

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEEDraft minutes of the 101st meeting held on 15th October 2008

Park Inn Hotel, Southampton Row, London, WC1B 4BH

Members:	Professor C. Higgins (Chair)	
	Professor J. Collinge	
	Professor A. Ghani	
	Professor N. Hooper	
	Mr. P. Jinman (Deputy Chair)	
	Dr. R. Knight	
	Ms. D. McCrea	
	Professor J. Manson	
	Professor G. Medley	
	Professor J. Nicoll	
	Dr. R. Salmon	
	Professor A. Williams	
Assessors:	Mrs. S. Eades	(Defra)
	Dr. S. Hayes	(NAW)
	Dr. J. Hilton	(FSA)
	Mr. M. Noterman	(DH)
	Dr. A. Douglas	(AFBINI)
Technical Experts:	Mr. P. Burke	(Defra)
	Professor N. Gill	(HPA)
	Dr. I. Hill	(FSA)
	Dr. J. Hope	(VLA)
Secretary:	Dr. P. Grimley	
Secretariat:	Dr. T. Barlow	
	Mr. B. Cole	
	Dr. D. Cutts	
	Dr. A. Patey	
Also in attendance	Dr. A. Adkin	(VLA)
	Professor M. Baylis	(University of Liverpool)
	Professor S. Bird	(MRC - Biostatistics Unit)
	Dr. P. Comer	(DNV)
	Dr. V. Del Rio Vilas	(VLA)

ITEM 1 – INTRODUCTION

1. The Chair welcomed everyone to the 101st meeting of SEAC. He explained that, in accordance with the SEAC Code of Practice, there would be a reserved business session in the afternoon to discuss preliminary unpublished data. However, short summaries of all the discussions would be published on the SEAC website.
2. The Chair thanked Professors Matthew Baylis and Sheila Bird and Drs Amie Adkin, Philip Comer and Victor Del Rio Vilas for attending to contribute to the discussions.
3. The Secretary explained that open meetings allow the public an opportunity to observe the committee at work and provide an insight into how an advisory committee provides independent scientific advice to Government. Government officials with responsibility for transmissible spongiform encephalopathy (TSE) policy may be invited to contribute to discussions.
4. Members were reminded that they are obliged to declare any commercial or other interests they may have at the relevant agenda items. Members were asked to inform the secretariat of any changes to the register of members' interests. Expense claims should be submitted as soon as possible after meetings and must be submitted within three months of meetings.
5. Apologies for absence had been received from Professors Margaret Stanley and Corinne Lasmezas.
6. The next SEAC meeting was scheduled for 12th December 2008 at a venue to be confirmed. In the future, meetings would be held in government buildings where possible, for reasons of cost. This would not compromise the committee's independence and meetings would still be open to the public.

ITEM 2 – APPROVAL OF MINUTES FROM SEAC 100 (SEAC 101/1)

7. The minutes of SEAC 100 were agreed as a correct record with the following:
 - Paragraph 26, first sentence changed to “...to give an estimate of infection...” and third sentence changed to “Most combinations of the data...”

ITEM 3 – CURRENT ISSUES

8. SEAC was informed about the following issues:
- A mother and son in Spain had died of variant Creutzfeldt-Jakob Disease (vCJD). This is the first recorded instance of more than one case of vCJD within one family. As both the mother and son lived in a region of Spain with a history of BSE, had frequently shared meals of cattle brain, and as no other risk factor has been identified, it seems most likely that both infections were acquired from dietary exposure. Furthermore, the similar times of onset of disease of the cases did not suggest transmission had occurred from one to the other.
 - Screening tests on 200 goats from an English herd of 1500 goats culled because of a large classical scrapie outbreak had identified one goat where a diagnosis of BSE could not be excluded. Further testing of samples of this goat by the Strain Typing Expert Group had not allowed a different diagnosis. The Group had recommended that mouse bioassays of isolates of brain and lymphoid tissue from this goat and its herd mates be conducted in order to make a definitive diagnosis. The goat had been born in October 1999 before the introduction of the European Union-wide feed ban in 2001. A report of epidemiological and analytical investigations of the 200 goats from the herd that had been screened will be available shortly.

ITEM 4 – UPDATE ON vCJD PREVALENCE STUDIES

9. Professor Noel Gill (Health Protection Agency (HPA)) provided an update on the National Anonymous Tonsil Archive (NATA). Approximately 62 500 NATA samples (12 500 samples in the 1961-1985 birth cohort and 9 500 in the 1986-1990 birth cohort) had been screened. None was positive for the presence of abnormal prion protein (PrP^{Sc}). Immunohistochemical analysis of 10 000 samples from the 1961-1985 birth cohort was progressing. No discrepant results had been found to date. An application for a second retrospective survey of appendix samples is currently under consideration by a Research Ethics Committee.
10. Professor Gill explained that the establishment of a post mortem tissue archive, which is dependent on the collection of samples from Coroners' autopsies, does not have the support of Coroners needed to take it forward. The HPA and Department of Health

(DH) had met with the Coroners Advisory Group (CAG) at the Ministry of Justice a number of times to discuss how the archive might be set up. A system had been devised which would have a minimal impact on the work of Coroners by involving National Health Service Blood and Tissue (NHSBT) in asking consent for tissue collection. In addition, legal advice confirming that Coroners could collaborate in the archive had been obtained. However, the proposed archive was considered unacceptable by CAG and also by Coroners discussing it at the recent Coroners Annual General Meeting. It was considered by them an abuse of the Coroners position and their role which is to establish cause of death. Furthermore, Coroners are still uncertain about the legal implications of their involvement in an archive.

11. The committee was extremely disappointed about the lack of support from Coroners for the post mortem tissue archive. As SEAC has repeatedly stated, the archive is key to obtaining better estimates of the prevalence of subclinical vCJD. These estimates are vital to make meaningful assessments of the risks to public health from vCJD and of the need for, and effectiveness of, current, and further, very costly public health protection measures. SEAC acknowledged the strenuous efforts made by the HPA, DH and NHSBT to set up the archive. SEAC remains strongly in favour of establishing the archive as the committee is unable to give meaningful estimates of risk of secondary transmission of vCJD in the absence of prevalence data.

ITEM 5 – PROPOSALS TO REDUCE TESTING OF CATTLE SLAUGHTERED FOR FOOD – IMPACT ON RISK TO HUMAN HEALTH (SEAC 101/2)

12. The Chair introduced the item, stating that at SEAC 100, the Food Standards Agency (FSA) had asked SEAC to consider a risk assessment by the Veterinary Laboratories Agency (VLA) of the human health risk from increasing the minimum age at which cattle are tested for BSE. At that meeting, members raised a number of questions that had been addressed in correspondence since SEAC 100. A draft conclusion on the issue had been circulated to SEAC for comment and agreement. The finalised conclusion would be presented by the Chair to FSA Board immediately following SEAC 101.
13. Members were satisfied that the questions raised at SEAC 100 had been addressed. Members concluded that the risk assessment was suitable and gave a reasonable estimate of the risk to human health from increasing the age of BSE testing of cattle for human

consumption. This risk was very low as long as the prevalence of BSE remains low. Therefore, it is important that surveillance continues to remain capable of detecting changes in the prevalence and incidence of BSE, the possible emergence of a further BSE epidemic and, possibly, the emergence of a new TSE in cattle.

14. Professor Sheila Bird (MRC – Biostatistics Unit) noted that the age at which cattle are tested could influence how early a new epidemic of BSE or of another TSE in cattle might be detected.
15. Members noted that the results from a simpler analysis of the effect of increasing the age of BSE testing produced by the European Food Safety Authority (EFSA) were not inconsistent with the results produced by the VLA analysis.
16. SEAC agreed the following conclusion which was to be provided to the FSA Board:

SEAC considered the results from a mathematical model that had been used to estimate the number of infected cattle that may be undetected as a result of raising the minimum age at which healthy slaughtered and fallen stock cattle must be tested for BSE. The model itself, produced by VLA, was previously reviewed by SEAC¹.

The increased risks to human health estimated by the model from raising the age at which healthy slaughtered cattle are tested for BSE (up to 60 months, the highest age modelled) are very small. The model estimates that much less than one BSE case would be missed annually in the GB herd by increasing the age of testing to 60 months for the healthy slaughter surveillance stream. Although uncertainties are inherent in such modelling, the validation of the model that has been conducted provides assurances about the reliability of the results. Similar results from a different analysis by EFSA^{2,3} provide additional confidence in the findings. The EFSA analysis estimates that less than two BSE cases would be missed annually in the whole of the EU15⁴ by increasing the age of testing to 60 months for the healthy slaughter surveillance stream.

¹ Reviewed at SEAC 95, December 2006.

² Risk for Human and Animal Health related to the revision of the BSE Monitoring regime in some Member States. Scientific Opinion of the Panel on Biological Hazards. The EFSA Journal (2008) 762, 1-47.

³ Further consideration of age-related parameters on the Risk for Human and Animal Health related to the revision of the BSE Monitoring regime in some Member States. Opinion of the Panel on Biological Hazards. The EFSA Journal (2008) 763, 1-8.

⁴ Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, United Kingdom.

These risk assessments hold provided the incidence of BSE in cattle remains low. Therefore, regulations should not be modified unless effective surveillance remains in place. Surveillance is the only means of monitoring changes in the incidence and prevalence of BSE, the effectiveness of control measures in preventing an epidemic and the possible emergence of new prion diseases. As control measures to prevent cattle and human infection are modified, continued active and passive surveillance become increasingly important to ensure that the remaining controls are effective in minimising the risk to human and animal health.

ITEM 6 – RISK ASSESSMENT OF SRM CONTROLS AT ABATTOIRS AND CUTTING PLANTS (SEAC 101/3)

17. Dr Judith Hilton (FSA) explained that SEAC had reviewed an earlier version of the risk assessment at SEAC 95. The present version incorporated changes that had been suggested by SEAC. The assessment examined the effect of changes to the level of supervision of specified risk material (SRM) controls not the effect of changes to the controls themselves. Supervision levels had been established at a time when the incidence of BSE was much higher than currently so a more risk-based approach to supervision was now being considered. SEAC were asked to review the revised model and comment on its suitability to inform considerations by the FSA Board of changes to the levels of supervision of SRM controls.
18. Dr Philip Comer (Det Norske Veritas Consulting) gave an overview of the risk assessment and how it had been modified since SEAC 95. A panel of experts from the Meat Hygiene Service, industry and government had been convened to provide more robust estimates for parameters in relation to slaughter processes and the effectiveness of supervision of controls. The revised model included estimates for peripheral nervous system (PNS) infectivity and an assessment based on a worst case scenario. The risk assessment estimated that the total infectivity entering the food supply from Over Thirty Month Cattle to be 0.35 bovine oral ID₅₀s per year. The largest contributions were from head meat, Dorsal Root Ganglia (DRG) and PNS tissue. A worst case scenario of a maximally infected carcass entering the food supply would result in about two bovine oral ID₅₀'s (range 0.2 to 36) entering the food supply, assuming SRM controls remain as at present. Changes to post mortem cattle identity checks made little or no difference to the level of infectivity that may enter the food supply, including in

the worst case scenario where no ante-mortem and no post-mortem identity checks were performed.

19. Professor Bird was content with the methodology used and the conclusions drawn from the assessment, noting that the conclusions would be valid provided the prevalence of BSE remains low. Data from the BSE pathogenesis studies had allowed the assessment to be refined. The data derived for the upper and lower limits of parameters agreed by the expert panel should be treated with caution as often such groups were poor at estimating extremes accurately. Some empirical data could be collected to assess the accuracy of some of these parameters. However, any inaccuracies were unlikely to greatly affect the overall conclusions. Research could also be conducted to estimate better the level of spinal cord contamination and CNS contamination of head meat.
20. Members noted the wide range of values used for PNS infectivity.
21. A member asked if it was possible to translate the estimates of infectivity into a number of potential additional cases of vCJD. Dr Comer explained that such estimates would rely upon a number of assumptions where there would be large uncertainties, producing results with very large uncertainties. Human exposure expressed as bovine oral ID₅₀ may be more easily understood, aiding decision making. A member noted that the possibility of human-to-human transmission made estimating the potential number of vCJD cases for a given level of dietary exposure to BSE more complex. Members agreed that it was important to communicate to consumers the reasons why such estimates are so difficult to make.
22. Members were content with the risk assessment and the conclusions drawn from the results. However, as with all changes to controls, it would be important for risk managers to consider whether changes to one control affect the effectiveness of other controls.

ITEM 7 – ATYPICAL SCRAPIE CASE-CONTROL STUDY (SEAC 101/4)

23. The Chair explained that that the VLA had undertaken a case-control study to identify potential risk factors associated with atypical scrapie. Defra had asked that SEAC consider a report of the study, its findings and the possible implications. Three SEAC

members had considered the study methodology prior to the meeting and their views had been presented in the papers.

24. Dr Victor Del Rio Vilas (VLA) presented an overview of the study conducted between July 2005 and November 2007. The aim was to characterise cases of atypical scrapie, particularly with regard to their holdings of origin and to examine any association between variables related to the holdings and the occurrence of atypical scrapie. Forty case holdings and 119 control holdings were analysed. Data were collected from interviews with farmers with a questionnaire, producing 260 analytical variables. A statistical analysis of the data collected showed that a small number of variables, including certain animal feeds, were associated with an increase in the odds of atypical scrapie being present. Some variables appeared protective against atypical scrapie.
25. Professor Matthew Baylis (University of Liverpool) noted that the selection of controls for such a study should match as closely as possible the selection of cases. Bias may have been generated by the criteria used to select the controls. Further analyses using a number of different selection criteria for controls may be informative.
26. Professor Bird noted that the selection criteria for controls differed for the abattoir and fallen stock surveillance streams. More detailed information should be provided on how the cases and the controls were selected. A larger study with more cases and controls should be conducted. At present, the study may be too small to make conclusions about risk factors. Bias from genetic factors that are known to influence susceptibility to atypical scrapie should be considered.
27. Dr Del Rio Vilas explained that the number of cases had been restricted by verification of whether animals were home bred or not; in many cases this verification was not possible. Such verification was also a requirement for the selection of controls. He explained that the study should be considered as an exploratory investigation of potential risk factors to develop hypotheses rather than identifying risk factors conclusively.
28. A member congratulated the VLA for obtaining data to make this study possible. Whilst it would be preferable for the study to be enlarged and further analysis of the data conducted, the underlying design of the study was reasonable. The findings should not be dismissed. As the breed of sheep had been shown to be significantly associated with atypical scrapie, as would be predicted on genetic grounds, this provided some assurance about the value

of the study in identifying real risk factors for atypical scrapie. Nevertheless, more work is required to investigate further the possible associations identified.

29. A member noted that, for such a small study, a large number of variables had been investigated. Therefore, it is possible that statistically significant associations could have been found by chance. Thus, at this present time, it might be premature to carry out further studies to look for corroborating evidence of associations until the statistical analysis undertaken had been reviewed further. A member also noted that some of the significant associations identified may be linked together by husbandry practices and the structure of the sheep industry in the UK.
30. Professor Baylis suggested that, given the results of this and other studies, potential dietary risk factors for atypical scrapie could be examined.
31. In summary, SEAC agreed that the study was important and the underlying design appropriate. However, further work, particularly on the selection of cases and controls, statistical analysis of the data and the reporting of the study, was required before conclusions could be drawn.

ITEM 8 – DRAFT SEAC STATEMENT ON RELAXATIONS TO THE TOTAL FEED BAN (SEAC 101/5)

32. The Chair explained that Defra, the devolved Rural Affairs Departments and FSA had asked SEAC to consider the potential for TSE infections and epidemics to arise as a result of the possible implementation of various future options for modifying TSE-related feed controls. A draft statement had been produced and had been revised following discussion by the committee on a number of occasions.
33. A member noted recent research⁵ on the possible transmission of prions to fish. Groups of sea bream and sea bass had been fed with BSE or scrapie. Although no clinical signs of infection had been observed, plaque-like aggregates had been found in the brain of sea bream, but not sea bass, although no other immunohistochemical evidence of prion disease had been found.

⁵ Salta, E., Panagiotidis, C., Petrakis, S., Eleftheriadis, E., Karagiannis, D., Aggelidis, P., Teliouis, K., Kaldrimidou, E., Krey, G., Sklaviadis, T. Evaluation of the possible transmission of prions to the two closely related teleost species, sea bream and sea bass. Abstract P3.18. Prion 2008 Abstracts (Sponsored by Min de Ciencia y Innovacion, Spain, INIA, the Commission, 6th Framework Programme & Neuroprion), Madrid, Spain. 8-10 October 2008.

Further studies to determine transmissibility of these infections were underway. Transmission studies in zebra fish were also being planned.

34. Members agreed that the statement should be altered to make reference to these data noting that the research had not yet been published in a peer-reviewed publication. Members also agreed to substitute the word “relaxation” with “modification” throughout the statement. With these changes, SEAC agreed that the statement be considered final and published on the SEAC website.

ITEM 9 – ANY OTHER BUSINESS

35. The Chair explained that the Chief Medical Officer for England had asked SEAC to consider the plausibility of a hypothesis proposed by Professor Alan Ebringer (King’s College London) that prion diseases may be the result of an autoimmune reaction initiated by exposure to certain bacteria. As SEAC had considered the hypothesis in the past, concluding then that it was not supported by the evidence available, the Chair asked the committee whether it knew of any new data to support the hypothesis.
36. The committee noted that there are no new published data to support the hypothesis. The National CJD Surveillance Unit (NCJDSU) had collaborated with Professor Ebringer in a study to test the hypothesis on human samples, which had produced results that did not support the hypothesis. This study had not been published. As there were no new data to support the hypothesis the Chair concluded that the hypothesis did not warrant reconsideration by SEAC.

The Chair closed the open meeting, thanking all those who had presented information to the committee and all who attended the meeting.