FOR MEMBERS' USE ONLY

DRAFT OF 17 JULY 1998

(Comments as late for by end of August)

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

Minutes of the 51st meeting held on 15 June 1998 at MAFF, Tolworth.

Present

Members;	**Professor Sir John Pattison (Chairman)**	
	Dr R Will (Deputy Chairman)	
	Professor J Almond	
	Professor R Anderson	
	Dr C Bostock	
	Mr R Bradley	
	Professor A Ferguson	
	Professor H Kimbell	
	Dr M Painter	
	Mr D Pepper	
	Professor P Smith	
	Dr W Watson	
Technical Advisors:	**Dr D Matthews (MAFF)**	
	Mr J Wilesmith (CVL)	
Observers;	**Dr M Bale (HSE)**	
	Dr P Barrowman (JFG)	
	Dr A-M Coriat (MRC)	
	Dr L Heppell (BBSRC)	
	Dr A Leigh (DH)	
	Dr N Wingfield (JFG)	
Secretariat;	**Mr T Eddy (MAFF)**	
	Mr P Jones (DH)	
Also in attendance;	**Mr P Comer (DNV)**	**- Items 2 & 3**
	Mr J Spouge (DNV)	**- ditto**
	Mr A Hare (DH)	**- ditto**
	Mr J Townshend (DH)	**- ditto**
	Dr J Metters (DH - DCMO)	

ITEM 1 - PRELIMINARIES

1.1 The Chairman informed Members that the proceedings were being recorded to assist in the production of minutes. A transcript would not be produced but the record could be used by the Chairman to resolve disputes over the contents of the minutes.

1.2 The Chairman welcomed Dr Metters, Mr Comer, Mr Spouge, Mr Hare and Mr Townshend to the meeting. He went on to announce that following a request from the Joint Funders Group he had agreed that representatives from the MRC and BBSRC should be re-invited to attend meetings and welcomed Dr Coriat and Dr Heppell. Apologies were received from Professor Aguzzi, Professor Brown, Professor Collinge, Dr Goodfellow, Professor Hueston and Dr Kimberlin.

1.3 The Chairman offered the Committee's congratulations to Professor Kimbell on her professorship and to Dr Will on his imminent professorship. He informed members that a number of people known to the Committee had received honours in the recently announced Queen's Birthday Honours list, including Dr Moira Bruce of the NPU, who had been awarded an MBE.

ITEM 2 - RISK ASSESSMENT ON BLOOD (SEAC 51/1; 51/1A & 51/B)

2.1 The Chairman reminded Members that at the October meeting of SEAC the Committee had recommended to Government that it began to develop a strategy for the leucodepletion of blood and that a risk assessment should be carried out to help inform future decisions. DNV had been commissioned to carry out this work and their draft report had been circulated to Members (SEAC 51/1). The Department of Health had sought comments from a number of referees and a meeting had taken place a week earlier at which the referees comments (SEAC 51/1A) had been discussed with DNV. The Department of Health's Economics and

Operational Research Division (EOR) had also carried out some work on some scenarios for secondary transmission of nvCJD via blood (SEAC 51/1B).

2.2 The Chairman explained that Mr Comer would give a short presentation on DNV's draft report. This would be followed by a report by Dr Wingfield of the outcome of a meeting to discuss the referees' comments and then Mr Hare would be invited to present the EOR report. Members would then have the opportunity to seek clarification on the reports. Once all the reports had been presented there would be a discussion of the issues that had been raised.

Presentation by Det Norske Veritas (DNV) (SEAC 51/1)

2.3 Mr Comer explained that in his presentation he would concentrate on the highlights from DNV's draft report and indicate where comments from the referees had been, or needed to be taken into account. He explained that in producing this report it had been necessary to use assumptions for which there was no clear scientific evidence and he emphasised the limitations of the work because of the many uncertainties.

2.4 In his presentation Mr Comer set out the various factors that had been used to produce the report and copies of the slides that he used are attached as Annex A.

2.5 The Chairman asked members if they had any points on which they wished to seek clarification.

2.6 Members sought clarification in respect of the pooling of blood and in particular the fact that the report did not appear to support the seemingly logical view that if infected whole blood, where most infectivity was likely to be, went into a pool to be used to make blood products then there was a risk that infection would be spread among more of the population. Mr Comer explained that data on partitioning of infectivity into blood products had come from

the unpublished results of experiments conducted by Brown and Rohwer. These did not explain how infective material that went into a pool seemed to disappear.

2.7 Members reported that in their experiment Brown and Rohwer had successfully transmitted infectivity from one animal to another by transfusion, however, only in one animal out of a batch. It was, therefore, not clear whether this was an artificial or a real result. Although it was necessary to treat these unpublished results with some caution Members agreed that it appeared that infectivity in blood had been shown via intra-cerebral injection in an animal model. They agreed that for the purposes of DNV's work and further discussion it would have to be assumed that there was infectivity in blood. It was understood that Brown and Rohwer were in the process of repeating this experiment and looking at what happened at each stage of the production of Factor VIII.

2.8 Mr Comer agreed that he would need to discuss this matter further with the Bio Products Laboratory (BPL) and accepted the Chairman's suggestion that it would also be useful to discuss this matter with the researchers involved. It was noted that Professor Brown had been asked for comments on the DNV report but that none had been received.

ACTION: DNV

Expert Group comments SEAC 51/1A

2.9 Dr Wingfield gave a report of the meeting he had convened to discuss the report and the comments that had been received from the referees to whom it had been sent. He explained that the meeting had identified the following issues as major criticisms in the presentation of the report and some of the conclusions reached;-

i) The way in which the large number of uncertainties including the lack of epidemiological data and negative results from experiments on primates had been treated.

ii) Having accepted that there were so many uncertainties the conclusions presented in the report pointed to very firm outcomes that could not be substantiated. It was felt that rather than a specific outcome the range of possibilities should be explained that took account of the uncertainties.

2.10 In discussion members pointed out that although there may be populations of lymphocytes in the spleen and other lymphatic tissue, like tonsil and Peyer's patch, they did not necessarily always circulate in the blood stream. There were probably eight to ten routes by which lymphocytes trafficked but it was likely that most circulated no more than three times. The Chairman questioned whether it was necessary to differentiate between sub-populations of lymphocytes when attempting to quantify risks.

2.11 In summing up the conclusions of the meeting he had arranged Dr Wingfield said that it was thought that parts of the report, notably Chapter Three, detracted from the overall effect of the report. DNV had been asked to give further consideration to this matter. The pooling effect had also been identified as an area that needed closer examination.

2.12 The group had agreed that the report had been useful in identifying where the gaps in knowledge were and areas where further experiments or better information was needed, for example, experiments on primates, experiments involving spiked and normal blood, better data on patients who receive transfusions.

2.13 The group had agreed that there was a need to enhance good transfusion practice. Although the exclusion of donors who had previously received blood might have some benefits there were also considerable disadvantages, particularly relating to the continued supply of adequate amounts of donated blood.

2.14 In response to some of these points members explained that most of the plasma that was retrieved was disposed of; the majority of it is water. It was agreed that this would need careful presentation so as not to deter donors from giving blood.

2.15 Little was known about the recipients of blood, anecdotal evidence suggested that as many as 50 per cent of patients who received blood died within 18 months of receiving blood. It was accepted that there was a need for better epidemiological data. Members also referred to research that appeared to show that outcomes for some patients who receive blood during surgical treatment were worse than for those who did not receive transfusions.

Presentation of paper SEAC 51/1B

2.16 Mr Andre Hare from the Department of Health's Economic and Operational Research (EOR) Division was invited to present the paper. Mr Hare explained the basis of the work they had carried out and then went on to present the EOR paper. Copies of the slides that he used are attached at Annex B.

2.17 In response to questions from members Mr Hare explained that they had looked at scenarios for secondary transmission for nvCJD but had not considered other TSEs. They had assumed infectivity from 1989 but the approach they had adopted would enable other factors to be taken into account as they became clearer.

2.18 Members returned to the question of blood that is pooled to make blood products. After further discussion it remained unclear what effect the processing of blood had on reducing the level of infectivity. Other members questioned the robustness of the approach that had been adopted.

2.19 In many respects the EOR results were similar to those reported by DNV and reflected the wide range of uncertainties. The EOR work had also shown those areas where more work needed to be done. As better information became available it would be possible to do further modelling.

2.20 The Chairman thanked Mr Comer and Mr Hare for their contributions and thought that their reports would help the Committee have a more focused discussion.

2.21 The Chairman opened the general discussion by suggesting that the Committee had three issues to consider. Firstly, should the Committee recommend the leucodepletion of blood? Secondly, that there was insufficient information on which to make a decision - others may wish to decide whether leucodepletion should be carried out. Thirdly, conclude that the data suggests that leucodepletion is not necessary.

2.22 The issue of the potential risk from donors who had previously received blood was discussed. Members were informed that former recipients of blood were among the most assiduous of donors. The Committee on the Microbiological Safety of Human Tissues and Organs used in Transplantations (MBST) had considered this matter. They had concluded that as preventing previous recipients from giving blood would lead to an immediate crisis in the blood service they could not endorse this proposal. The MBST would re-consider this issue if SEAC thought it necessary.

2.23 Members were informed that the Chief Medical Officer had called a conference to discuss many of these issues and in particular to draw to the attention of the professions to the need to make better use of donated blood and the need to reduce the use of transfusion to those cases where it was only clinically necessary.

2.24 Members then discussed the recent announcement that plasma was to be sourced from outside the UK. It was explained that the Committee on Safety of Medicines reached this decision in the knowledge that there were alternative sources for this material. These is no similar alternative source for whole blood for transfusion.

2.25 The Chairman sought the Committee's views on the exclusion of previous recipients from continuing as donors. Members concluded that on the basis of the information that was

available any advantage that might be gained by the introduction of such a measure was far out-weighed by the disadvantages.

2.26 Members were also informed that it seemed likely the USA and Canada would announce shortly that they were to cease accepting blood from British donors. If this should happen then the question of the safety of blood would become a real issue in the United Kingdom.

2.27 Some members expressed the view that because of the many uncertainties and the likely cost involved a further option may be to wait a few more years by which time better data might be available as the results of further research became known.

2.28 Some members explained that leucodepletion would bring other benefits that would add to the overall quality of blood for transfusion. It was also pointed out that some EU countries had already taken action to leucodeplete blood. There was also a possibility that EU-wide action on the safety of blood and blood products might be proposed in the future. Other members felt that in light of the unknown numbers of people who might be incubating nvCJD, and the uncertainties involved, precautionary action was advisable. Members also discussed the possibility of using leucodepleted blood just for certain groups of people. After taking account of the practical difficulties of this approach the Committee rejected this suggestion.

2.29 In response to the need to take account of financial consequences of SEAC's decisions the Chairman explained that he had sought advice on this matter in the past. He had been advised that SEAC existed to advise the Government only on the scientific aspects of TSEs. He reminded members that some of the Committee's decisions in relation to the BSE epidemic had been considerably more expensive than those presently under consideration that were aimed at the protection of public health.

2.30 After further discussion including a proposal for the targeting of leucodepleted blood to certain groups members concluded that despite the many uncertainties it appeared that if

there were infectivity in blood, and it was appropriate to consider that there was, then it was most likely to be in lymphocytes. A practical solution, that was likely to reduce the risk, was the leucodepletion of blood. Members concluded that they should recommend this course of action to Ministers. In making this recommendation members recognised that it would be some time before all blood could be leucodepleted and that care would be needed in its implementation in order to protect the supply of donated blood.

ACTION: DH

2.31 In concluding the discussion on this item the Chairman asked if the DNV risk assessment was to be published. It was the intention that it should be published but before doing so it would be necessary to take account of the comments that had been received from the referees and those made by SEAC. Although no time-table for publication had been determined DNV were aware of the need to move with some speed.

ACTION: DNV

ITEM 3 - SPIKING EXPERIMENT ON BLOOD (SEAC 51/2)

3.1 The Chairman explained that this item was linked to the issue that had just been discussed. The Committee had recommended that there needed to be further research in this area and the proposal set out in SEAC 51/2 could be considered as falling within that recommendation. The Committee were being asked to consider what priority this proposal should be given.

3.2 Dr Wingfield reported to members that because of concerns within the Bio Products Laboratory about uncertainties with the animal model the proposal was still at a preliminary stage.

3.3 Members discussed the merits of the proposal. The view was expressed that as it presently stood the proposal appeared to duplicate work being done elsewhere.

3.4 The Committee concluded that they would need further detail before making any firm recommendation about the priority given to this proposal. They also indicated that they would wish to see how this proposal fitted in with other work already in hand, particularly in the USA and Canada.

ITEM 4 - UPDATE ON CJD AND BSE CASES

Update on CJD cases

4.1 Dr Will informed the Committee that the number of confirmed nvCJD cases stood at 26 and that there were a small number of possible cases awaiting neuropathology and a few more suspects. There was no evidence to date of an upward or downward trend in the incidence of the disease.

4.2 He advised the Committee of his concern that BSE in humans with a genotype other than methionine/methionine might have a different pathology from that which is currently recognised as typical for nvCJD. This concern had arisen because there was an apparent excess of sporadic CJD in the UK in people under 50 years of age compared with other European countries. Dr Will advised members that material from a wide range of cases had been provided to Dr Bruce for transmission studies in mice and to Professor Collinge for strain typing. Of the 84 cases which had been strain typed to date only those already recognised as nvCJD had shown the type 4 pattern.

4.3 Of the 4 cases of classical CJD in farmers in the UK, 3 had a methionine/methionine genotype and one an methionine/valine genotype.

4.4 Dr Will confirmed that there is not yet a discernible change in ratio between suspect and confirmed CJD cases, explaining that it is not possible to formulate such a ratio for nvCJD

cases as an nvCJD suspect cannot be defined. The CJD Surveillance Unit does monitor referrals under 50 years, however, and no change has yet been seen in the number of suspects in this category. An internet site is planned on which data on suspect CJD cases will be updated quarterly.

BSE Update - SEAC 51/3

4.5 Dr Matthews referred members to SEAC 51/3, an update on research results, and summarised developments for members:

PATHOGENESIS EXPERIMENT (SE1901)

4.6 In the BSE pathogenesis experiment assays of all kills up to and including kill 10 were complete. Assays from the 11th kill would be complete in December. No new tissues had tested positive, although trigeminal ganglion, which had been positive from the 9th and 10th kills had now also tested positive in a single mouse from the 11th kill.

4.7 Dr Matthews said that the 4 outstanding bone marrow assays from kill 10 were negative on histopathology but would also be checked by immunocytochemistry. The results of assays of bone marrow from kill 11 were anxiously awaited by policy makers and it was hoped that there would be results of histopathology if not of immunocytochemistry available for the July SEAC meeting.

ACTION: Dr Matthews

4.8 Dr Matthews was asked whether it was intended to look again at negative assays from earlier kills by immunohistochemistry, in particular specific tissues from kills immediately prior to those at which the tissues had assayed positive. He explained that evidence from CVL and NPU had shown that immunohistochemistry was not a reliable method of resolving assays unless there was other evidence of transmission such as clinical signs. The CVL were still refining their technology for the use of immunohistochemistry in this

connection and the intention was to wait until the assays on the final kill, kill 11, were completed and then to target negative assays in key tissues which had included "inconclusive" mice. Some tissues from kills either side of 30 months were already being re-assayed in cattle, some in RIII3 mice and spinal cord by the DELFIA test. It was expected that results from all strands of the re-assessment should be coming together by the end of the year.

COMPARATIVE BIOASSAY (SE1821)

4.9 In this experiment no more cases had been diagnosed in the cattle which had been inoculated intracerebrally with brain tissue. The cattle which had been intracerebrally inoculated with pooled spinal cord and lymph-node were still clinically normal 65 months post inoculation.

ORAL SCRAPIE TO PIGS (SE1822)

4.10 There was no evidence of transmission 54 months post exposure although two control animals had died of intercurrent disease. Bioassays were still underway in pigs that had been killed 24 months post exposure.

ASSAY IN CATTLE OF TISSUES FROM PATHOGENESIS EXPERIMENT (SE1824)

4.11 The list of tissues from the pathogenesis experiment that have been put into cattle has been expanded. Dr Matthews would reformat the data for the next meeting to enable the Committee to identify more easily how long each single tissue assay had been in progress.

ACTION: Dr Matthews

IC/ORAL CHALLENGE OF CHICKENS WITH CATTLE BRAIN TISSUE - SUB-PASSAGE AFTER 5 YEARS INTO CHICKEN AND MICE (SE1805/6)

4.12 The sub-passages were now 24 months post inoculation with no sign of disease.

been confirmed in an animal born after the SBO ban. Mr Wilesmith confirmed that the epidemic in cats is declining, although it does not yet appear to have finished and agreed to provide data on the epidemic curve in cats for the Committee. This information is already published in Hansard.

ACTION: Mr Wilesmith

GENERAL QUESTIONS FROM MEMBERS ON RESEARCH

4.16 With reference to the BSE attack rate study (SE1918) members asked whether the mean incubation period had been looked at as a function of dose. It was noted that there was no dramatic difference in incubation between animals which had received 300g. and those which had received 1g. and data on the fate of animals which had received lower doses in the new attack rate studies was awaited with interest.

4.17 Members were also interested in whether, in SE1918, clinical duration had been correlated to dose, with low doses possibly giving a longer clinical duration or intermittent clinical signs. Mr Wilesmith said that clinical signs would be retrospectively allocated at the end of the experiment, as they considered this would be more accurate and less prone to bias than if this was done on an ongoing basis. Members considered that such data could be very important in relation to possible silent infections. Dr Matthews explained that the higher levels of observation and lower levels of stress to which cattle in this experiment were subjected, compared to cattle on farm, were significant factors which should be borne in mind in comparing clinical duration data for naturally and experimentally infected cattle. Cattle from the first intracerebral challenge showed clinical signs as early as half way between exposure and death.

ITEM 5 - RATE OF DECLINE OF THE BSE EPIDEMIC (SEAC 51/4)

BSE PATHOGENESIS IN SHEEP (SE1929)

4.13 Oral challenge of Romney sheep with 5g of BSE infected brain. No evidence of CNS lesions from 1st interim kill (4 months post exposure). The full experimental design will be presented for the next meeting.

ACTION: Dr Matthews

ORAL EXPOSURE OF CATTLE TO UNTREATED SCRAPIE BRAIN AND MBM CONTAINING SHEEP BRAIN (SE1942)

4.14 This experiment was initiated in March 1998. The full experimental design will be provided for the next meeting.

ACTION: Dr Matthews

FSEs IN CHEETAHS

4.15 Members were advised that there have been 2 more cases of FSE in cheetahs. These were born in 1992, after the SBO ban. There have now been 8 cases in all: 5 born at Marwell, 2 born at Whipsnade and 1 in Ireland. 2 cases have occurred in litter mates, suggesting that the cheetahs are being infected during kittenhood. In view of the fact that cheetahs do not like to crunch bones it was considered unlikely that they had been fed cattle carcase remains containing brain or spinal cord. Mr Wilesmith has a further epidemiological investigation into cheetahs planned. Considerable concern was expressed at the high transmissibility of the disease to the species, with approximately 10% of the population of the UK in 1992 having died of the disease. This suggested that between 20% and 30% of cheetahs had been infected during the BSE epidemic. Mr Wilesmith told the Committee that it was not certain that this was in fact BSE but agreed that it was reasonable to assume this to be the case. Professor Collinge was putting material from cheetahs into RIII mice. The high incidence in cheetahs was contrasted with the low incidence in domestic cats, in which only one case had

5.1 Dr Matthews explained that SEAC 51/4 was not an epidemiological paper but a copy of a paper which had been put to the EU Commission which had been based on data provided by John Wilesmith. SEAC noted from the paper that the rate of decline in the BSE epidemic this year is lower than that seen in previous years. Up to the end of May, the number of reported cases was down about 19% on the same period last year, compared with reductions of around 41% in previous years. This suggested that there would be around 2,500 confirmed cases during the whole of 1988; a number slightly higher than had been predicted by the Oxford group or the epidemiology unit at the VLA. Data in the annex to SEAC 51/4, which showed no reduction in the number of cases occurring in 3 and 4 year old animals from the 1990/1 to the 1991/2 birth cohorts suggested that the exposure to infected feed had not reduced as much as expected from 1990/91 to 1991/2. The figures showed that the expected year on year decline in cases had resumed with the 1992/3 cohort.

5.2 The Committee were advised that the drop in the rate of decline could be more apparent than real, as the OTMS and selective culls had taken out animals in 1997 which would otherwise have gone on to develop disease, thus contributing to an artificially increased rate of decline last year.

Against the backdrop of a declining incidence of BSE, the decline in number of negative cases presented and slaughtered was also discussed. Various explanations for the drop were identified and discussed. These were:

- the possibility that veterinary officers now have more time to spend on clinical diagnosis and repeat visits resulting in increased recognition of discriminatory signs and fewer negative animals being put under restriction as suspect cases;

- BSE may no longer be the most likely differential clinical diagnosis and more cattle may be treated or destroyed rather than be presented as BSE suspects;

- it was theoretically possible, but unlikely, that a significant proportion of cases that were diagnosed negative earlier in the epidemic would have been found positive if different diagnostic criteria had been applied.

5.3 Mr Wilesmith told the Committee that the epidemic could now be broken down essentially into two parts: Born Before the Bans (BBBs) and BABs. The BAB epidemic is worst in the Northern Region and East Anglia. A disproportionate number of the cases from the 1991/2 cohort were occurring in East Anglia, particularly in Norfolk, but were not concentrated on particular farms. This suggested cross contamination with pig and poultry feed at local mills, which had indeed been found through the routine ELISA screening of cattle feed for the presence of ruminant protein. It was noted that this finding, although disappointing, reinforced the view that MBM was the source of the epidemic.

5.4 Turning to the BBB epidemic, Somerset was identified as a hotspot. This was thought to be related to the fact that there was a concentration of cull cow slaughter in the area, as it contained a slaughterhouse which specialised in exporting carcases of such animals to France. Their offals would have been rendered and consumed as MBM relatively locally.

5.5 The high sensitivity of the geographical information was stressed with regard to the confidentiality of the database. The point was also made that although some mills could clearly be shown to have had a problem with cross contamination, no renderers or feed manufacturers could be considered to have been completely exempt from responsibility for exposure.

5.6 Members considered that the data suggested important policy options for the selective cull, in terms of geographical focus and herds to be targeted, which could speed up the end of the epidemic.

5.7 Dr Matthews informed members that a decline in the percentage of negative cases was also occurring in Switzerland, and that this was believed to be largely due to improving

differential diagnosis. He also said that it was hoped to quantify the extent to which suspects were not being placed under restriction by submission of returns on such instances to Tolworth.

5.8 One member had seen information submitted to the OIE on BSE in the Channel Islands in 1995 born animals, and asked for further details of the methods of confirming cases in Jersey and Guernsey. Dr Matthews explained that, because of health and safety concerns regarding the removal of brains, Guernsey have not in the past confirmed clinical diagnoses of BSE by post mortem, although this is done with cases from Jersey. Guernsey (via the UK authorities) had recently reported to the OIE 2 cases of BSE born in 1995, which had caused considerable concern to MAFF as no GB cases had been reported. Dr Matthews had subsequently discussed these cases with the Guernsey States Veterinary Officer who had attended the animals. He had said that he had considered it unlikely that they were suffering from BSE, but they were dangerous animals and had nevertheless been recorded as BSE suspects and destroyed. An agreement had been reached for the whole heads of any further such cases to be submitted to the CVL for brain examination.

ITEM 6 - RECORDING AND FORMAT OF MINUTES (SEAC 51/5)

6.1 **SEAC 51/5** contained a proposal that meetings should be audio-recorded, that an index of each tape should be produced and held by the secretariat for reference, and that written minutes should be produced which are unattributable to individual speakers apart from those who are making presentations. The Chairman said that he favoured the proposal and hoped that its adoption would lead to faster production of minutes. Members were asked for their views. The possibility that full transcript of meetings could be produced by the company who are producing the record of the Public Inquiry was discussed. Members were impressed by the technology, but recognised that checking of the transcript, which needed to be done before a final version could be produced was very time consuming. It was also thought that the system might be prohibitively expensive. Members voted unanimously in favour of the formal proposal.

ITEM 7 - OPENNESS: PROPOSAL FOR A WEBSITE (SEAC 51/6)

7.1 The Committee considered a proposal (prepared by the Secretariat) for a SEAC website. The suggestion had arisen following the discussion at Frensham Ponds where it was agreed that it would be useful for some output from the meeting to be put in the public domain. The Chairman thought that a website could be the beginning of an ongoing information system, supplementing the public statements, and which would describe the work undertaken on routes of exposure in the context of the work of the Committee. The Chairman thought that this would be preferable to providing a one-off report on risk assessment from the Frensham Ponds meeting.

7.2 One member thought it important to put the Committee's uncertainty into the public domain, in a form selected and approved by the Committee and considered that a website would be the best way of disseminating information widely, cheaply and quickly and would also attract a younger audience. Another member agreed strongly with the educational importance of a website, quoting two presumptuous and misleading statements from the Daily Telegraph editorial of Thursday 11 June.

7.3 Dr Metters was encouraging: SEAC was seen as a good example, promoting the current philosophy of improved openness of advisory Committees.

7.4 Concerns were expressed about the resource implications of setting up and running a website: members anticipated that feedback would be high and had reservations unless extra personnel could be provided.

7.5 The Chairman said that consideration needed to be given to the level of material to go on a website. The aim should be to provide a general upgrading of people's understanding of the entire subject. Consideration had been given to updating the 'blue book'; this could be

superseded by a commitment of the resources instead to the setting up and running of a website. It was suggested that links to other sites should be integral to a SEAC website, thus reducing the need for expanded sections.

7.6 The Chairman said that the next stage would be to seek Ministerial approval for a) the concept and b) extra resources.

ACTION: Secretariat

ITEM 8 - MINUTES OF PREVIOUS MEETINGS, MATTERS ARISING AND CHAIRMAN'S CORRESPONDENCE

Minutes of previous meetings

Meeting of 23 May 1997

8.1 The Chairman explained that the note of the discussion on the cattle/human species barrier for BSE in these minutes had proved very difficult to agree. To resolve the problem he had added paragraph 22 to explain why the note of that agenda item had been unusually detailed. The minutes were cleared.

Meeting of 2 December 1997

8.2 The minutes were agreed subject to the following amendment: paragraph 26 line 12: reinstate the word "advice" which had been inadvertently deleted.

Meeting of 12 January 1998

8.3 The minutes were agreed.

Meetings of 8 February 1998 and 9 March 1998.

8.4 The Chairman decided that the two sets of minutes before members should be considered to be agreed unless any comments on the drafts were sent to Mrs Townsend at MAFF by 29 June.

Matters Arising

SURVEILLANCE FOR EVIDENCE OF BSE IN OTMS CATTLE - SEAC/INF/51/31

8.5 Members were asked for their views on a proposed study to survey OTMS cattle for evidence of BSE. A draft study design, subject to the securing of funding, was tabled for the Committee's approval (SEAC/INF/51/31). Dr Matthews explained that the study had originally been planned to give policy makers an idea on how much pre-clinical BSE there may be in the national herd, to inform future discussions on the possible rolling back of measures. However, the study would also provide a useful preliminary study into the possible existence of a sub-clinical form of the disease, although its scope for this purpose would be limited. The proposal could not yet be precisely costed as some of the companies approached to submit bids for testing the samples had not yet replied, but a rough estimate was that the study would cost between £1 million and £1.8 million.

8.6 Mr Wilesmith said that the expectation was that there would be up to 5,000 animals with pre-clinical infection out of the 750,000 adult animals being slaughtered in the year (an incidence calculated at about 0.6 - 0.7%). Some members considered that a finding, in the proposed study, of significantly more cases than expected would highlight the possibility that some of the infections could be a sub-clinical strain. Dr Matthews warned members that the proposed study would be of very limited value in the search for sub-clinical BSE as it might not be targeting the right tissues, and even if it did they might not produce PrP BSE.

8.7 The Committee were told that to detect a prevalence of 0.1% with a sensitivity of +/- 0.1% the proposed study would need to investigate around 4,000 animals. If significant slippage in the start date, planned for August this year, could be avoided the sample would include animals from the selective cull.

8.8 The heads of cattle, mostly killed by captive bolt, would be collected from abattoirs involved in the OTMS slaughter (there are currently 22), for submission to Veterinary Investigation Centres (VICs). For logistical reasons the Orkneys and Northern Ireland would be excluded from the survey. Samples of cervical spinal cord, brain stem and cerebellum would be extracted at the VICs via the foramen magnum and these would be sent to the CVL for aliquoting and onward submission to the testing laboratories. Members suggested barbiturate overdose should be used to kill the cattle, instead of captive bolt, so as to preserve the brain structure, and improve the quality of the possible analyses, but Dr Matthews explained that disruption to the slaughterhouse routines would not be acceptable, or even justifiable, bearing in mind the restricted scope of the study.

8.9 Three companies had been approached about testing. They were Enfer Scientific, Prionics and E G & G Wallac (DELFIA test to be done at VLA). None of their tests had been fully validated and it was known that their performance varied significantly with target sites, the method of preparing samples and antibodies. Members considered the advantages and disadvantages of the various tests and the range of tissues which should be sampled. It was thought that if diagnostic features for infection could only be detected very close to the onset of clinical signs, the study would not be very helpful. Dr Matthews said that Dr Hope of the NPU had studies underway on tissues from the pathogenesis experiment which were critical to this issue. Tonsil and spleen were suggested as possible additional tissues for sampling, with a view to providing data which might be useful with regard to the possible existence of a sub-clinical strain of BSE.

8.10 The age of the animals to be sampled was also considered to be very important. The current draft experimental design contained no proposal for targeting animals of known age, as

OTMS animals were only subject to an age declaration by the farmer which might be inaccurate. It was suggested that the choice of pedigree animals would overcome this problem, as their ages were known and they would be likely to be older than the average OTMS animal at slaughter, which would be an advantage for the study. The intention was to confine the sampling to dairy animals.

8.11 In view of the current spatial clustering of BSE cases members suggested that a geographical element to the study might be useful. Mr Wilesmith told SEAC that the origin of the animals would be known, but it was recognised that this would not confer the same advantages as the targeting of particular areas.

8.12 The Committee concluded that this research was of high priority, and acknowledged the wish to get it started in August if possible. The Chairman considered that further thought should be given to the details of the animals to be tested, the tissues to be sampled and the tests to be employed, and requested that the issue should be taken forward in correspondence.

8.13 In the course of the discussions on research into pre-clinical and sub-clinical BSE, members asked about a Swiss study of clinically normal animals from the same cohorts as animals in which BSE had been confirmed. The study by Bruno Oesch et al, recently reported in the New Scientist, showed that 6 of the animals sampled were infected with BSE although clinically normal. Mr Wilesmith told members he considered that they overestimated the incidence of BSE being detected as, in his opinion, the wrong denominators had been used. Dr Matthews had a copy of Dr Oesch's report on the cohort sampling and test validation done in Switzerland and had asked Dr Oesch for permission to copy the paper to SEAC. He had not yet received a reply. He was able to tell members, however, that the Swiss Reference Laboratory results of histopathology and immunohistochemistry had found 6 animals positive which were clinically normal whereas the Prionics Western blot test had picked up 4 of these, but had given positive results on 2 samples which had been negative on histopathology and immunohistochemistry.

Chairman's correspondence

8.14 There was no Chairman's correspondence for discussion.

ITEM 9 - ANY OTHER BUSINESS

9.1 No other business was discussed and the meeting was closed at 5.05 p.m.

Secretariat June 1998