



SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE
Final Minutes of the 75th meeting held on 11th September 2002

At

The Queen Elizabeth II Conference Centre
Broad Sanctuary
Westminster

London Members:	Professor P Smith (Chairman)	
	Professor J Ironside (Deputy Chairman)	
	Professor R Anderson	
	Professor C Bostock	
	Professor G Bulfield	
	Professor R Carrell	
	Dr D Cunningham	
	Mr P Jinman	
	Professor H Kimbell	
	Professor C Masters	
	Professor I McConnell	
	Dr J Safar	
Technical Advisors:	Mr P Soul	(Defra)
	Dr H Gates	(Defra)
	Dr I Malik	(DH)
	Ms A Conroy	(FSA)
	Dr S Dixon	(FSA)
Observers:	Dr A Allman	(BBSRC)
	Dr P Crook	(EA)
	Dr K Finney	(MRC)
	Dr J Nielson	(HSE)
	Dr N Coulson	(Defra)
	Dr M Simmons	(NAW)
	Professor J Wilesmith	(VLA)
	Miss K Dell	(FSA)
	Mrs M Holt	(DH)
Secretaries:	Dr C Boyle	(Incoming Secretary)
	Dr M Bailey	(Defra)
	Dr R Jecock	(DH)
	Mr D Carruthers	(FSA)

Secretariat:	Dr R Pugh	(Defra)
	Dr A Leigh	(DH)
	Mr M Hall	(DH)
	Dr I Hill	(FSA)
	Dr C Ravirajan	(Defra)

Also in attendance:	Professor J Wilesmith	
	Professor H Dalton	(Defra Chief Scientist)
	Dr D Matthews	(VLA) Paper 75/5
	Dr N Gill	(Chair, SEAC Epidemiology Sub-Group) Paper 75/3
	Professor J Lowe	(University of Nottingham Medical School) Paper 75/3
	Mr N Dean	(DH) Paper 75/3
	Miss S Osbourn	(Home Office) Paper 75/3
Mr G Wells		

Item 1 – Chairman’s Introduction

- 1.1 The Chairman welcomed Members and the public to the open meeting. For the benefit of the public, he began with a brief explanation of the function and remit of SEAC.
- 1.2 The Chairman explained that the Committee currently had 13 Members who were independent experts in their own fields. Members were selected in accordance with the required public appointment procedures.
- 1.3 The Chairman informed the public that SEAC had a new website at www.seac.gov.uk. Previously information on SEAC had been contained within the Defra website. Discussion papers for future meetings will be placed on the website prior to each meeting.
- 1.4 The Chairman explained that it had been decided to hold committee meetings in public to provide an opportunity for the public to observe the Committee at work and to see the process of how an independent scientific advisory committee discusses and debates issues in order to formulate advice to Government.
- 1.5 The Chairman stressed that open committee meetings were first and foremost, business meetings, and that the public were invited to attend in an observer capacity only. The Chairman requested that if a member of the audience wished to raise a specific point they should do so at this meeting during the allotted Q&A session or by writing to the SEAC Secretariat after the meeting.
- 1.6 In respect of the date chosen for this meeting, the Chairman explained that it had been organised before the events of September 11th last year. The Chairman noted that he would be asking the Committee to observe a minute’s silence at 1:46pm in remembrance of events of September 11th 2001.
- 1.7 The Chairman asked Members and the public to note that a Q & A session had been allocated for this meeting. This had been done because there was a similar session at the first open meeting a year ago and this was the first meeting after which all meetings of the committee would be open. He pointed out, however, that such a session would not form a regular part of the agenda for future meetings, but would be scheduled on an occasional basis, due to the pressures and time constraints on SEAC’s agendas.
- 1.8 The Chairman noted that paper 75/4, concerning the recent reviews by the Office of Science and Technology and the Food Standards Agency on Codes of Practice For Scientific Advisory Committees, had been withdrawn due to pressures on the agenda. He confirmed that it was planned that the paper would be discussed at the next meeting.
- 1.9 The Chairman introduced Dr Catherine Boyle, who had been appointed as the new SEAC Secretary. He explained that the Secretariat was in the process of being reorganised to create an independent unified Secretariat that would work closely with the sponsoring departments.

- 1.10 The Chairman thanked the out-going Secretaries: Mandy Bailey (Defra), David Carruthers (FSA) and Rowena Jecock (DH), for their important contributions to the work of the Committee during their terms of office in support of SEAC.
- 1.11 An apology for absence had been received from one Member, Professor Adriano Aguzzi.

Item 2 – Approval of Draft Minutes from 13 June SEAC meeting (SEAC 75/1)

- 2.1 Members considered the Minutes from the previous meeting in June. These had been published in draft form following the last meeting and released at the time of the press briefing. They were subject to any corrections and final agreement at the present meeting.
- 2.2 The Chairman brought to the Committee's attention a letter that had been received from Dr Stephen Woodgate, the Chairman of the UK Renderers' Association Technical Committee. The correspondence raised issues with respect to the portion of the minutes concerning the committee's discussion on intra-species recycling, in particular the item on tallow.
- 2.3 The Renderers' Association did not agree fully with the conclusions drawn by SEAC, particularly with reference to the statement detailed in paragraph 7.3 of the minutes. The Committee had been informed that most UK tallow is used in soap manufacture. The Renderers' Association had challenged this statement, stating that only 5% of UK tallow is used in soap production. Dr Woodgate stated that the splitting and distillation of tallow for oleochemical production utilised approximately 25%, the food industry utilised 15% (e.g. as a frying, medium and shortenings) and approximately 50% is used as a renewable fuel in place of oil, gas or coal. The Chairman proposed that a footnote be added to the minutes, setting out the information provided by Dr Woodgate. Members agreed this.
- 2.4 Apart from the inclusion of other minor amendments, Members agreed the Minutes. A final version would replace the draft version on the SEAC Webpage.

Action: SEAC Secretariat

Item 3 – Science in Defra – Implications for the management of TSE Research

- 3.1 Professor Howard Dalton (Defra's Chief Scientific Advisor) presented this item. He welcomed the opportunity to respond to the review of Defra-funded research and surveillance on TSEs, which was chaired by Professor Ian McConnell¹; he also took the opportunity to explain his role in Defra and strategies that were being formulated to enhance the quality and use of science within Defra.

¹ Defra TSE Research and Surveillance Year 2000 Review

- 3.2 Professor Dalton informed the Committee that a wide-ranging review of the organisation of the support and use of science research in Defra has been established. The aim of the review is to address objectives set by Ministers, which will build an organisation giving a much higher importance to science activities. It also aims to respond to external requirements which have emerged, for example, from the Phillips Inquiry Report and the Office of Science and Technology Guidelines on scientific advice and policymaking.
- 3.3 Professor Dalton explained that Defra's vision for science is to create a Department which has gained the trust of the public, and respect of the scientific community, whilst at the same time delivering science which will inform evidence based policies. In order to achieve this, the 'challenge function' of the Chief Scientific Advisor (CSA) is seen as crucial, and will seek to ensure that science programmes are fit for purpose and of a high quality. To this end, a Scientific Advisory Council is being set up to assist the CSA in the 'challenge function'.
- 3.4 As part of the 'challenge function', all Defra funded research programmes are subjected to regular review by independent panels of scientists. In addition, the TSE Research Unit has been operating a system of external peer review for research proposals since 1999. Further to the recommendation of the review report¹, this system is now being formalised by the formation of a Research Programme Panel. The panel will comprise up to 12 independent scientific experts, including at least one statistician who will advise on experimental design. It is anticipated that this panel will be able to receive proposals by the end of 2002, and all proposals will be peer-reviewed. Ad hoc subsidiary peer-review panels will be set up whenever there is call for research proposals in an area which is outside the collective expertise of the Programme Panel. The output from the subsidiary panels will feed into the Programme Panel.
- 3.5 The Programme Panel will work with the TSE Research Unit to assist in the co-ordination of the Research Programme. Members were informed on Defra's plans to co-ordinate the TSE Research Programme with that of other national and international funders. This will be achieved by the continued participation in the UK Joint Funders' Co-ordination Group, the High Level Committee, and representation on the EU Expert Group for TSE Research. More recent contacts with the United States Department of Agriculture (USDA) will also be developed.
- 3.6 In addition, the TSE Research Unit, with its detailed knowledge of the Research Programme, will continue to be proactive in effecting collaborations between interested parties. Members were informed that the Defra funded research programme is now an international programme, with projects in the UK, Europe and the USA. Meetings and workshops are also organised to encourage collaboration. These include the bi-annual UK Joint Funders Workshop, as well as bespoke workshops organised by Defra on specific topics (e.g. TSEs and the environment, and the use of mass spectrometry and NMR in diagnostics).
- 3.7 The promise of quality assurance on the science from a potential contractor is very important to Defra. Members were informed that the Science Directorate, in
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combination with the Office of Science and Technology (OST) and other Government departments, is in the process of establishing a strategy for quality control for Government funded research.

- 3.8 The Committee was informed that Defra viewed effective communication of science as very important in achieving the aims of 'Science in Defra' initiative. The review report noted that publication rates were variable, and whilst the production of high quality publication is important, it was recommended that other methods of disseminating information were investigated. The Committee was informed that a list of all current and historical projects funded by the UK Joint Funders is listed on the MRC website:
www.mrc.ac.uk/index/current_research/current-tse_portfolio_search.htm
- 3.9 In addition to the release of final reports of research projects on the Defra website, the TSE Research Unit (Defra) is planning to develop a website to include a summary of the state of knowledge of science in TSEs, research questions currently being addressed and any further areas which require research.
- 3.10 In agreement with the review report, Defra shares concerns regarding the recruitment and retention of scientific staff within the field of TSEs. The Committee was informed that, although Defra does not operate a PhD studentship scheme, requests for funding PhD studentships within research project proposals would be welcomed. In addition, the TSE Research Unit would keep a watching brief on Defra's ongoing Veterinary Research Fellowships, and assess the merit of such a scheme for TSE research.
- 3.11 Finally, the Committee was informed that, in response to the review report regarding biological samples, Science Directorate is setting up an Independent Archive Advisory group (IAAG). This group will comprise independent experts, and representatives from Science Directorate (who fund the archive) and the Veterinary Laboratory Agency (VLA), who manage the archive. IAAG will advise on release of tissues, quality control and publicity for the archive.
- 3.12 The Committee welcomed the steps taken to address the recommendations arising from the review – particularly the 'challenge function' and the strategies for wider dissemination of research results. The provision of information in lay terminology was also considered to be important. The Committee suggested that there should be improved co-ordination between research on animal and human health.
- 3.13 The Chairman concluded by welcoming the opportunity to be updated on the progress of the science in Defra initiative, and the progress of the Defra funded TSE Research Programme.

Item 4 - BSE cases born on or after 1 August 1996 (BARB cases) (SEAC/INF/75/24)

- 4.1 Professor John Wilesmith provided the Committee with information on preliminary epidemiological analyses of the first 17 cases of BSE born after 31 July 1996. These cases are referred to as BARBs (**B**orn **A**fter the **R**eal **B**an). This date corresponds to the time at which mammalian MBM could no longer be fed to any

farmed livestock and, following the recall of any stocks on farms, it became an offence to possess mammalian MBM on premises where livestock feed is used, produced, prepared or stored.

- 4.2 Of the 17 cases of BSE, 16 cases were born in Great Britain and the remaining case in Ireland. Eight of these animals were initially detected as possible clinical cases, 7 as a result of screening slaughtered casualty animals and one was an apparently healthy animal slaughtered in the Over Thirty Month Scheme (OTMS).
- 4.3 The age at onset of clinical signs of BARB cases was higher (57 months) than that of BAB² cases (43 months). Also, the first 20 BSE cases in the previous 12 month birth cohort to BARBs (1 August 1995 to 31 July 1996), had a similar mean age of onset to BABs.
- 4.4 None of the dams or siblings of the BARB cases had succumbed to BSE, and BSE had never been reported in 4 of the 16 natal herds. In addition, for four of the cases, BSE had not been suspected in the four natal herds.
- 4.5 The study showed that the geographical distribution of BARB cases was different from that of BAB cases – which had previously been linked to cross contamination of cattle feed in mills which also processed pig feed. The greatest incidence of BAB cases occurred in eastern England. In contrast, the incidence of BARB cases was more widespread, with predominance in counties in which dairy herds were concentrated.
- 4.6 Professor Wilesmith was of the view that contamination of feed might explain the aetiology of disease in BARBs. He speculated that imported feed could have been cross-contaminated with mammalian MBM, as the ban on feeding mammalian MBM in the EU was not put in place until January 2001. Cross-contamination of feed ingredients could occur during handling, storage and transport. As mammalian MBM is imported for the manufacture of pet food, this could represent another potential source for cross contamination.
- 4.7 The Committee was informed that the collection of epidemiological data will continue, together with further tracing of feed ingredients to examine common links and sources. Case-control studies may also be performed.
- 4.8 The small numbers of BARB cases to date was considered to be indicative of a much reduced rate of transmission. The Committee acknowledged that the cross contamination of feed is a plausible hypothesis. However, they considered that the possibility of environmental transmission could not be eliminated on the basis of the current evidence. In addition, previous work investigating whether disease can be transmitted by means of embryo transfer has shown that embryos taken from BSE infected cows and implanted in TSE free recipient dams, did not cause

² In the UK it has been illegal to feed ruminants with ruminant derived protein since July 1988 and to feed any farmed livestock, including fish and horses, with mammalian meat and bone meal (mammalian MBM) since 04 April 1996. Any animal born after July 1988 is referred to as a BAB case (born after the ban) and any animal born after 1 August 1996 is referred to as a BARB case (born after the real ban).

disease in either the recipient dam or the resultant offspring. However, this experiment does not demonstrate that vertical transmission, in the form of perinatal transmission, in cattle does not occur, and therefore Members considered that maternal transmission could not be ruled out. Rare differential genetic susceptibility to very low levels of BSE infectivity in feed or the environment was also an hypothesis that could not be ruled out). The Committee was informed that the BARB cases did not have the same sire and thus any hypothesised genetic susceptibility could not have been inherited from a common source. The pathological characteristics of the BARB cases were similar to earlier cases of BSE, suggesting that they have a similar aetiology. Strain typing studies of BARB cases have not been undertaken and the Committee considered that these would be of interest. Molecular strain typing would have the advantage of producing results rapidly.

Item 5 – Over Thirty Months (OTM) Review progress report

- 5.1 Members were provided with information on the progress of the Food Standards Agency review of the Over Thirty Month (OTM) rule. This rule forbids the sale in the UK of meat for human consumption from cattle aged over thirty months at slaughter. The FSA is carrying out the review with the assistance of a stakeholder group, which includes representatives of the farming and meat industries and consumers, and a risk assessment group. The latter is a joint FSA/SEAC group chaired by Professor Peter Smith, the Chairman of SEAC, and includes SEAC members and additional independent scientific experts. This group aims to provide a peer review function of modelling of the BSE epidemic, both past and in the future, with the OTM rule in place and with possible options for amendment.
- 5.2 The resulting predictions from this work will be used by the stakeholder group to inform their discussion of the risk management options. The advice they will ultimately provide to the Agency will also take into account the practicalities of enforcement, and the costs and benefits of alternative options.
- 5.3 It is anticipated that results from the first stage of this will be presented to SEAC at the November meeting. This work will provide the basis for further modelling work to provide a measure of infectivity entering the food chain (i.e. taking account of the SRM controls). Following the presentation of the results from GB, the work will model the epidemic in Northern Ireland (as the OTM rule applies to the UK) and the Republic of Ireland, which country is the major source of imports of beef into the UK.
- 5.4 It is anticipated that the modelling work will be completed in early 2003. The stakeholder group will then consider the results of this research as part of the overall review in formulating their conclusions on the review. The Agency will issue any new proposals on the future of the OTM rule for public consultation, which will include a public meeting. Recommendations on any proposed amendments to the OTM rule will be presented to the FSA.
- 5.5 Members stressed the importance of considering the potential risk from imported beef as well as UK beef including any non-compliance with the SRM requirements.

Item 6 - vCJD update

- 6.1 The Committee conducted its regular review of epidemiological information on vCJD. The Committee was informed that the total number of definite or probable vCJD cases in the UK, as at 11th September 2002, was 127, 12 of whom were alive. There were 69 male and 58 female cases in the UK. The greater number of male cases was not statistically significant. The mean age at death was 29 years with a range from 14 to 74 years and the mean age at onset was 27 years. The median duration of illness was 14 months with a range of 6 to 39 months. The longer periods of illness were associated with younger cases. It remained the position that all of the cases tested for the prion protein (PrP) genotype, (105 in total) were Methionine/Methionine at codon 129 of the PrP gene (37 per cent of the UK population being Methionine/Methionine).
- 6.2 There were 6 cases in France, 1 in the Republic of Ireland, 1 in Italy, 1 in the USA and 1 in Canada. None of the cases from France, nor the case from Italy, had a history of residence in the UK. The Committee noted that the level (around 10 per cent) of exports of UK beef to France in the 1980s and early 1990s was likely to be of significance. The cases in France had a similar age distribution to those in the UK. The cases reported in Ireland, US and Canada had a history of UK residence in the late 1980s. More details on the cases were being sought by the National CJD Surveillance Unit in liaison with national investigations in those countries.
- 6.3 The Committee noted the results from an analysis from the Public Health Laboratory Service (January 1994 – June 2002), which showed that the trend in the number of vCJD cases since 1995 continued to be significant, at an increasing rate of 18 % per year for onsets and 20 % per year for deaths. These figures were consistent with an overall increase in the upward trend in both onsets and deaths. To date no new onsets of vCJD have been reported in 2002. The Committee was informed that details of the analysis were available on the National CJD Surveillance Unit website: www.cjd.ed.ac.uk. The Committee agreed that it was too early to forecast longer-term trends of the disease incidence with any certainty.

Item 7 - Transmission of prion diseases by blood transfusion (SEAC 75/2)

- 7.1 Professor Chris Bostock described the work detailed in the recent publication of Hunter *et al.* (2002)³. This research was funded by the Department of Health.
- 7.2 The study examined the transmission of TSEs by blood transfusion in (susceptible) healthy sheep from sheep either experimentally infected with BSE or naturally infected with scrapie. The transmission of BSE to a single animal in this study had previously been reported in the *Lancet* (Houston *et al.* 2000). The study is ongoing

³ Hunter, N., Foster, J., Chong, A., McCutcheon, S., Parnham, D., Eaton, S., MacKenzie, C. and Houston, F. (2002). Transmission of prion disease by blood transfusion. *Journal of General Virology* **83**.
www.socgenmicrobiol.org.uk/JGVDirect/18580/18580ft.pdf

and may take up to 5 years to complete. The recent publication³ described a second case of transmission of BSE and four new cases of transmission of natural scrapie in the same study.

- 7.3 As detailed in Hunter *et al.* (2002), 24 transfusions from BSE-inoculated sheep were carried out. In each case, 450 mls of blood was transfused into recipient sheep. Of these, 17 received whole blood and 7 received a fraction enriched in white cells (buffy coat). Both cases of BSE transmission occurred in sheep that received whole blood taken from the donor before clinical onset of disease; these recipient animals succumbed to BSE 610 and 538 days post transfusion. The donors were likely to be approximately half way through the incubation period.
- 7.4 The Committee was informed that, since the publication of Hunter *et al.* (2002), two further sheep had succumbed to BSE; one of these sheep had been transfused with buffy coat, while the other had been transfused with whole blood. Of the remaining 20 sheep that received transfusions, one died of unrelated causes and 19 animals remain apparently healthy. The healthy animals are at varying times post-transfusion – ranging from less than 100 to over 1000 days.
- 7.5 Members were informed that among the 21 sheep transfused with blood from scrapie infected animals (761 to 1080 days of age), 4 had developed scrapie between 614 and 737 days post-transfusion. One animal received the buffy coat preparation from the blood of an animal with clinical disease. The remaining 3 animals received whole blood from donors not yet showing clinical signs. Of the remaining 17 transfused sheep, one died of unrelated causes and two further sheep were showing clinical signs of scrapie; one of these had received buffy coat, while the other had received whole blood.
- 7.6 The Committee noted that it would not be possible to confirm that the negative controls are free of TSEs until the end of the study, when they would be culled and analysed post mortem for signs of subclinical infection. Of the 10 positive controls that received BSE-infected cattle brain homogenate intravenously, 5 have developed disease or appear to be in the early stages of the disease.
- 7.7 Members were informed that the electrophoretic pattern of PrP^{res} in the brains of the transfused sheep indicated that the patterns were characteristic of the disease (BSE or scrapie) observed in the donor animals. In addition, PrP^{sc} detection by immunohistochemistry in a limited number of tissues (including some lymphoid tissue) showed differences between BSE infected and scrapie affected animals. Furthermore, in the lymphoid tissues tested to date, PrP^{sc} staining was weaker in transfused animals and i.c. challenged animals compared with animals exposed via the oral route. However, the lack of involvement of the lymphoid tissues has been observed previously in some sheep orally infected with BSE (Jeffrey *et al.*, 2001)⁴. The Committee was informed that tissues from donor and recipient sheep are also being strain typed in mice.

⁴ Jeffrey, M., Ryder, S., Martin, S., Hawkins, S.A.C., Terry, L., Berthelin-Baker, C. and Bellworthy, S.J. (2001). Oral inoculation of sheep with the agent of bovine spongiform encephalopathy (BSE).I. Onset and distribution of disease-specific PrP accumulation in brain and viscera. *Journal of Comparative Pathology* **124**, 280-289.

- 7.8 The Committee discussed the study and implications for human health. The Committee agreed the study emphasised the importance of the potential for transmission by means of transfusion, but considered that it was difficult to extrapolate these findings directly to the human situation. The volumes of blood transfused were comparable with those used in the treatment of humans. Some Members noted that the incubation periods were greater in sheep which had received buffy coat than in those that had received whole blood, indicating that there may be significant levels of infectivity in non-white cell components blood. This raised the question as to whether leucodepletion programmes to protect human health were sufficient. The Committee agreed however that these are interim results and stressed that over interpretation should be avoided. The Committee was informed that this study had not leucodepleted blood, and accepted that in the process of preparing the buffy coat, it is possible that cell damage may have occurred with resultant loss of infectivity from the buffy coat fraction.
- 7.9 Members asked for details of blood transfusion bags used in this experiment and the length of time the blood samples were stored prior to transfusion. One member expressed concern that if dextran sulphate was present in these bags, then this could decrease infectivity in the samples collected. This concern relates to experimental studies in rodents, which has shown increased incubation periods following treatment with dextran sulphate. Professor Bostock stated that he would check the nature of the bags used, and confirmed that blood would have been stored in these bags between 1 to 3 days prior to transfusion to the recipient sheep.
- Action: Professor Bostock**
- 7.10 These initial studies had been undertaken with first passage BSE in sheep. Some members expressed a view that secondary amplification of infectivity may occur in passaging BSE from sheep to sheep and that this might also be relevant to humans. Consideration should therefore be given to undertaking similar studies in later passage animals.
- 7.11 Members queried whether haemophiliacs⁵ and others who receive large quantities of blood products, and children, might be at greater risk. Department of Health (DH) officials reminded the Committee of precautionary measures already put in place, aimed at protecting the blood supply from risks arising from pre-clinical disease in donors. The DH had:
- instituted universal leucodepletion (removing the white cells) of all blood for transfusion from 31st October 1999.
 - instructed fractionation laboratories in 1998 to make blood products only from plasma imported from countries where there is no evidence of the presence of the BSE agent (eg the United States).
 - instructed the National Blood Service (NBS) to import US Fresh Frozen Plasma (FFP) for neonates and children born after 1.1.96 as soon as practicable.

⁵ At the SEAC meeting held on 14 November 2002, Members were informed by the Department of Health that the individual risk for haemophiliacs is likely to be low. Members were reminded that since 1998 all plasma for plasma products preparation has been obtained from outside of the UK, from countries where BSE is not present.

- 7.12 DH had also recently issued guidance to the NHS on the appropriate use of blood. The Committee viewed the precautions as prudent, and recognised the need to balance protection of the blood supply against availability of blood and blood products, which are only used when there is an acute clinical need.
- 7.13 The Chair concluded that this study does not directly inform on risk, but there remains a theoretical risk for human health from the transfusion of blood or blood products, which the DH has been addressing. More targeted fractionation studies on blood should be performed to determine which fractions contained infectivity, and whether this varies according to the stage in the incubation period. These studies should include testing for infectivity in leucodepleted sheep blood. The Committee agreed it would be important to encourage international input into the experimental design of future studies.
- 7.14 On the issue of the effect of age of donor and recipient sheep, or any other experimental variable on the interpretation of results, the Committee concluded that this was of scientific interest but was a second-order priority.

Item 8 - Public consultation on:

a) Removal, retention and use of human organs and tissues, and

b) Death certification and coroners' services

(SEAC 75/3)

- 8.1 The Committee was informed that the Home Office and the Northern Ireland Courts Service had commissioned an independent review of death certification and coroners' services in respect of England, Wales and Northern Ireland. The Committee also learned that the Department of Health and the Welsh Assembly Government had issued a consultation document on the law on human organs and tissues in England and Wales.
- 8.2 The Committee reiterated previously expressed concerns about compromising public health surveillance for CJD because of the low numbers of post-mortems being conducted in the elderly. They expressed concern about the lack of depth of current investigations to determine what constitutes a "cause of death" and considered that there were strong public health arguments for increasing the rate at which post-mortems were conducted. In some instances such investigations would be appropriate, from a public health perspective, even without consent from surviving relatives. Members noted that the low rate of post mortem investigations was further exacerbated by concerns over tissue retention, which had led to reluctance of coroners to validate the cause of dementia at post mortem by histology, even when this related to the cause of death. The Committee expressed concern at reports that there was inconsistency shown by coroners around the UK in deciding whether to hold a post-mortem and an inconsistency in the depth of examination to determine the actual cause of death. The Committee acknowledged that the low number of pathologists had contributed to the problem but was unlikely to be the major factor.
- 8.3 The Committee emphasised the value of a full post-mortem examination in relation to surveillance for TSEs. As a minimum requirement, this could entail strategic sampling

of the brain. They welcomed the proposal in the review document regarding the possible creation of a new Medical Audit Service in which a medical auditor would become responsible for ensuring proper investigations were conducted to establish the underlying cause of death. The medical auditor would have “the power to decide the purpose and scope of further medical investigation, including scrutiny of existing case notes and/or ordering post-mortems.” The Committee considered that this could be a useful tool to enable sampling to be done for surveillance purposes, extending wider than CJD.

- 8.4 In addition, the Committee expressed support for a proposal to develop a national protocol governing the use and arrangements for post-mortems for coroners and/or medical auditors, allowing full scope for independent professional and judicial judgement, but having legal status and produced by a publicly accountable body after consultation with expert and family interests. The medical audit should be charged with establishing procedures to a high medical standard, capable of being reviewed. The Committee supported the establishment of a properly constituted statutory body which could commission enhanced post mortem surveillance in some jurisdictions according to societal and public health requirements. If a problem was identified through such local enhanced surveillance, then it could be rolled out to wider jurisdictions. The Committee agreed that this system should be amenable to subsequent review, that its powers extend to ordering an enhanced examination of the body and that its terms of reference should be expanded to include the commission of specific studies. Members also agreed that any national protocol should stipulate that the coroner should have to justify why a post-mortem or why specific investigations should not be undertaken.
- 8.5 The Committee stressed the importance of systematic disease surveillance of human prion diseases. The Committee noted that without surveillance and specialist laboratory techniques, it would not have been possible to have identified the first cases of vCJD in 1996. Furthermore, they pointed out that for these rare diseases, some of which can be difficult to identify at an early stage, and which in older people may possibly be masked by other neurological conditions which give rise to similar symptoms, good surveillance required not only reporting by clinicians who see patients, but also confirmation by post mortem examination, wherever possible with the agreement of the family concerned.
- 8.6 The Committee agreed that considerate and sensitive explanation to relatives of the purpose of hospital post mortems, which emphasised the importance of approved public health surveillance programmes, where these might be facilitated by data gathered at post mortem, normally persuaded relatives to co-operate.
- 8.7 The Committee accepted that public health surveillance programmes often involved testing, without compromising clinical care, small samples of tissue that were discarded routinely. Members noted the value of the unlinked anonymous technique (whereby results can not be traced back to individuals) to help monitor HIV, hepatitis C and infections preventable by vaccination and which can also provide valuable information on the surveillance of human TSEs. The Committee considered that in some instances the importance of the information that could be collected in this way for public health surveillance purposes was such that informed

consent was unnecessary (provided the samples were collected in an unlinked and anonymous way).

- 8.8 The Committee considered elements of a draft interim statement on the use of organs and tissues in clinical research incorporated by the Department of Health in its consultation document. The Committee agreed that all these research principles ought to be embedded in proposed new legislation/guidance, although Members considered that the principle of absolute consent should not be brought into legislation and they strongly endorsed the use of unlinked anonymous surveys.
- 8.9 The Committee noted that retrospective unlinked anonymous studies to detect abnormal prion protein in stored tissue had been in progress since 1998, in order to begin to assess the prevalence of this protein in a particular subset of the population. The majority of these tissues would be appendix and tonsil taken from living people. The Committee accepted that the unlinked, anonymous technique absolved responsibility for clinical care. They noted the distinction between tissue taken from a living patient and a post-mortem case but considered that the unlinked, anonymous technique might usefully be employed with both. While the MRC guidelines made provision for unlinked anonymous testing as long as ethics committee approval was obtained, the Committee agreed that the consultation document should make specific reference to the use of the unlinked anonymous technique in the study of existing stored tissue. The Committee considered that unlinked and anonymised tissue samples, used for properly approved public health surveillance programmes, provided valuable information on the surveillance of human TSEs and agreed that the value of such programmes would be compromised if patients were allowed to opt out.
- 8.10 The Committee agreed that there should be no restrictions on how long tissue samples could be kept. Tissues might need to be retained for TSE surveillance or research purposes, and should apply to both existing and future collections of tissue. They considered that this should apply to material taken at coroners' post-mortems as well as tissues from patients.
- 8.11 Members also agreed that quality assurance schemes were an important part of maintaining high quality clinical services generally and endorsed the consultation document's explanation of current practice that, provided patients have consented to a particular intervention, tissue samples may be used for quality control purposes without specific consent being obtained. This was because, in the field of human TSEs, appropriate positive and negative control samples were essential in development and quality control of, for example, diagnostic tests for TSEs. However, the Committee was of the view that if an audit would involve specific sample identification, then it may be necessary to seek consent under these conditions.
- 8.12 The Committee noted that as part of the Chief Medical Officer's recommendation in January 2001 for a fundamental and broad revision of the law on the taking, storage and use of human tissue from the living and the dead, he recommended that formal controls be introduced on the import and export of body parts. Pending this review of the law, he recommended that a Code of Practice be introduced to require proper records to be kept of imports and exports of all human body parts for

teaching, education, research or other non-therapeutic purposes. The Committee commended the aim of the Code of Practice to ensure that body parts had been obtained ethically, that the appropriate consents had been obtained, and that they had been subject to screening, where possible and feasible, to minimise the risk of infection. Members expressed the view that it would be an unnecessary additional requirement to include small, unfixed tissue samples, for example exchanged between professional colleagues for diagnosis, in this code. However, they thought that larger tissues such as skeletons should be included.

- 8.13 The Committee strongly disagreed with the Code of Practice recommendation that the import/export of brains, spinal cord or cerebrospinal fluid should be avoided. Members believed that this would greatly hinder participation in overseas research projects, funded by the European Union and World Health Organisation Diagnostics Group, and limit investigation into other diseases which can be tackled better by international co-operation. SEAC agreed that if import/export were disallowed, this would undermine the UK's participation and lead role in international research and surveillance of CJD.

Item 9 - Western Blot Technique – (SEAC 75/5)

- 9.1 A plan for the evaluation of the VLA's modified format of the Prionic Western blot technique was discussed and agreed at the SEAC meeting on 10 April 2002. This technique aims to differentiate between scrapie and experimental BSE in sheep. The Committee was provided with an update from the VLA on the progress of the evaluation process.
- 9.2 The Committee was informed that the VLA had completed the repeatability study of the assay and had concluded that, it is sufficiently robust for strain typing in sheep, provided that the test was used with care. The VLA had consulted Dr Simon Cousens, from the London School of Hygiene and Tropical Medicine, concerning the statistical methods used; he had suggested some further statistical analyses, and had agreed with the VLA's conclusions following these analyses.
- 9.3 Statistical analyses of the results from Stack *et al.* (2002) (SEAC 75/5) demonstrated that the mean molecular weights for the unglycosylated band could be used as a discriminatory variable for different strains – with the unglycosylated band of experimental ovine BSE and CH1641 scrapie being lower than other sources of scrapie.
- 9.4 The Committee noted that the VLA Archive had received a number of experimental sheep passaged BSE infected brains from the Moredun Research Institute. This is sub-passage material, and it is necessary to first test this material to ensure that the BSE strain remains stable on sub-passage. Testing of the retrospective scrapie brain samples could then start in October 2002.
- 9.5 Further studies performed at the VLA confirmed that autolysis could compromise Western blot results. It was reported that molecular weights of samples tested fresh were usually higher than in tissues which were autolysed, and this potentially could give rise to false positives for BSE. This therefore has important implications for the

handling of brain material collected for the prospective scrapie testing surveillance programme.

- 9.6 It had been anticipated that the VLA had access to 1700 scrapie sheep brains collected since January 1998, which could be used for retrospective testing. However, the Committee learned that the actual number to be tested will depend upon if there is sufficient material remaining for testing, as some of this material has been used in other research projects over the intervening years. It is anticipated therefore that approximately 1000 samples would be available for testing. In accordance with the plan agreed by SEAC in April 2002, the VLA plan to test ARQ homozygous sheep as a priority, as experimental studies suggest that this genotype is the most susceptible in terms of BSE transmission.
- 9.7 The Committee was informed that the VLA, in its capacity as an EU Community Reference Laboratory, has subsequently received a request from the EU Commission to translate the SSC's 'Strategy to Investigate the Possible Presence of BSE in Sheep' into instructions for all National Reference Laboratories. This would facilitate the development of a common protocol.
- 9.8 The SSC also propose to set up "ring trials" to analyse any tissues with a 'BSE-like' signature using different molecular methods. The VLA welcomed this proposal, as it was important to validate its technique and check potentially positive samples with other laboratories. However, a note of caution was raised over the lack of experimental sheep BSE material available for use as positive controls in these experiments. The Committee was informed that the planning of the ring trial would commence in September 2002, and all available strain typing tests would be included. Additionally, the SSC also proposes to establish a review panel of experts on molecular typing to review and interpret the results from the ring trial.
- 9.8 The Committee was content for the proposed work at the VLA to commence, and proposed that a sub group of SEAC could be set up to review the ongoing work on molecular strain typing, and report back to the main Committee.

Action: SEAC Secretariat