



## **SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE**

Open minutes of the 98<sup>th</sup> meeting held on 29<sup>th</sup> July 2007

Royal Horticultural Halls and Conference Centre  
Greycoat Street  
London  
SW1P 2QD

Members:	Professor C. Higgins (Chair)	
	Mr. J. Bassett	
	Professor J. Collinge	
	Dr. A. Ghani	
	Professor N. Hooper	
	Mr. P. Jinman (Deputy Chair)	
	Dr. R. Knight	
	Professor C. Lasmézas	
	Professor J. Manson	
	Ms. D. McCrea	
	Professor G. Medley	
	Professor J. Nicoll	
	Dr. R. Salmon	
	Professor M. Stanley	
	Professor A. Williams	
Assessors:	Dr. P. Christie	(SEHD)
	Ms. S. Eades	(Defra)
	Dr. A. Gleadle	(FSA)
	Dr. S. Hayes	(NAW)
	Mr. M. Noterman	(DH)
Technical Experts:	Mr. P. Burke	(Defra)
	Miss. A. Conroy	(FSA)
	Dr. S. Dixon	(FSA)
	Dr. D. Matthews	(VLA)
	Dr. J. Stephenson	(DH)
SEAC Secretary:	Miss K. Richards	
Secretariat:	Dr. T. Barlow	

Mr. B. Cole  
Dr. D. Cutts

Also in attendance    Mr. S Dobra (DH)  
                                  Dr. F. Hill (NHS)  
                                  Dr. S. Jenkins (BPL)  
                                  Lord J. Rooker (Defra)

## ITEM 1 – CHAIR’S INTRODUCTION

1. The Deputy Chair welcomed everyone to the 98<sup>th</sup> meeting of SEAC. He explained he would chair the meeting pending the arrival of Professor Chris Higgins. He welcomed Professor John Collinge for his first meeting following his reappointment to the committee. Lord Jeff Rooker, Minister for the Sustainable Food and Farming, and Animal Health, would be in attendance later in the morning.
2. The SEAC Secretary explained that open meetings allow the public an opportunity to observe the committee at work and provide 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. The committee would hold a reserved business session in the afternoon to allow discussion of unpublished research on straining typing of sheep TSEs. This was in accordance with the SEAC Code of Practice. Short summaries of the open and reserved business discussions would be published on the SEAC website.
3. The SEAC Secretary congratulated Professor Higgins on his reappointment for a second term of three years as SEAC Chair. A light touch review of SEAC was scheduled for later in the year with the appointment of an independent reviewer imminent. Members and officials were encouraged to participate in interviews if approached by the reviewer.
4. The SEAC Secretary noted that as of 2<sup>nd</sup> July 2007 the total number of definite or probable variant Creutzfeldt-Jakob Disease (vCJD) cases both dead and alive in the United Kingdom (UK) was 165 (114 deaths from definite vCJD, 161 deaths from definite or probable vCJD). The current number of born after the reinforced ban (BSE) bovine spongiform encephalopathy (BARB) cases was 147 cases in Great Britain (including one imported from the Republic of Ireland) and 23 cases in Northern Ireland.
5. Apologies for absence had been received from Professor David Brown. The next SEAC meeting is scheduled for Friday 4<sup>th</sup> October 2007 and will take place at Mercure Holland House Hotel, Newport Road, Cardiff<sup>1</sup>.

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<sup>1</sup> Following the meeting it was decided that SEAC 99 be postponed until Friday 14<sup>th</sup> December 2007.

6. Members were reminded that they are obliged to declare any commercial or other interests they may have at the relevant agenda items and 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.

## **ITEM 2 – APPROVAL OF MINUTES FROM SEAC 97 (SEAC 98/1)**

7. The minutes of SEAC 97 were agreed as a correct record with the following amendments:

- Professor Stanley was present at the meeting.
- paragraph 25, change *“Members noted that in the absence of any data which suggests a link between types of CJD and atypical scrapie such a scenario would not change the assessment of risk.”* to *“Members suggested that these data would be best interpreted together with data indicating the presence or absence of a link between types of CJD and atypical scrapie.”*
- Paragraph 28, change *“Strong evidence of a risk would only be obtained if similar results from comparative studies were obtained in more than one model were obtained, this would provide strong evidence of a risk.”* to *“Strong evidence of a risk would only be obtained if similar results from comparative studies in more than one model were obtained.”*
- Paragraph 33, change *“Members concluded that negative results are very hard to interpret, however negative results from current and retrospective surveillance and transmission studies would be suggestive of a negligible risk.”* to *“Members concluded that negative results are very hard to interpret as it is always difficult to provide proof of absence, however results from current and retrospective surveillance indicating the historical occurrence of atypical scrapie and the absence of a link between a particular form of CJD together with negative results from transmission studies would be suggestive of a negligible risk.”*

## **ITEM 3 – CURRENT ISSUES**

8. On his arrival, Professor Higgins chaired the rest of the meeting. SEAC was informed about the following issues:

- A recent opinion from the European Economic and Social Committee (EESC) on the disposal of animal carcasses and the possible use of processed animal proteins in the feeding of livestock. Contrary to UK press reports, the EESC had not recommended the feeding of ruminant material to ruminants but had suggested that the European Commission pursues research on the possible human health risks of using meat and bone meal from non-ruminants in feed to non-ruminants of a different species. The committee considered it important that the Department of Environment Food and Rural Affairs (Defra) should seek the views of SEAC should such a policy be proposed as part of the TSE Roadmap.
- Following the discussion at SEAC 97 of potential transmission of vCJD via dentistry, a reference group had been convened by Department of Health (DH) to consider this issue in depth and produce a more comprehensive risk assessment. Professor Graham Medley (Chair of the reference group) explained that the group had met on 14<sup>th</sup> June 2007 and included members of the dental profession as well as decontamination and TSE experts. The types and numbers of dental procedures and of instruments used were identified as a key areas for investigation. DH is undertaking a more rigorous assessment of the type and quantity of residues on dental instruments following standard decontamination. It was envisaged that results of a reasonable worst case assessment of the risk of vCJD transmission via dentistry would be presented at SEAC 99. However, this assessment would be preliminary as results from ongoing experimental research to inform the risk assessment were not expected until 2008.
- Ms Ruth Gasser (DH) was invited to address issues relating to dental practice that had been raised at SEAC 97. Ms Gasser explained that the dental profession, both private and National Health Service (NHS), is regulated by the General Dental Council (GDC). Concerns raised about fitness to practice would be considered by the GDC. In addition, the GDC coordinates continuing professional development (CPD) and dentists must undertake CPD which includes training in decontamination to continue to practice. All NHS dentists are legally required to adhere to satisfactory decontamination and infection control procedures, including quality assurance programmes. Primary Care Trusts (PCTs) have responsibility for inspections and monitoring compliance. DH is considering how private dentistry may also be similarly regulated. DH will publish a document in the Autumn 2007 on decontamination

that includes a supplement on dentistry detailing the standards expected. DH is also developing an audit tool for PCTs for infection control and decontamination. Members asked whether a standardised audit for procedures existed for private and NHS dentists. Ms Gasser explained that inspections of NHS practices include all aspects of practice including decontamination and infection control with a recommendation that they occur at least every three years. Private practices are not currently inspected, however DH is considering how such practices could be inspected. Members considered it very important that all dentists be inspected and audited to ensure that appropriate decontamination and infection control procedures are applied and dentists comply with relevant guidance, for example on single use instruments. Members asked what data are available on the numbers of dental procedures conducted privately. Ms Gasser explained that, as dentists are now paid through contracts and not for items of service, these data are not collected centrally. Members considered that these data are vital to inform risk assessment and risk management. A member suggested that data on the numbers and types of procedures conducted in private dentistry may be available from claims to private health care insurers. The Chair noted that it may not be possible to determine whether the potential spread of vCJD infection via dentistry is being curtailed unless dental practice is monitored and audited. In addition, meaningful risk assessments are dependent on obtaining data on the type and numbers of procedures conducted in private dental practice. Members also considered it very important that dentists be made aware why appropriate decontamination and infection control procedures are important. It was agreed that the Chair should write to the Chief Dental Officer to try to obtain clarification on these issues, critical to the risk assessments carried out by SEAC.

- The Food Standards Agency (FSA) TSE Research Review had been completed recently with two SEAC members taking part in the review process.
- The Deputy Chair had briefed the FSA Board in relation to the assessment of changes to the audit and inspection of specified risk material controls that SEAC considered at SEAC 95. The Board had been assured that if SEAC became aware of data that would affect that assessment, SEAC would notify the Board.

9. The Chair welcomed Lord Rooker to the meeting. Lord Rooker thanked the committee for its work over the years in assessing the science on TSEs, which is, and has been, of great value to government decision making.

#### **ITEM 4 – vCJD INFECTIVITY AND PLASMA DERIVATIVES (SEAC 98/2)**

10. Mr Stephen Dobra (DH) asked SEAC to assess the timing of possible infections from plasma derivatives that may have been contaminated with vCJD when derivatives were produced using plasma sourced in the UK, and to re-examine the likely removal of vCJD infectivity during the production of plasma derivatives at that time. The committee was also requested to consider what additional research might be needed to assess the likely clearance of vCJD infectivity during plasma processing. The existing assumptions used to estimate the level of infectivity in plasma derivatives are based on a previous analysis by Det Norske Veritas (DNV) that has not been reviewed for a number of years.
11. Dr Stephen Jenkins (Bio Products Laboratory [BPL]) provided an overview of studies at BPL to assess the clearance of vCJD infectivity during plasma derivative production processes. These studies are similar to other published studies and use microsomal fractions of brain homogenate from hamsters with 263K hamster scrapie spiked into plasma or plasma derivatives to measure the clearance of infectivity during processing. The results, which were derived from experiments that had not been repeated, were consistent with clearance factors estimated in the DNV analysis for most plasma fractions with the exception of albumin and immunoglobulin. There were also some minor differences in BPL processes compared with those outlined in the DNV analysis in terms of the size of pooled products and these do not appreciably affect the analysis of risk.
12. Professor Frank Hill (United Kingdom Haemophilia Doctors Organisation) provided an overview of the data that is being collected for the National Haemophilia Database on patients that have received batches of blood derivatives implicated for vCJD contamination. These data are being linked to patient records to determine what treatments patients received and when these occurred. Work is ongoing to assess how complete these data will be. Data is also being collected from death certificates for the database about the cause of death and availability of post mortem samples if an autopsy has been conducted. The National CJD Surveillance Unit has agreed to analyse any samples that may be

available for evidence of vCJD infection. A questionnaire has been sent to haemophilia centres to assess how many individuals have received implicated plasma derivatives. To date, no patients that received implicated derivatives have developed clinical vCJD.

13. Members noted that the best data on the risk of infection from plasma derivatives would probably be provided by the National Haemophilia Database.
14. A member noted that the DNV report assumes the period of risk for possible infections arising from plasma derivatives as being from the start of the BSE epidemic, around 1980, until around 1998 when plasma for plasma derivatives was sourced from countries considered to have little or no BSE. There are good data to suggest that the quantity of BSE infected material entering the food chain was greatest from about 1987 to the mid-1990s. However, there are many uncertainties around the size of the pool of vCJD infections that may have been generated and when the blood in vCJD infected individuals becomes infectious. Therefore, it would be unwise to narrow the window between 1980 and 1998 in which infections might have occurred. However, scenarios could be developed to assess how the level of risk during this window could change by considering the profiles of the BSE and vCJD epidemic curves.
15. Members noted that studies in hamsters and sheep suggested that blood becomes infectious at least half-way through but may be infectious much earlier in the incubation period.
16. The Chair asked, if exposure to vCJD in plasma derivatives had started to occur during the 1980s, why no clinical vCJD cases had been observed from these exposures. A member suggested that the absence of any cases of vCJD associated with plasma derivatives is not indicative of the absence of infections in the early part of this time window. The three clinical cases of vCJD associated with blood transfusions have been observed probably because they received a high dose of infective agent and were all of the most susceptible (MM) genotype, and therefore these infections would have a relatively short incubation period to clinical disease. However, the dose of infectivity from transfusion of plasma derivatives may be relatively low and so these infections may develop into clinical disease over much more extended periods of time. Members suggested that the lack of clinical cases of vCJD associated with use of implicated derivatives could exclude some scenarios for transmission of vCJD via plasma derivatives.

17. Members considered that data from spiking experiments are highly unreliable as the infectivity associated with a brain homogenate has different physico-chemical properties to infectivity present endogenously in blood. Therefore, a brain homogenate spike would behave very differently in the experiments to assess clearance factors compared with endogenous infectivity in plasma. It is not worth carrying out further spiking experiments until studies with 'real' clinical materials have been undertaken. Members noted that many published studies only measured reductions in abnormal prion protein and did not measure reductions in infectivity. In addition, studies to assess the clearance of infectivity during plasma processing fail to identify where the cleared infectivity is trapped. On the basis of the data presented, which are limited by the experimental approaches used, the committee concluded that there is no strong evidence that the risk assessments made in the DNV analysis should be superseded.
18. Members noted that the assumptions made in the DNV report had been endorsed by SEAC, the Committee on Microbiological safety of Blood, Tissues and Organs and the Committee on the Safety of Medicines. Members agreed that without substantive new data on the level of infectivity in blood and the clearance of infectivity in plasma during plasma processing the assumptions in the DNV report could not be re-evaluated. A member noted that a one log clearance factor is assumed in the DNV analysis as the worst case scenario by DNV and suggested that this should be reassessed.
19. Members agreed that studies to measure reductions in endogenous infectivity in blood and plasma during processing are required and that these studies should identify where the infectivity removed resides. It was noted that studies in sheep using endogenously infected blood to address these issues are underway but results will not be available for several years.
20. Members asked that, if infectivity is trapped by filters, could these filters, if reused, contaminate subsequent batches of plasma derivatives. Dr Jenkins explained that filters used at BPL are only used once, however ultra-filtration cassettes are reused but are disinfected with sodium hydroxide treatment between uses.
21. A member noted that the DNV risk analysis is used to estimate the risk of infection for those individuals that have received implicated plasma derivatives. Currently, those estimated to have a 1% or greater increased risk of infection above background are informed of this risk as it is considered that the benefits of informing them of

the possibility of infection outweigh the disbenefits. However, the 1% threshold was originally derived pragmatically by the CJD Incident Panel essentially when considering the context of patients who might have been put at risk through the use of surgical instruments previously used on patients with CJD. It was suggested that research in areas such as the psychology or sociology of risk perception could be conducted that might lead to a better founded judgement as to where this threshold should be set.

22. Mr Dobra asked for the committee's view on the potential infectivity of cryoprecipitate. Plasma for cryoprecipitate is sourced from UK blood donations unless for use for children under 16 years of age and usually a number of donations are pooled. The committee expressed surprise that UK sourced plasma is used and agreed that it would consider a risk assessment on cryoprecipitate provided by DH at a future meeting but could not make any further comment in the absence of data.
23. The Chair summarised the discussion noting that SEAC agreed:
  - there are no substantive new data to allow a reassessment of the infectivity of plasma derivatives from fractionation of contaminated plasma.
  - only research that measures the clearance of endogenous infectivity in blood would support a reassessment of the infectivity of plasma derivatives.
  - the National Haemophilic Database could provide important data to assess the risks of transmission of vCJD via plasma derivatives.

## **ITEM 5 – REPORT FROM THE SEAC EPIDEMIOLOGY SUBGROUP**

24. Professor Graham Medley (Chair of the SEAC Epidemiology Subgroup) explained that the Subgroup met on 5<sup>th</sup> June 2007 to discuss the generation of data and samples to allow a more accurate assessment of the prevalence of subclinical vCJD in the UK. The Subgroup reviewed the testing methodology and preliminary results of analysis of the first tranche of samples from the Health Protection Agency (HPA) National Anonymous Tonsil Archive (NATA). The Subgroup agreed that the methodology was appropriate, although uncertainties remain about the sensitivity of tonsil testing to detect subclinical vCJD. As analysis of the samples was incomplete, no firm conclusions can be reached, however the results to date are consistent with previous understanding of the prevalence of subclinical vCJD. SEAC is to

be presented with a more extensive dataset at SEAC 99. Work by the HPA and the blood services to determine the feasibility of using prototype blood tests for a survey of anonymous blood donations is ongoing.

25. Professor Medley explained that the Subgroup was also informed about progress to establish an archive of post mortem samples from coronial autopsies. This approach is considered very important as it would provide data on older age groups of the population, on which only limited data will be provided by NATA. Although the Chief Medical Officer (CMO) is very supportive of an archive of post mortem tissues, the Subgroup was informed that Coroners may be reluctant to take part as the archive would place an additional burden of work on them.
26. Mr Mark Noterman (DH) explained that the HPA is currently conducting a feasibility study for a post mortem tissue archive with several Coroner's Jurisdictions to ensure that the mechanisms to obtain consent from relatives of the deceased and sample collection and analysis are robust and reliable. Once this study had been completed, a letter would be sent to all Coroners' Jurisdictions, on behalf of the CMOs and the Department of Justice, to request that they participate in the archive.
27. The Chair asked if it was known how supportive Coroners may be. Mr Noterman explained that CMO had written to the Coroners' Society, the Coroners Officers' Society and the Royal College of Pathologists asking them to support the implementation of the archive. No responses had yet been received. It would be useful if the SEAC Chair could lend his support for the archive in the letter to Coroners. The Chair noted that Professor Sir David King (the Government's Chief Scientific Advisor) also considers the autopsy study important.
28. A member asked whether tissues from individuals that have donated their body to science could be collected for subclinical vCJD prevalence studies. It was noted that the number of such individuals is too few for such studies.
29. A member suggested it would be important for infectivity studies to be conducted on any positive samples identified in NATA. A member noted that the MRC Prion Unit was conducting infectivity studies on appendix tissue from the retrospective appendix/tonsil survey<sup>2</sup>. However, because the quantity of material was so limited

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<sup>2</sup> Hilton *et al.* (2004) Prevalence of lymphoreticular prion protein accumulation in UK tissue samples. *J Pathol.* 203, 733-739.

and had been subject to fixation, it is unlikely infectivity would be detected. It was noted that tonsil material appropriately stored and of sufficient quantity for infectivity studies is being collected by NATA.

30. Members noted that assessment of the sensitivity of tests used in NATA was important and noted that positive control samples collected from humans and animals were being made available to make these assessments. Members asked to see these data, if available, at SEAC 99.

#### **ITEM 6 – CODE OF PRACTICE FOR SCIENTIFIC ADVISORY COMMITTEES (SEAC 98/4)**

31. The SEAC secretary introduced the item stating that the Office of Science and Innovation is consulting on a revised Code of Practice (CoP) for Scientific Advisory Committees (SACs)<sup>3</sup>. The CoP promotes good practice in the operation of SACs and their relationships with government and helps to interpret the 2005 guidelines on Scientific Analysis in Policy Making. Revisions to the CoP were recommended in November 2006, by the House of Commons Science and Technology Committee in its report on 'Scientific Advice, Risk and Evidence Based Policy Making'<sup>4</sup>. The aim of the consultation is to ensure that evidence and advice from that evidence is robust, credible, reliable and objective and that the public is aware of this advisory process. Specific revisions related to quality assurance of committees, the role of lay members and SAC relationships with government departments. A formal response from SEAC to the consultation would be prepared in light of the committee's discussions.
32. A member noted that from a public and consumer perspective SEAC has always been seen as an exemplar of good practice for example by holding its meetings in public and communicating its statements and decisions using clear language. It was noted that the House of Commons report is not in favour of consumer or lay representatives on all scientific committees as a matter of course and it advises that their roles are re-evaluated. The member noted that lay members are in fact important in ensuring that information produced by committees can be understood by non-experts. However, it is important to make clear that a single consumer representative cannot represent the thoughts of all consumers. Periodic review of scientific advisory committees, such as is

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<sup>3</sup> <http://www.dti.gov.uk/files/file39981.pdf>

<sup>4</sup> <http://www.publications.parliament.uk/pa/cm200506/cmselect/cmsctech/900/900-i.pdf>

undertaken with SEAC, is important as a quality assurance mechanism.

33. The Chair agreed that many of the procedures considered best practice for SACs have evolved from the work of SEAC. He noted that some committees were reluctant to hold meetings in public. However, opening up meetings to the public and ensuring information is put in the public domain had not impeded discussions by SEAC and had removed concerns that information maybe being withheld. Only on rare occasions when unpublished data are being considered should discussions be held in reserved business sessions. This should be noted in the response to the consultation.
34. Members considered that although lay members could not be expected to make detailed comments on scientific detail, they could provide a global view on issues considered by committees. Lay members also have an important role in assisting the committee in ensuring that the outputs from a committee are communicated in a way that is understood by non-experts. Formal training, support networks and advice had become available for lay members on advisory committees. The committee strongly supported the need for at least one lay member but noted that it is important to clearly define their selection and role. It was considered that lay members, like other members of the committee, should not represent organisations but be appointed as individuals.
35. A member raised the issue of adequate compensation arrangements for those attending committee meetings. Members in private practice may incur costs in contracting a locum while serving on a SAC. A member noted that there is a huge difference in the compensation between different SACs and suggested that fees should be standardised. In addition, there is no mention of the relationship between committee members and their employers in the revised CoP. The document should consider and recognise that employers release employees for periods of time to serve on SACs in order to maintain this source of expertise in the future. The SEAC Secretary noted that, as part of the application process, applicants were asked to verify that they had the time required to sit on the committee and that their employers were content for them to serve on a SAC. The CoP should consider compensation arrangements and the employers of SAC members to ensure the best people are attracted to serve on SACs.

36. The Chair raised a concern about the proposed grouping of non departmental public bodies such as SEAC under the Defra web address as part of government's rationalisation of websites. Members considered this inappropriate as SEAC is an independent body and a Defra web address may negatively impact on this independence. It was added that a Defra web address would also be unsuitable as SEAC also reports to DH, FSA and the Devolved Administrations. The SEAC Secretary stated that she had already submitted a business case for SEAC to be exempted from this website rationalisation. The Chair committed to write to those responsible for the rationalisation to make them aware of the committee's concerns.
37. The Chair noted that he has links to Chief Scientific Advisors (CSAs) from DH, Defra and FSA and the government's Chief Scientist, Sir David King. He considered it important that SEAC retains this ability to interact independently with all CSAs to give the committee a further, informal, line of communication with departments.

#### **ITEM 7 – ANY OTHER BUSINESS**

38. The Chair explained that the SEAC Steering Group had decided that, due to the low numbers of people viewing the webcasts of SEAC meetings, this would be the last webcast meeting. The webcasts of this and previous meetings would continue to be available via the website. If a future discussion was considered of great public interest, it may be possible to film that discussion. The SEAC Secretary reassured the members, officials and the public that sound recordings of meetings would continue and be available to the public on request.
39. The Chair closed the meeting, thanking all those that had presented information to the committee and all those that attended the meeting.