SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

DRAFT MINUTES OF THE 23RD MEETING, HELD ON 5 JANUARY 1996 AT THE CENTRAL VETERINARY LABORATORY, NEW HAW

Present:	Professor J R Pattison (Chairman)	
	Dr R G Will (Deputy Chairman)	
	Professor J Almond	
	Mr R Bradley	
	Professor F Brown FRS	
	Professor J Collinge	
	Dr W D Hueston	
	Dr R H Kimberlin	
	Dr M Painter	
	Mr D B Pepper	
	Professor P Smith	
	Dr W A Watson	
	Dr D Matthews (MAFF)	Observers
	Dr A Wight (DH)	
	Mr T E D Eddy (MAFF)	Secretariat
	Mr M T Skinner (DH)	
In attendance:	Mrs M Wilson (BBSRC)	
	Dr Dukes (MRC)	
	Mrs T Gumhill (MAFF)	
	Mrs S Townsend (MAFF)	

A. APOLOGIES FOR ABSENCE

1. These were received from Professor Allen and Dr J Havercroft (MRC).

B. PUBLICITY

2. Professor Pattison welcomed the new members. There was a discussion on publicity and enquiries from the media in general and in particular on the outcome of SEAC meetings. It was agreed that statements made to the press should be clearly identified as personal views where they differed from those of the Committee. Members

should always be accessible to discuss their own field of expertise. Professor Pattison suggested that members should let MAFF/DH know when they have spoken to the media.

3. Dr Kimberlin asked whether it was the intention of the Committee to keep the minutes of the meeting private. Mr Eddy advised that the Government would not make the minutes available to the public unless the Committee felt it was appropriate. He pointed out that the interim research results discussed by the Committee were confidential and it would be unfortunate if these discussions were inhibited. Professor Pattison agreed. The Committee had access to confidential data, and if this confidence was broken the Committee had to accept that such data would no longer be forthcoming. Such a situation would seriously affect their effectiveness in advising Government.

4. Professor Smith felt that data that underpinned a decision made by the Committee would need to be made public. The interim results of the pathogenesis study were cited as an example. Mr Bradley explained that these were already made publicly available through the European Community's Scientific Veterinary Committee. It was agreed that a general decision could not be made on confidentiality as the matter was too complex and that items would need to be assessed as they arose.

5. It was agreed that the minutes would remain confidential. Individual members were, of course, free to continue to speak on the subject as they saw fit but the Chairman emphasised the point that the role of the Committee was to advise Ministers in the two Departments and that he did not intend to make public the Committee's conclusions until they had been conveyed to Ministers.

6. Dr Hueston advised that he was occasionally contacted by the UK press and found it difficult to comment on their questions as he did not have access to the articles referred to. He asked whether copies of press cuttings could be sent to him. Mr Eddy agreed that this could be arranged but pointed out that he had been swamped with cuttings over the last few weeks.

Action:Mr Eddy

C. MINUTES OF MEETINGS ON 8 SEPTEMBER, 4 OCTOBER AND 23 NOVEMBER 1995

7. The three sets of minutes were discussed in detail and a number of amendments were agreed. Revised minutes are appended.

D. MATTERS ARISING

Gelatin (SEAC 23/6)

8. Professor Pattison asked the Committee to confirm that the they were content with the previous advice they had given on gelatin, bearing in mind gelatin was derived from bovine vertebrae. Mr Eddy explained that the EC had provided for gelatin and certain other specified products to be exempt from the mammalian protein ban.

9. Dr Kimberlin felt there was no need for the committee to alter its advice. The key issue was the removal of spinal cord. As spinal cord was an SBO it should not be present in vertebrae being used for the production of gelatin. Additionally, because production techniques include degreasing and acid hydrolysis the degree of inactivation should reduce the risk from any small pieces of spinal cord remaining in the vertebrae to negligible levels.

10. Whilst Dr Hueston did not doubt the advice given by Dr Kimberlin he was of the view that the Committee needed more information. Professor Pattison considered that there was a need for a further discussion paper on gelatin prior to thorough discussion at a later meeting. It was suggested that the paper should cover two things:

(a) the nature of the gelatin industry in the UK with as much detail as we can give on the plants and methods used;

(b) a quantitative assessment, if possible, of the extent of inactivation expected from the processes used in the gelatin industry;

11. Dr Kimberlin agreed to help on b). He also told the Committee in confidence that the European Gelatin Manufacturers (GME) have commissioned their own research on inactivation during the manufacturing process and he recommended that MAFF should approach for release of the data in confidence. Mr Bradley agreed to assist MAFF in producing a background paper.

Action: Mr Eddy

MRM

12. Mr Eddy reported that the latest report on abattoirs dated 15 December showed two instances where spinal cord had been found

attached to carcases. One was on the 4 December where two carcases, which were the subject of deferred inspection, had been identified as containing spinal cord and one was on the 14 December where a tiny fragment (two mm long; so small that it may not have been visible when wet) was identified.

13. Professor Almond commented that it was not these instances that the Committee needed to be particularly concerned about. He was far more concerned about the amount of spinal cord, which he initially estimated to be between 10 and 20% , which gets smeared over the carcase and left on the saw due to inadequate cutting. He also felt that some of this material was later smeared on subsequent carcases, which were not necessarily bovine. Mr Pepper said that the normal procedure is for the saw to split the spinal column off centre so that the cord remains on one side. The cord can then be easily removed in one piece. He disputed the estimated 10 - 20%residue which had been suggested. Dr Will also reported on conversations with the son-in-law of the suspect CJD case who worked in a slaughterhouse. The son-in-law also worked in a slaughterhouse and had direct experience of cutting carcases in half. He claimed that this could be done reasonably well with young animals and with a new bandsaw blade, usually at the start of a working day. As the day wore on however, and particularly with older cows with harder bones, it became more difficult and cross cutting and mistakes did occur. He also felt that spinal cord was not always properly handled and occasionally missed the SBO bin and would end up on the floor where it might well be collected up for rendering rather than be treated as SBO. Mr Bradley also mentioned a different sort of saw which he felt was an even greater risk. Dr Painter also commented that a colleague of his, who was an EHO, thought that the Committee were "kidding themselves" if they thought that spinal cord was totally removed from all carcases. *Professor Collinge was extremely concerned to hear that spinal cord was being incompletely removed from a number of carcases.* He suggested research into new mechanical methods for removing spinal cord from carcases. Dr Will was of the opinion that there must be some way of determining the amount of spinal cord going through a slaughterhouse to ensure that all is accounted for. Mr Eddy advised that as part of the new SBO procedures in slaughterhouses an audit on the spinal cord was being carried out. Part of the new procedures is to weigh the spinal cords.

14. Dr Hueston suggested that the way forward was to use HACCP principles. There was a case for commissioning engineers to look at new technology in the slaughterhouse, but this would take a long while. In the meantime HACCP principles could be put in place. Mr Bradley

suggested that it would be useful if the Committee could see slaughterhouses operating procedures if they were to advise further on this issue. He also reminded the Committee of previous research done at Bristol Veterinary School using V shaped cuts to remove the spinal cord encased in bone and laser directed sawing. He would investigate the position. Dr Painter drew attention to the concept of ALARA in the nuclear industry (as low as reasonably attainable) and suggested that the matter should be considered with a view to minimising risks as far as practicable.

Action: Mr Eddy and Mr Bradley

15. Mr Bradley suggested that there might be a case for restricting the killing of cull cows to particular slaughterhouses with tighter controls, but Mr Pepper pointed out that this could lead to longer journey times and welfare problems. In order to maintain their current advice on MRM the Committee felt they needed to be reassured about the MRM process and the application of the SBO controls. Mr Eddy advised that it was still early days for the new MRM controls but pointed out that the controls had been applied to all MRM, they were not restricted to MRM produced for human consumption and that MRM plants processing bovine MRM were now required to register. Mr Bradley also pointed out that 80% of bovines slaughtered are under the age of 2½ years. The Committee agreed to consider the matter again at the next meeting.

Tallow

16. The subject of tallow arose in relation to the discussion on MRM. Dr Matthews briefly explained the tallow process and advised that the use of SBO tallow for human and animal food was banned. Professor Pattison requested that a paper on tallow be put forward to the Committee for discussion at the next meeting.

Action: Mr Eddy

Dr Dealler's Paper

17. Dr Kimberlin asked whether Dr Dealler's paper had been analysed. Professor Pattison advised that Mr Wilesmith had written a critique but that it was difficult to understand and that the paper would also need to be analysed by Dr Hueston. The Committee were of the opinion that it would be useful to have several critiques - in effect a peer review. Dr Hueston agreed that this suggestion would add more weight to SEAC's rebuttal of the paper (if that was in fact the outcome) and

offered to co-ordinate and analyse other critiques. The Committee suggested a number of candidates who could be asked to analyse the paper. Robert Curnow, Jack Cusick (ICRF), Paul Brown, Dr Dykhuizen and the Royal Statistical Society were suggested. Mr Eddy was asked to arrange for the analyses to be prepared.

Action: Mr Eddy

Blood Transfusions

18. Dr Collinge drew attention to Japanese research results from Tateishi (1985) which suggest that blood could be a vehicle for transmission of CJD in humans. Dr Will agreed to let members see a copy of a major new paper by Dr Paul Brown currently in press and offered to provide data to DH on CJD cases who were blood donors. Although recipients of blood from CJD cases could thereafter be traced through and monitored, the Committee felt that it would be inappropriate to notify them in view of the very small risk involved in relation to the stress caused. The Committee considered it important to record details of blood donations by patients who die of CJD.

E. Update on CJD Situation (Agenda item 8)

19. Dr Will reaffirmed that the incidence of CJD in dairy farmers in Europe showed an excess over the incidence for the population as a whole except in the Netherlands. There was no excess if data for all farmers were used.

20. He confirmed that there is now a CJD suspect in a 52 year old from York who had a history of having been an abattoir worker. The patient was exhibiting progressive cognitive symptoms simultaneously with ataxia. Dr Will's current view was that the patient was "no more than a suspect" at this stage and the EEG was non-specific. The patient worked in a mixed abattoir for 18 months in 1989, largely in the lairage, occasionally stunning cows, where he would also wash out the stunning pen and would not normally have worn gloves. He occasionally pithed animals but had much less exposure than other abattoir workers and was essentially a stockman. The son-in-law was not aware of any injury received in the abattoir that required medical attention. Most of this information was provided by the son-in-law who is also an abattoir worker, and would therefore have a very good grasp on abattoir practices and his father-in-law's job.

21. Professor Smith said that, with the figures provided by MAFF of 11,500 workers in the red meat slaughterhouse industry 30 per cent

annual turnover, and a potential exposed population of 60,000 over ten years, one would expect 0.2 cases over a five year period. He felt that it was not possible to come to any conclusions on the basis of this case alone even if CJD was confirmed. Nevertheless, taking into consideration the affected farmers as well, and even though the abattoir worker was in an apparently relatively low risk category, the "box" of "at risk" occupations was getting full compared to expectation on pure chance, and could not be dismissed. The Chairman agreed but reminded people that the case was only a suspect at this stage.

22. Dr Will reviewed the age distribution of cases. He continued to have no concern about the incidence of disease in those aged over 30 but the number of cases under 30 was worrying. Between 1970 and 1989 there had been no cases under 30 except for those due to growth hormone treatment. Since 1990 there have been four definites and one possible. These comprised the 17 and 19 year olds which were already published, a 29 year old diagnosed on the basis of cerebral biopsy, a 29 year old diagnosed post mortem and a 29 year old who was still alive and classified as no more than "possible". There were also a 30 and 38 year old confirmed and a 35 year old suspect, who now looks unlike CJD. In one of the 29 year olds and the 30 year old the pathology is unique with very extensive plaques in both the cerebellum and cerebral cortex and Dr Will considered there is a very high chance that these two are genetic.

23. Dr Kimberlin asked whether the lack of previous cases had been due to misdiagnosis but Dr Will thought this unlikely because the disease was unusual in the young. He had checked through 35 cases of suspect but negative SSPE and had found none which looked like CJD and no evidence to suggest that SSPE was being misdiagnosed. Other members were of the view that CJD in patients under 30 would not have been misdiagnosed because of the rarity of symptoms in this age category. When asked if he knew of a second case in an abattoir *worker* as mentioned in the press Dr Will stated that the 30 year old case had visited an abattoir for two days whilst a 38 year old case had worked in a butcher's shop for a year in 1975 and a 29 year old case had a husband who worked in an abattoir. He was unaware of any other cases suspected in abattoir workers and was not aware of any further teenage cases as recently alleged by Dr Narang. Dr Will reminded the Committee that if two of the cases in young adults were genetic then the figures were perhaps not so worrying at this stage, given the fact that there had been two in France although over a 15 year period, and two in Japan and other cases reported in the Netherlands and Australia under 30.

24. He told Professor Almond that he thought that was unlikely to be CJD. The longer she remained alive the less likelihood there was that she was suffering from CJD. Dr Will advised that mortality rates for CJD were 90% within 1 year, 95% within 2 years and 98% within 3 years. In conclusion Dr Will admitted that he could not prove that cases had been missed in the past and that was still a possibility but it would be unwise to assume that it was the only explanation. One problem was that there was some evidence of the reluctance of next of kin to agree to post-mortems in young patients which made diagnosis, particularly in the past, difficult.

25. Dr Will was not unduly concerned at the overall number of CJD suspect cases that had occurred in the under 30 age bracket, what he did find worrying was that all the cases had occurred over a very short period. Professor Collinge was extremely worried at the occurrence of this number of young cases in such a short period, which could suggest a link to BSE. He requested that a formal statistical analysis be carried out to assess this further. The committee concluded the situation demanded the continuation of the intensive monitoring of CJD.

F. Human Growth Hormone (hGH) and Scrapie (Agenda item 7)

26. There was discussion of a DH paper covering reports from Dr Milner suggesting that scrapie may have been responsible for hGH CJD cases. Equipment used to mince pituitaries prior to extraction of human growth hormone had also been used for the maceration of sheep brains. This was felt unlikely to be a significant factor since there was no evidence of scrapie ever having crossed the species barrier to humans; human growth hormone produced in other countries, including those without endemic scrapie, had also caused CJD in recipients. The Committee discussed the fact that material from some CJD cases in hGH recipients was under study. It was inconceivable that there had not been comparable failures in laboratory procedure in all other countries with similar problems and yet there was no suggestion that hGH had been infected with scrapie in this way elsewhere. The Committee did not, therefore, feel that this was something which was likely to be a significant factor. Transmission from humans, with no species barrier, was the most likely cause of all of the hGH derived cases.

G. MRC Workshop (Agenda item 3)

27. The final report of the Workshop on MRC Priorities for Research in the SEs relevant to Human Health, which was held on 19/10/95 was

tabled by Dr Dukes as SEAC 23/3. Dr Dukes told the Committee that MRC would welcome their comments. Although MRC had a policy of funding research into TSEs it had received few applications in the past. They still have interests in the field, but these overlap those of BBSRC and DH and to a lesser extent MAFF. The priorities identified in the report are broad and in general complement those of the other funding bodies. He explained that MRC are strengthening their Committee structures and are reviving the Murray Committee.

28. Professor Almond expressed his agreement with the report but saw an urgent need for liaison between MRC and BBSRC to address the overlap of interests. Mrs Wilson was in agreement with the document presented and felt that all that remained was to decide what should be funded by whom. Dr Dukes said that a meeting of funders is taking place on 31 January at which funding and departmental needs relating to strain typing and transgenics would be discussed. Professor Collinge said that he has a grant for transgenic work but not for strain typing. The subject of core funding of the Neuropathogenesis Unit (NPU) was raised. Dr Dukes told SEAC that the Neurosciences Board consider that NPU work should be dealt with no differently from other areas of important science and said that the research councils need to decide how to manage their resources. He felt that SEAC's interest should be to ensure that the science is not affected at the NPU, possibly by influencing the provision of funds for overheads not covered by project-based funding.

29. Professor Pattison expressed concern that research establishments would find it hard to manage if funding of the infrastructure was weakened. Professor Almond alluded to the redundancies to be announced that same day at the NPU. Dr Dukes explained that these were not due to the changes in MRC funding.

30. Dr Wight asked whether the list of priorities, which was long, would be ranked and whether SEAC should be asked to suggest priorities. The Chairman thought it would be helpful if this could be done. Dr Dukes thought that the 'priorities' would be better termed 'opportunities' and advised the Committee that the Neurosciences Board would take the matter further.

H. Research Update (Agenda item 4)

31. Dr Matthews presented SEAC 23/1, which was largely unchanged from the previous meeting, but gave a verbal update on the significant points of interest.

32. Epidemiology - a study of the age specific incidence table indicated a disappointing plateauing of incidence in animals born after 1990, although it was too soon to see if this was fully reflected in older age groups.

33. Epidemiology, cohort study - 44 animals were now confirmed to have had BSE in this study, a total of 16 others were dead and BSE negative. Fewer than 150 remained alive, with most slaughtered after their seventh birthday. Pathology was pending for these. Although it had previously been considered that the coding of the experimental animals could be broken at around this time for interim analysis of the results; given the small number of confirmed cases in the experiment the committee were advised that this was not considered necessary.

34. Pathogenesis - there was little further to report in this experiment as final results of bioassay of kill 5 were still awaited. Ileum was still the only tissue containing infectivity at this kill. Problems with the change from RIII to C57 Black mice between kills 5 and 6 were mentioned. Due to concerns about the longevity of RIII mice, and that insufficient numbers might survive to the negative end point, bioassays from kill 6 onwards have been carried out in C57 Black mice. These, being s7s7 mice, should have been equally susceptible to BSE but had been obtained from a commercial source, not NPU. Initial signs in this experiment, and in others at CVL, suggested that the CVL C57Bl colony may not be behaving as consistently as those at NPU.

35. Attack rate - definite clinical signs had now been seen in the 1g challenge group. Pathology was awaited.

36. Exposure of pigs to BSE - were there any policy consequences following the detection of infectivity in ileum, jejunum and cerebrum of clinically affected pigs challenged by IC/IV/IP route? In the oral challenge experiments, the pigs were still healthy at 66 months PI. In the scrapie oral challenge experiment, now 24 months PI, there were fears that the starting titre was lower than desirable, but titration was still in progress.

37. Embryo transfer experiment - all mouse bioassays with embryos and uterine flushings had now ended, but a few pathology results were outstanding. It looked as if there was to be no evidence of transmission.

38. Comparative bioassay - table 10 - with respect to spleen and lymph node challenges, all mice were now dead with no clinical or

pathological evidence of transmission, and the cattle were 35 months PI and healthy. In the challenge involving brain tissue, there were clear differences in sensitivity between mice and cattle, but the experiment was not considered sufficiently advanced to allow definitive interpretation. Dr Kimberlin expressed interest in the results so far. His calculations (based on the assumption that cattle listed as showing clinical signs would be confirmed histologically) suggested a 150 fold difference in sensitivity between cattle and mice at this stage.

39. Tissue transmissions - table 4. In view of the number of source animals used (all now listed in the table were available) and the number of mice surviving beyond a negative end point, the CMO was concerned that there might be a need to repeat some challenges. The Committee's views were sought.

40. Rendering experiments - table 9 - in the scrapie rendering experiment, while some mice remained alive in the bioassay, it was clear that all systems other than the batch pressure (natural fat) process (Chapter II in EC regulations) had failed to inactivate scrapie (and perhapsBSE) to a degree. Although the Committee might consider that there was sufficient evidence to interpret the experiment already and to advise on policy, it was an EC funded experiment and the results would also be interpreted by the EC Scientific Veterinary Committee sub-Group shortly.

41. Mr Bradley noted that there was no detectable infectivity in any nervous tissue up to 18 months post challenge in the pathogenesis study. With reference to the SEAC statement of 23/11/95 on the use of bovine vertebrae from animals over 6 months of age in the production of MRM, he asked if the Committee would support a statement to make it clear that the six months limit which had been recommended was based on operational practicalities rather than scientific data. The Committeee was prepared to support such a statement but not to go so far as to confirm the safety of CNS up to any particular age in the light of the preliminary evidence from the comparative bioassay.

I. Research Priorities (Agenda item 6)
(Dr Kimberlin and Dr Will were unable to stay for all the discussion)

42. Paper 23/4 was tabled at the meeting. Research priorities were discussed extensively, but incompletely, by the Committee. Dr Will told the Committee that the CJD Unit was under-resourced with respect to maintaining efficiency of surveillance. It had been funded to investigate 50 cases a year and had in 1994 investigated 115. The

Committee recommended that Ministers should ensure that the Unit has sufficient funds to allow it to carry on with its epidemiological studies.
ACTION: Dr Wight

43. The Chairman explained that MAFF had had its research budget for 96/97 increased by a million pounds and that the Committee had been asked to recommend areas to be covered. Some areas might be more appropriately funded by other funding bodies. The Committee reiterated the need for additional strain typing facilities to examine CJD, BSE and scrapie in order of priority and to develop transgenic mice for this purpose(see paragraph 28). It was also necessary to develop mice transgenic for the bovine PrP gene and to produce more models with the human PrP gene i.e. those with additional polymorphisms and copy numbers. Dr Collinge mentioned that he had applied to the Wellcome Trust for funding to expand his facilities and for extra staff and their decision was expected in February. The Committee placed considerable importance on directing some funds towards new facilities for strain typing to create additional capacity in this area. The Chairman wished to see the straintyping currently in progress using conventional mice continued in parallel with development and validation of strain typing using transgenic mice.

44. Mr Eddy advised that MAFF had prepared a summary of research that they believed was most important and would welcome SEAC's advice on the proposals contained in appendix 2 of SEAC 23/4. The Committee reviewed the high priority projects. On the highest priority, Project 1, bioassay of some tissues from the pathogenesis experiment by inoculation of cattle, it concluded that it would be sensible to test muscle, liver and kidney from both kill 8 and kill 5. The Committee suggested that the additional cost of testing tissues from kill 5 as well as kill 8 could be offset by not testing specified bovine offals from kill 3 as proposed. It agreed that project 9 (audit trail of cattle and sheep tissues from abattoirs) was urgent, while 12 (reassessment of performance of C57Bl mice in bioassay) and 6 (oral exposure of sheep to BSE - pathogenesis and subsequent transmission) were of slightly lower priority. Project 13 (longitudinal survey of pathology) was useful although the Committee wondered whether it justified the expense and whether it could be scaled down to provide money for other work.

45. The Committee also suggested that it might be useful to commission some further work about the cause of the epidemic and the explanation for the continuing number of BAB cases. Dr Matthews advised that Mr Wilesmith has been asked to reinterpret the original data from the case control study to see whether new cases in the study herds

had affected the significance of original results. In particular Mr Wilesmith was hoping to look at non BSE herds and feed mills but feed mills had not co-operated for legal reasons.

46. Further discussion would be necessary on research priorities once the Committee had had an opportunity to fully consider the paper (23/4) tabled at this meeting.

J. Questions put to SEAC by MAFF (Agenda item 5)

47. Mr Eddy explained that the Minister had asked SEAC for its views on a number of questions. He wanted to be able to say that the answers he was giving were those advised by SEAC and to publish them as such. The Committee agreed that it would be sensible to put together replies and that individual members might be asked to give some thought to individual questions with a view to circulating draft replies before the next meeting. The Chairman advised that it would be necessary to have a further meeting at the end of January to take these questions forward. He stressed the need to ensure that the agenda for this meeting was kept as short as possible to ensure that the Committee had sufficient time to form its view.

K. ANY OTHER BUSINESS (Agenda item 9)

48. It was agreed that meetings should be held at the end of January and during March.