cervids to CWD infection.
- the origins of CWD are unclear. CWD is unlikely to have been directly derived from scrapie. Most likely CWD arose as the result of a spontaneous change in PrP but there is no direct evidence.
- there is good evidence that CWD is transmitted laterally between animals, possibly via contaminated environments, and natural transmission is sufficiently effective to maintain epidemics in both captive and free-living cervid populations. However, the precise mechanisms of transmission are unclear.
- the pathogenesis of CWD appears similar to scrapie. Therefore, some of the precautionary measures that have been applied to infection in sheep and goats may also be appropriate to cervids.
- there is no evidence that CWD can be orally transmitted to cows and there is some evidence to suggest a significant species barrier to infection of cows, sheep and goats.
- there is no evidence of transmission of CWD to humans from consumption of venison but data are extremely limited and it would be very difficult to detect a low level of infection.

Additionally, although there are few data, there is some evidence to suggest the presence of a species barrier to transmission to humans. Studies of transgenic mice expressing human forms of PrP may give more information about a possible species barrier.

- modelling studies of the geographical distribution and make-up of deer populations and of venison imports and consumption may help to inform assessment of surveillance programmes and exposure estimates.
- although a theoretical possibility exists, there is no evidence to suggest that BSE is present in UK deer. However, it is important to closely monitor the findings of an on-going study to look at the potential susceptibility of red deer to BSE.

ITEM 5 – HORIZON SCANNING

35. The Chair explained this agenda item had been included to give the assessors from DH, FSA and Defra an opportunity to provide SEAC with brief overviews of topics that might require the committee's consideration in the future.

Department of Health

36. Mrs Eileen Lawrence (DH) explained that protection of public health was the key priority for DH and this was reflected in the department's recently published research strategy on TSEs. Important research areas that may require input from SEAC in the future included the advancement of the treatment and care of vCJD patients, the development of diagnostic tests for vCJD, surveillance to provide more accurate estimates of the size of the vCJD epidemic and measures to reduce the risks of secondary transmission by medical procedures. As part of this work the Health Protection Agency (HPA) was in the process of setting up an archive of tonsil tissues for research and surveillance of human TSEs. Research was also in progress to develop a diagnostic test for abnormal PrP, as earlier detection of the disease might facilitate better treatment and prevent secondary transmission of the disease. Additionally, advisory groups had been set up to look at developing more effective methods of decontamination for surgical instruments and the effectiveness of changes to decontamination procedures. Furthermore, the National Institute for Clinical Excellence (NICE) was currently developing guidance, which would be available next year, on vCJD risks during surgery and the Committee on the Microbiological Safety of Blood and Tissues was continuing to look at the potential risk of transmission of vCJD from

blood and tissues. Although these groups were looking at specific measures, it is likely that aspects of their work would require risk analysis from SEAC.

37. In addition, DH would continue to ask SEAC's opinion on the implications of new research findings on the epidemiology of vCJD. For example, the recent research findings that suggested possible age and genotype related differences in susceptibility to vCJD. Similarly, SEAC's view may also be sought on research on other human and animal TSEs that may inform understanding of vCJD.

Food Standards Agency

38. Mr Alan Harvey (FSA) noted that there were a number of cross-cutting issues for FSA, DH and Defra such as the development of non-invasive TSE tests. Thus, there would be occasions where advice on a particular aspect of TSE science may be sought by more than one department. Mr Harvey explained that the Agency would continue to ask SEAC to carry out risk assessments on food safety issues to enable government to make risk management decisions. SEAC's view would also be sought on new findings on sheep TSEs and the theoretical possibility of BSE in sheep as well as the implications of new research on contingency plans to protect public health from emerging TSE risks. A subgroup comprising key FSA stakeholders and members of SEAC might also be convened to discuss emerging research results, which could inform contingency plans.
39. Mr Harvey noted that as BSE continues to decline across Europe, surveillance programmes and associated control measures may be reviewed and the FSA would ask SEAC for advice on any new proposals in these areas from the European Commission.

Defra

40. Dr Peter Barrowman (Defra) explained that Defra was working towards both a reduction of scrapie cases by 40% and eradication of BSE by 2010. It would continue to ensure that animal by-products such as tallow, were disposed of in an environmentally sound and safe manner. It was anticipated that advice from SEAC would be sought on aspects of this work. SEAC would also be asked to advise on the risks associated with possible future relaxation of various BSE control measures, such as Specified Risk Materials (SRM) legislation and the feed ban. In addition, Defra had recently initiated an independent review of BARB cases (BSE cases Born After the Reinforced Ban) and SEAC would be asked to

comment on the findings of this review. SEAC would also continue to be presented with the findings from Defra research into possible BSE in sheep and goats, the possibility of different strains of BSE, the resistance of sheep genotypes to scrapie and the 'atypical' scrapie cases.

41. The Chair thanked the assessors and requested that the departments continue to liaise with the secretariat to ensure that the committee had sufficient advance notice of issues that would require consideration by SEAC.

ITEM 6 - AOB

42. The Chair explained that at SEAC's 75th meeting, the FSA had agreed to notify the committee when a cattle bioassay study, to define the pathogenesis of BSE in cattle, would be terminated.
43. Mr Harvey informed the committee that the FSA planned to terminate the cattle bioassays it was funding at the VLA, both on grounds of animal welfare and to focus funding on research to develop non-invasive live animal diagnostic tests. Members were informed that the initial challenge groups in the cattle bioassay studies were reaching 8 years post inoculation (p.i.) and that the original proposal indicated that 7 years p.i. would be the anticipated end point for the study. Analyses by Wells *et al* provided at Annex 1 of SEAC paper 85/3 showed that termination of the studies at approximately 7 years p.i. would not result in any measurable loss of data. A culling strategy was planned to start in December 2004 and would be completed in March 2007 as each of the challenge groups reached 7 years p.i.. A series of tissues would be archived to include brain, spinal cord (cervical, thoracic and lumbar), distal ileum, Peyer's patches and tonsil. Members were asked to comment on the scientific rationale for termination of the study.
44. The committee was content with the scientific rationale for termination of the cattle bioassays but stressed the importance of archiving appropriate tissues for further study.

ITEM 7 - PUBLIC Q&A SESSION

45. The Chair invited members of the public who had submitted questions in advance of the meeting to ask their questions and then invited questions from the floor.

Question 1

46. With reference to the case of probable transmission of vCJD via blood transfusion, the committee was asked if there had been any control studies in subjects of a similar age and clinical condition to assess the possible presence of abnormal prion protein in spleen tissue.
47. On behalf of the committee, Professor Ironside explained that this particular patient had been traced through the Transfusion Medicine Epidemiology Review (TMER) study funded by DH. As part of this study, spleen tissue from post mortem of normal controls and patients with other neurological diseases had been performed and in none of these cases was abnormal PrP detected, although the cases were limited in number. Also, no abnormal PrP had been found in other DH-funded studies to examine the brain and other tissues collected from autopsies of elderly and younger individuals.

Question 2

48. In view of recent findings from studies of transgenic mice expressing forms of human prion protein, which suggested BSE infection may be influenced by polymorphisms at codon 129 of PrP gene, the committee was asked for data on the number and genotype of sporadic CJD cases, and if the pattern had changed within the last 15 years.
49. In answer, Professor Ironside presented information on sCJD deaths from 1985 to 29 November 2004 that indicated the number of sCJD deaths per annum in the UK was increasing, but explained that this was possibly due to better case ascertainment, particularly in the elderly. Comparable data have been obtained in European countries and Australia, which showed similar changes in the incidence of sporadic CJD. France, Germany and Italy had higher relative mortality rates for sCJD than the UK, over the period examined (1 Jan 2004 to 30 September 2004).
50. Professor Ironside explained that during the period 1 May 1990 to 29 November 2004 there were 756 sCJD cases (dead and alive), with genotype data available from 476 cases. The codon 129 genotype distribution was 65% MM (310 cases), 17% MV (80 cases) and 18% VV (86 cases).
51. Professor Ironside noted there had been increases in the VV and MV proportion of cases over time but believed this to be largely due

to increased surveillance in young patients, presenting with a variety of neurological signs and symptoms, with a higher proportion of VV or MV genotypes. Between 1 May 1990 and 31 Dec 1995, 75% of sCJD deaths were genotype MM (96 cases), 11% were MV (14 cases) and 13% were VV (17 cases). Between 1 Jan 96 and 31 Dec 2003, 62% of sCJD deaths were genotype MM (191 cases), 19% were MV (59 cases) and 19% were VV (58 cases).

52. Professor Ironside commented that in the UK, clinical, biochemical, pathological and genetic analysis was performed for each case of CJD. Additionally, material from many of the cases, particularly from younger patients, had been experimentally transmitted to mice to investigate the possibility that a BSE strain may be responsible for the disease, but so far this had been negative. However, it was not assumed that vCJD would necessarily be the only manifestation of BSE-associated disease in humans, particularly in those people with different genotypes of PrP. However, it was reassuring that the PrP western blot profile of the second blood transfusion-associated case in an individual of the MV genotype was clearly identifiable as vCJD and was similar to that found in MM genotypes.

Question 3

53. The committee was asked when a non-invasive blood test for vCJD would be available for the haemophilia community. The Chair referred to DH for comment.
54. Dr John Stephenson (DH) replied that a diagnostic non-invasive blood test was a research priority for DH. However, no test was currently available. DH was also in liaison with companies working on such tests. Dr Stephenson indicated that Professor Christine Lee at the Royal Free Hospital, London was co-ordinating the surveillance of haemophiliac patients in the UK and could be approached for further details.

Question 4

55. The committee was asked whether the ethical issues had been considered if a blood test for vCJD became available.
56. Dr Stephenson explained that the National Blood Centre was setting up a test assessment facility to prepare the blood services for the introduction of such testing. In addition, DH had asked the Health Protection Agency and the Nuffield Council for Bioethics to

set up a workshop to consider the ethical issues of blood testing for vCJD infection.

Question 5

57. The committee was asked if research on immune system reactions, which may be an early marker of TSE disease, was being pursued.
58. Dr Steve Dixon (FSA) explained that the FSA is funding work to search for metabolic biomarkers of TSE infection and to look at the use of erythroid differentiation-related factor (EDRF) as marker of TSE disease. Dr Barrowman indicated that results of a Defra funded metabolomics study of BSE infection at the Institute for Grassland Research may be available later this year. Dr Matthews indicated that an infra red spectroscopy TSE test is being validated by EFSA on post mortem tissue from clinically-affected BSE cases. If successful, the test would be evaluated using samples from animals with preclinical disease.

Question 6

59. In response to a question received in advance of the meeting about the case of possible BSE in a French goat, the Chair explained that this issue had been covered earlier in the meeting, under item 3 (paragraphs 12-14 above).
60. The committee had also been asked by the questioner if it endorsed the 26 November 2004 European Food Safety Authority (EFSA) statement on goat milk². The Chair replied that SEAC had not changed its view that goats milk from healthy animals is unlikely to pose a significant risk to human health, and that therefore the EFSA statement was consistent with previous advice from SEAC.
61. The questioner had also asked whether new EC legislation required that samples from goats and sheep that had tested positive for a TSE be tested by bioassay. Dr Matthews explained that from 31 January 2005 all cases in small ruminants that had initially tested positive would then be tested by discriminatory western blot or ELISA. If an abnormal result was obtained, the samples would be submitted to a ring trial using ELISA, western blot and IHC. Only if the outcome from all these tests was unusual would a bioassay be considered.

² Statement of the EFSA Scientific Expert Working Group on BSE/TSE of the Scientific Panel on Biological Hazards on the health risks of the consumption of milk and milk derived products from goats [E F S A | European Food Safety Authority](http://www.efsa.europa.eu)