



**SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE**  
Minutes of the open session of the 93<sup>rd</sup> meeting held on 6<sup>th</sup> July 2006

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

Members: Professor C. Higgins (Chair)  
Mr. J. Bassett  
Professor D. Brown  
Dr. J. Chambers  
Professor N. Hooper  
Mr. P. Jinman (Deputy Chair)  
Professor C. Lasmézas  
Professor J. Manson  
Professor G. Medley  
Professor J. Nicoll  
Dr. P. Rudge  
Professor M. Stanley  
Professor A. Williams

Assessors: Dr. P. Christie (SE)  
Dr. A. Douglas (DARDNI)  
Dr. A. Gleadle (FSA)  
Mrs. E. Lawrence (DH)  
Dr. M. Simmons (NAW)

Technical Experts: Dr. P. Barrowman (Defra)  
Dr. P. Bennett (DH)  
Mr. P. Burke (Defra)  
Professor N. Gill (HPA)  
Dr. I. Hill (FSA)  
Dr. D. Matthews (VLA)  
Dr. J. Stephenson (DH)  
Professor J. Wilesmith (Defra)

SEAC Secretary: Miss K. Richards

Secretariat: Dr. T. Barlow  
Dr. D. Cutts  
Dr. N. Ebenezer  
Dr. P. Keep  
Dr. C. Ravirajan

Also in attendance Mr. K. Millar (FSA)  
Professor D. Jeffries (Chair of the Advisory  
Committee on Dangerous Pathogens TSE  
Working Group)  
Dr. N. Tomlinson (DH)

## ITEM 1 – CHAIR’S INTRODUCTION

1. The Chair welcomed everyone to the 93<sup>rd</sup> meeting of SEAC. He congratulated Professor James Ironside, who had been Deputy Chair of SEAC for a number of years, on being appointed Commander of the British Empire.
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 The committee will hold a reserved business session in the afternoon to allow discussion of unpublished studies on BSE in cattle. This is in accordance with the SEAC Code of Practice. Short summaries of the open and reserved business discussions will be posted on the SEAC website next week.
3. On behalf of the committee and secretariat, the Secretary congratulated Professor Chris Higgins on his appointment as Vice Chancellor of Durham University. Professor Higgins will continue as Chair of SEAC.
4. A list of website addresses of recently published reports relevant to TSEs, and a report of the ‘Social Science Insights for Assessment’ workshop held by the Royal Society and Food Standards Agency (FSA), were tabled. The SEAC Chair had presented a case study of SEAC involvement in the review of the Over Thirty Month Rule at this workshop. The report outlines five principles to enable more effective risk assessment, risk management and risk communication processes.
5. On the 4<sup>th</sup> July 2006, the Secretary attended the Medical Research Council (MRC) New Therapies Scrutiny Group (NTSG) as an observer. The Group had received updates from two NTSG working groups and an unpublished MRC study, which would be discussed in the afternoon in the reserved business session.
6. The next SEAC meeting will be held on Thursday 21<sup>st</sup> September 2006 at the Hilton Hotel in Belfast.
7. Apologies for absence had been received from Ms Diane McCrea.
8. 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.

## **ITEM 2 – APPROVAL OF MINUTES FROM SEAC 92 (SEAC 93/1)**

9. The minutes were agreed as a correct record of the SEAC 92 open session.

## **ITEM 3 – CURRENT ISSUES**

10. SEAC was informed about the following issues:
  - Publication of the Department of Environment, Food and Rural Affairs (Defra) response to the independent review of the origins of bovine spongiform encephalopathy (BSE) cases born after the reinforced feed ban (BARB cases) by Professor William Hill (University of Edinburgh)<sup>1</sup>.
  - Draft guidance produced by the CJD Advisory Committee of the National Institute for Health and Clinical Excellence (NICE) on how to best manage the risks of transmission of Creutzfeldt-Jakob Disease (CJD) and variant Creutzfeldt-Jakob Disease (vCJD) via surgical procedures had been revised following a public consultation and had been issued for a second consultation. Members were invited to submit comments directly to NICE.
  - The Clinical Governance Advisory Group (CGAG), an independent group recently convened to advise the Department of Health (DH) on the appropriate counselling and care for individuals defined as 'at risk from vCJD for public health purposes'. Mrs Eileen Lawrence (DH) explained that CGAG would report to the four United Kingdom (UK) Chief Medical Officers (CMOs) and the membership and terms of reference would be circulated to SEAC. The first meeting had been very constructive with the Group agreeing that General Practitioners (GPs) of individuals at risk from vCJD are central to the support of these individuals but improvements could be made to the support available to both GPs and the individuals at risk. The Group expects to report later in the year.
  - The Chair reminded members that, following the SEAC recommendation<sup>2</sup> to the CMO that an expert group be

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<sup>1</sup> [http://defraweb/animalh/bse/pdf/hill-response\\_annex1.pdf](http://defraweb/animalh/bse/pdf/hill-response_annex1.pdf)

<sup>2</sup> <http://www.seac.gov.uk/statements/state260106.htm>

convened with urgency to consider the best way, including post mortem testing, of ascertaining the prevalence, age and genotype distribution of subclinical vCJD in the UK population, DH had asked the Health Protection Agency (HPA) to take this forward. At SEAC 92, SEAC had been informed that it would be given the terms of reference and membership of the group for comment by the end of May 2006. This information had not yet been provided. Professor Noel Gill (HPA) explained that, from discussions within the HPA and with key external parties, it had agreed the group should determine the practicability of large scale collection of post mortem tissues via the coroner's system. Identification of a suitable Chair and membership was underway, SEAC would be given an opportunity to comment on the composition and remit of the group. It was possible that the first meeting would be in September with one further meeting and the group reporting by the end of 2006. Members asked if the group would also examine the practicability of using donated and post-operative tissues for prevalence studies. Professor Gill explained that HPA considered that priority be given to discussion of testing tissues collected at autopsy since it was already collecting large numbers of tonsils for testing and collection of donated tissues would yield much fewer samples. However, if SEAC wanted the group to look at collection and testing of donated and post-operative tissues as well as tissues collected at autopsy, further discussions would be required to clarify the remit and membership. The Chair stressed that the principal objective should be to ascertain the approach that would provide the best possible and most rapid estimates of the prevalence of vCJD infection and urged that this group be convened as soon as possible. There had already been significant delays and SEAC had already been unable to give meaningful risk assessments to advise DH policy on several issues because of the lack of accurate information on prevalence.

- The SEAC Chair and Deputy Chair had briefed the FSA Board prior to its recent discussion on atypical scrapie and BSE in sheep. The Board's conclusions were published on the FSA website. The Deputy Chair thanked Drs Alison Gleadle and Irene Hill (both FSA) for organising the briefings to the Board. The Deputy Chair also attended the open Board meeting which had been very useful particularly in highlighting the uncertainties in the science of atypical scrapie. Dr Gleadle thanked the Chair and Deputy Chair for discussing these issues with the Board and noted it was likely that further

advice from SEAC would be required as new information on these issues becomes available. The Chair explained that as the human health implications of atypical scrapie are unknown, it would be advisable for the National CJD Surveillance Unit to remind neurologists to remain vigilant and refer unusual neurological cases to the Unit. The committee endorsed this proposal.

- The Chair noted that recent reports described two cases of BSE in cattle in the United States of America (USA) as being similar to atypical cases of BSE found in a number of European countries. The Chair suggested that the term “atypical BSE”, used in the USA report, is potentially confusing and that this would be discussed under any other business. Dr Danny Matthews (Veterinary Laboratories Agency [VLA]) explained that data from western blots of the USA cases resembled that of a small number of atypical cases of BSE in France. A study of the French cases had shown the condition to be transmissible to mice by intracerebral (ic) inoculation with the neuropathological phenotype maintained on transmission<sup>3</sup>. Claims have been made about the existence of atypical cases of BSE in other countries but these have yet to be confirmed. No study has yet examined the tissue distribution of abnormal prion protein (PrP<sup>Sc</sup>) or infectivity in such atypical cases of BSE.

#### **ITEM 4 – UPDATE ON CHRONIC WASTING DISEASE (SEAC 93/2)**

11. The Chair reminded members that at SEAC 85 (November 2004) the committee had discussed the human and animal health implications of Chronic Wasting Disease (CWD) in the UK and Europe. The main conclusions were that:

- there was no evidence that CWD or BSE is present in the UK cervid population, however a low prevalence could not be ruled out.
- there was no evidence that CWD is transmissible to humans from consumption of venison or to cattle, sheep or goats through non-experimental means.
- CWD poses relatively little risk to human health but as a risk cannot be entirely excluded a watching brief should be maintained.

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<sup>3</sup> Baron *et al.* (2006) Transmission of new bovine prion to mice. *Emerging. Infect. Diseases.* 12, 1125-1128.

12. As part of the watching brief, the SEAC secretariat had produced a review of the new information on CWD published since October 2004. The new data suggest that:
- more than one strain of CWD may exist.
  - the geographic distribution of CWD in cervids in North America may be increasing, although CWD has not been identified in surveys carried out elsewhere in the world.
  - the natural host range of CWD has broadened to include the moose.
  - although CWD has been transmitted to cattle after ic inoculation, cattle orally inoculated with CWD have shown no signs of infection after seven years.
  - CWD has been transmitted to non human primates but not to humanised mice by ic inoculation.
  - CWD may be transmitted through contaminated soils.
  - CWD infectivity has been found in the muscle of mule deer.
13. Mr Patrick Burke (Defra) explained that a European Union (EU) wide surveillance programme for TSEs in red deer and white tailed deer was intended to commence in Autumn 2006. The survey will include deer over 18 months old from five groups (i) animals that show clinical signs of disease, (ii) animals involved in road traffic accidents, (iii) fallen stock, (iv) culled deer and (v) healthy farmed/wild deer shot for human consumption. Male wild deer will be targeted as North American data suggest an increased prevalence of infection in male animals. Older farmed deer will also be targeted due to the increased probability of exposure to contaminated feed. Areas with a high historic or present incidence of BSE or scrapie or a high potential for historic consumption of BSE contaminated feed will also be targeted. Areas that received imports of deer from North America will also be targeted, although this does not apply to the UK. UK surveillance will be conducted over an 18 month period and will include 598 wild and 598 farmed deer. The committee asked how the numbers for the surveillance study were derived. Professor John Wilesmith (Defra) stated that the numbers were derived by the European Food Safety Authority (EFSA) expert group to enable detection of a certain prevalence of TSE infection<sup>4</sup>.
14. Members asked if experiments had been conducted to mimic natural transmission of CWD by continuously feeding cattle infectious material. Nobody was aware of such a study which

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<sup>4</sup> Information provided by Defra after SEAC 93: the numbers of deer selected enable detection of a prevalence of TSE infection in deer of  $\geq 0.5\%$ .

could be useful. It was noted that a study of cattle grazing in CWD endemic areas was ongoing but no transmissions had been observed.

15. A member asked if experiments have examined the susceptibility of European red deer to CWD. Dr Matthews stated that a study in the USA was examining the transmissibility of CWD to red deer but was of low priority as it is a minority species in North America. No such study is being conducted in the UK.
16. The committee noted that deer killed in road traffic accidents (RTA) may be a good source of material for TSE surveys as evidence from North America suggests such animals are more likely to be diseased. In addition, the annual culling of elderly sick deer in the Scottish Highlands may also be a good source of animals for TSE surveys. Research into the logistics of taking samples from deer in remote areas had been conducted that would aid the design of a survey. Dr Matthews noted that use of deer killed in RTAs is being considered but many animals would only be found several days after death reducing the quality of the samples that could be obtained. A member noted that much of the North American surveillance data was based on hunter killed asymptomatic animals.
17. A committee member asked about the age of the animals at the time of inoculation of CWD in the study using non-human primates. Dr Darren Cutts (SEAC secretariat) stated that the authors described the animals as adult when inoculated but a precise age of inoculation had not been stated.
18. The committee agreed with all the suggested changes made to the position statement in light of the new information as outlined in Annex 3 of SEAC paper 93/2 with minor grammatical changes. In addition, it was agreed the statement should include comments that distinct differences in the neuropathological phenotype had been found between the appearance of CWD and BSE in cattle and to clarify the number of humanised mouse strains inoculated with CWD in the transmission study cited.
19. The Chair commented that, although there was no evidence that CWD was a human health risk, a watching brief should be maintained. The Chair thanked Dr Cutts for surveying the literature and producing the paper. The updated statement would be placed on the SEAC website.

## ITEM 5 – ASSESSMENT OF FEED SUPPLY ROUTES (SEAC 93/3)

20. The Chair reminded the committee that at SEAC 87 (April 2005), SEAC endorsed a recommendation from the SEAC *ad hoc* Epidemiology Subgroup on UK BARB BSE cases that Defra perform a prospective evaluation of animal feed use and supply routes currently and in the recent past to provide information on their vulnerability to cross contamination.
21. Mr Burke presented an overview of a report on animal feed usage, the supply network and the feed industry. The main data sources for the report were reviews by the Advisory Committee on Animal Feedingstuffs (ACAF)<sup>5,6</sup> and Professor Hill's report on the origins of BARB cases<sup>7</sup>. The Hill report concluded that feed contaminated with mammalian meat and bonemeal (MMBM) is the major route of BSE transmission and that feed controls appeared adequate but required rigorous enforcement as small doses of infective agent can transmit BSE to cattle.
22. Mr Burke explained that a total of 20 million tonnes of feed is purchased annually in the UK, of which half is compound feed. Of the 10 million tonnes of compound feed that is purchased annually, 4.5 million tonnes are destined for cattle and these figures have remained constant since 1992. A quarter of the feed purchased is imported comprising 1.5 million tonnes from the EU and 3.5 million tonnes from non-EU countries. The feed chain is complex with movements of feed between countries and between premises.
23. Mr Burke explained that the risk of TSE infection from feed containing processed animal protein was likely to be low as this comprises material deemed fit for human consumption (category 3 material) produced to standards set in the EU Animal By-products Regulations. The risk of the presence of other types of MMBM, if present in feed, is uncertain, however MMBM is not necessarily synonymous with BSE infectivity. Animals fed home mixed feed, produced from relatively small amounts of purchased feed materials, may be relatively more vulnerable to BSE infection compared with animals fed commercial compound feeds due to a decreased dilution effect and short supply routes with decreased sampling opportunity. At SEAC 90 (November 2005), the committee had been informed that there was a possible link

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<sup>5</sup> Review of On-Farm Feeding Practices. <http://www.food.gov.uk/multimedia/pdfs/farm.pdf>

<sup>6</sup> Review of Feed Law Enforcement <http://www.food.gov.uk/multimedia/pdfs/acaffeedlaw.pdf>

<sup>7</sup> <http://www.defra.gov.uk/animalh/bse/pdf/hillreport.pdf>

between some clusters of BARB cases and the persistence of traces of feed produced before either the 1996 or 2001 feed bans in on farm feed storage systems.

24. Mr Burke outlined the voluntary feed assurance schemes and regulations covering the production and delivery of compound feed to farms. The National Feed Audit (NFA) run by the State Veterinary Service (SVS), monitors and enforces the 1996 feed ban in Great Britain. The NFA shows a high level of compliance with feed controls. A risk assessment model was used to design the audit and establish the appropriate level of visits required to premises involved in feed manufacture, handling, distribution, storage or use. Imported fishmeal is also tested for cross contamination with MMBM. However, it should be noted that the microscopy analysis test used in the EU to monitor the presence of MMBM in feed can only detect levels of MMBM > 0.01% (> 0.1% in the presence of 5% fishmeal). Detection of aggregate contamination in feed as opposed to homogeneous contamination, particularly at low levels, is difficult and it is not practicable to test all feed. Defra is funding development of new tests.
25. In conclusion, Mr Burke noted that an EFSA quantitative risk assessment<sup>8</sup> had concluded that if 10 million cattle were fed extensively on MMBM produced in a Geographical BSE Risk (GBR) category 3 country with reliable surveillance and removal of all specified risk material (SRM), fewer than two new BSE infections would be expected per year. The EU 2001 ban of animal protein in feed had been very effective. Defra was aware of only 14 BSE cases in cattle born after the 2001 feed ban in the first fifteen EU Member States<sup>9</sup>. The 10 new Member States may have implemented this feed control later than 2001. The EU adult cattle population is 43 million.
26. A member noted that the available data are not sufficiently robust to provide recent UK regional statistics for feed composition, supply and usage and considered these important data to obtain. Mr Keith Millar (FSA) noted that measures taken over the last five years had improved feed and food safety. The Feed Hygiene Legislation had introduced wider controls with approval and registration required for feed operatives throughout the animal feed supply chain. In addition to the introduction of assurance schemes, there is a greater awareness within the feed industry of

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<sup>8</sup> [http://www.efsa.eu.int/science/biohaz/biohaz\\_opinions/1148\\_en.html](http://www.efsa.eu.int/science/biohaz/biohaz_opinions/1148_en.html)

<sup>9</sup> The European Commission has since published its Annual Report of TSE Monitoring in 2005 which indicates a total of 17 BSE cases born in the EU after the 2001 feed ban to the end of 2005, 11 of which are in the EU15. UK has confirmed a further 3 such cases in 2006.

its relationship with the human food supply. It was important to note that vegetable products comprised most of imported feed material and little animal protein was imported.

27. Members noted sufficient statutory controls appeared to be in place but asked if the necessary information about the importance of feed controls was supplied to all the parties involved, especially the end users. Mr Burke explained that advice is provided by the SVS in the course of the NFA. Mr Millar added that feed compounders and farmers are very aware of the financial penalties for non compliance with feed controls. FSA had also instigated ongoing training for local authority trading standards officers who enforce the feed legislation.
28. A member asked if all compound feedstuffs were tested. Mr Millar responded that testing covers all types of compound feed and feed materials. Additionally, testing is specified by feed assurance schemes and feed compounders only source materials from members of such schemes. Feed materials imported from outside the EU are subject to the same controls that apply to EU produced material. A member asked if sampling also covered milk replacers for calves. Mr Burke offered to clarify this for the committee after the meeting<sup>10</sup>. In addition to tests relating to TSEs, testing also covered other contaminants such as heavy metals and mycotoxins. A member asked about contamination via drinking water. Defra advised that its epidemiological investigations into confirmed BARB cases examined water sources as a potential source of contamination. However, there was no previous evidence to implicate water sources with respect to BSE cases and testing water supplies for BSE infectivity was impractical.
29. A member asked for clarification of the term “protein concentrates” used in the report. Professor Wilesmith advised that this referred to protein rich commercial products derived from grain which are designed for home mixing. These products contain components such as soya and fishmeal.
30. SEAC welcomed Defra’s report and agreed it was a comprehensive summary of the current animal feed industry and a useful reflection on the feed supply process and the maintenance of controls. Members agreed that it is important to maintain as full knowledge as possible of the feed industry.

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<sup>10</sup> Information provided by Defra after SEAC 93: samples of farmed animal milk replacer are collected and tested in the NFA. It is difficult to quantify its use as feed types are not specifically recorded in the NFA.

## **ITEM 6 – PROPOSALS TO CONSULT SEAC ON THE PRIORITIES ARISING FROM THE EUROPEAN COMMISSION’S TSE ROADMAP (SEAC 93/4)**

31. The Chair explained that Defra and FSA had sought advice at SEAC 89 (September 2005) on the EU TSE Roadmap. Defra and FSA now sought comments on a list of issues arising from the Roadmap where it was proposed SEAC’s input would be required.
32. Mr Burke explained that members were asked to comment on suggestions from Defra and FSA to consult SEAC at various points in time on proposals arising from the Roadmap rather than the proposals themselves as many lacked detail at this time. Since SEAC discussed the Roadmap, the European Commission (EC) had consulted Member States and stakeholders, producing draft priorities, however the final document was yet to be published. Discussions on amendments to the EU TSE Regulation had been conducted in parallel. Progress on proposals described in the Roadmap largely depended on progress on amendments to the TSE Regulation. These include the BSE risk categorisation of countries, surveillance, SRM controls, tolerance of contaminants in feed, feeding fish meal to young ruminants and deferred cohort culling.
33. The committee generally agreed with the proposals to consult SEAC but stressed that it would be important for the departments to review their proposals and consult SEAC in almost all cases to be sure that emerging or unpublished data that may impact on the proposals are not missed. Dr Matthews noted that EFSA took unpublished data into account. Regarding tolerance of fishmeal in farmed animal feed, members agreed it would be advisable to undertake a risk assessment that SEAC should consider. This was particularly relevant in view of the proposal for a tolerance in feed for young ruminants that are known to be more susceptible to TSE infection. Mr Burke explained that the current proposal for a tolerance for fishmeal was based on a lack of evidence of an association between BSE and fishmeal in feed and of TSEs in fish. Dr Matthews noted that in the past fishmeal had been contaminated with MMBM but it would be very difficult to detect low level accidental contamination of fishmeal with MMBM. An EU project was starting to develop analytical methods to detect deliberate contamination with illegal material in feed, however detection of very low level accidental contamination was impracticable. The Chair suggested that as EFSA will consider a number of the issues, opportunities may arise for SEAC to feed into these deliberations.

## **ITEM 7 – METHODS TO EVALUATE NEW SURGICAL INSTRUMENT DECONTAMINATION TECHNOLOGIES (SEAC 93/5)**

34. The SEAC Chair explained that the Engineering and Science Advisory Committee into the decontamination of surgical instruments including prion removal (ESAC-Pr) is considering the evaluation and implementation of new decontamination technologies to reduce the risk of transmission of TSEs via surgical instruments. SEAC has been asked by ESAC-Pr to advise on the principles to consider when developing a strategy to evaluate new decontamination technologies, particularly on the most appropriate TSE agents and experimental systems.
35. Dr John Stephenson (DH) provided an overview of DH policy and research on TSE decontamination of surgical instruments. TSE agents are resistant to standard decontamination practices used in sterile service departments (SSDs) and contaminated surgical instruments have been shown to transmit prion disease. A key priority for DH is the provision of clean and sterile reusable surgical instruments. DH research covered three areas:
- estimating the risk of vCJD transmission via surgery by determining the thermal resistance of the BSE/vCJD agent, the protein load on surgical instruments leaving SSDs, the level of infectivity in human tissue and the prevalence of disease in the UK population. The programme had shown the vCJD agent is as resistant to thermal inactivation as the BSE agent, with autoclaving only reducing vCJD infectivity by two to three logs. A survey of appendix and tonsil tissue had provided estimates of the prevalence of vCJD infection. Infectivity studies on tissues from vCJD cases had allowed a categorisation of human tissues. Analysis of surgical and dental instruments had provided data on the variation in amounts of protein residues on instruments before and after cleaning. Unpublished research suggested the scrapie agent is 1000 to 10 000 fold more infectious when dried onto a metal surface than when in wet form.
  - development of methods to rapidly detect and quantify low levels of contamination on surgical instruments before processing to identify instruments that may need special treatment, and after processing to ensure the instruments could be used. Research had shown that the standard ninhydrin test for protein was of little value. A number of other methods including high sensitivity immunochemical, fluorometric, microscopic and magnetic acoustic resonance

detection methods had been developed with detection limits in the  $10^{-18}$  mole to  $10^{-15}$  mole of protein/mm<sup>2</sup> range. Infectivity assays using material bound to stainless steel wires and spheres had also been developed to validate novel inactivation technologies.

- development of novel cleaning and inactivation methods for instruments. Research suggested that alkali autoclaving at high or low temperatures removed infectivity and did not damage high quality instruments, however this process damaged low quality surgical instruments. Some laboratory detergents removed some, but not all proteins, from surfaces with some specialised commercial detergents particularly efficient. Use of thermostable enzymes in conjunction with detergents removed virtually all detectable protein and infectivity. High energy gas plasmas had been shown to remove detectable organic material from the stainless steel surfaces, cavities and long lumens of instruments. Current research was examining whether instruments could be coated to prevent adsorption of protein onto surfaces. There were promising results from tests on a diamond like surface.
36. Dr Stephenson explained that a number of decontamination products were being commercialised. Therefore, DH had convened ESAC-Pr to consider ways in which these new processes could be formally evaluated and, where appropriate, brought into practice in the National Health Service. ESAC-Pr and the Medicines and Healthcare products Regulatory Agency have recommended that current decontamination guidelines be followed until novel technologies have been formally evaluated. Taking into account advice from SEAC, ESAC-PR will produce generic performance criteria for such technologies. As a result new guidelines will be written by the Advisory Committee on Dangerous Pathogens (ACDP) TSE Working Group and issued by DH.
37. The Chair asked whether the variance in levels of protein contamination on surgical instruments reflected poor decontamination practice in some SSDs. Professor Don Jeffries (Chair of the ACDP TSE Working Group and member of ESAC-Pr) explained that variability in the level of residual protein on instruments was found between high quality SSDs and often variability in the level of residual protein was found between the same instruments. Residues did not correlate with the complexity of instruments. This variability may be due to protein residues drying onto instruments as it is suspected that residual tissue in dry form is harder to remove. The committee agreed it was very

important to examine the effect of allowing protein deposits to dry onto surfaces and its subsequent resistance to removal.

38. A member noted that no gold standard system exists that allows complete evaluation of technologies for TSE decontamination. However, based on a review of the published literature on the assessment of decontamination technologies, there are a number of key requirements for an evaluation system. The system should:

- quantify the reduction in the titre of infectivity as a result of the decontamination process. This would allow the effectiveness of a decontamination method to be assessed and compared with other decontamination technologies. It is important that the titration curve to allow quantification is generated using the same experimental system used to test the decontamination treatment. For example, if the decontamination method is tested on a brain homogenate, the titration curve should be generated from dilutions of the same homogenate. If the decontamination method is tested using homogenate bound to stainless steel wires, the titration curve should also be generated from stainless steel wires treated with dilutions of the homogenate. The method of experimental contamination of stainless steel varies widely between published studies with drying of material onto stainless steel used in some studies. This may be a potential source of variability in assessments of decontamination methods since dried material may be more resistant to decontamination than wet material. Consideration should be given to standardisation of experimental contamination of stainless steel.
- not be restricted to the use of hamster adapted scrapie prions as studies show that sporadic CJD and BSE prions appear to be more resistant to decontamination than the hamster scrapie strain. In addition, if it is intended that the decontamination technology be applied to instruments used exclusively on tissues outside the central nervous system (CNS), it is important that the technology be assessed using a TSE strain that has wide distribution, including the lymphoreticular system (LRS). As the most commonly used 263K hamster scrapie strain is poorly lymphotropic, alternative models using TSE agents with tissue distribution including the LRS should be used as well. These include mice with mouse adapted vCJD or BSE and bovinised mice with BSE or humanised mice with vCJD or sCJD. These models would more closely represent the human situation than the hamster scrapie model.

- include evaluation by bioassays as they are the most sensitive and relevant assays for evaluating the effectiveness of a decontamination technology to remove or deactivate TSE infectivity.
  - include preliminary screening of the effectiveness of a new decontamination technology prior to evaluation by bioassay. Cellular infection assays, although not yet fully developed, would be preferable as preliminary screens compared with biochemical assays. As the relationship between PrP<sup>Sc</sup> and infectivity is not well understood, the relationship between PrP<sup>Sc</sup> and infectivity may vary between TSE strains and PrP<sup>Sc</sup> and infectivity may be affected differently by decontamination treatments, biochemical assays may not accurately predict the effectiveness of decontamination. However, biochemical tests may be useful to determine the mechanism of decontamination or to monitor the effectiveness of a decontamination method once its effectiveness has been established.
39. Dr Stephenson noted that the mechanism of action of new decontamination treatments varies widely and asked whether evaluation systems need to be tailored to the type of decontamination technology or should a suite of systems be used that would be applicable to all types of decontamination technology. Members agreed that use of different systems to evaluate different decontamination treatments would make comparison of their effectiveness very difficult. Therefore, the same, rigorous evaluation system should be applied to all decontamination technologies under evaluation.
40. Members asked whether there was variation in the composition of stainless steel used in surgical instruments and whether this would introduce variation in the binding of prions. Dr Stephenson explained that there is variation in the composition of stainless steel and this affects the resistance of instruments to damage by cleaning processes. It was notable that alterations to the structure of the surface, for example by introducing a diamond-like surface, could modify protein binding. Dr Nigel Tomlinson (DH) noted that no study had compared the binding of proteins, or prion proteins, to the different types of stainless steel used to produce surgical instruments.
41. Professor Jeffries noted that a number of new decontamination products have been, or will soon be, CE marked<sup>11</sup> on the basis of

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<sup>11</sup> CE (Conformité Européene) mark is a declaration by the manufacturer that a product meets all the necessary requirements of the relevant EU legislation.

assessments made using systems that may not be relevant to human TSE agents. In evaluating new decontamination technologies, it was also very important to establish that new treatments do not leave residues on instruments that adversely affect patient safety and do not compromise removal of other infectious agents. As some treatments, such as aldehydes, had been shown to increase the resistance of proteins to decontamination, he asked if it was possible for new decontamination treatments to alter the phenotype of TSE agents. Members agreed that, as the nature of TSE agents is not well understood, treatments, which alter protein structure could, potentially, alter their infectious properties. Members considered it essential that the effect of decontamination treatments on TSE infectivity, not just PrP<sup>Sc</sup> or other protein levels, be evaluated. Since the binding of PrP<sup>Sc</sup> to stainless steel was relatively strong, assays to measure the effect of a decontamination treatment on removal of protein may not be a good marker for removal of PrP<sup>Sc</sup>.

42. A member asked if high pressure inactivation of TSE agents had been investigated. Dr Stephenson explained that a research application addressing this had been accepted by a review panel but it would not be funded due to research budget restrictions.
43. A member asked whether evaluation systems should assess the effectiveness of new decontamination technologies to remove dried on material, or would instruments in the future be kept in a wet environment until processed in a SSD. Professor Jeffries noted that experiments to examine the effect of leaving material on instruments to dry for various periods of time should be conducted, however this was precluded by current restrictions on research funding. He noted that guidelines in other countries recommended that instruments be kept wet prior to processing in SSDs. The UK Health and Safety Executive had advised that instruments could be kept wet in transit if appropriate sealed containers were used. Members considered it very important that these relatively simple experiments be carried out as the results could have a major impact on processing of surgical instruments. The committee noted that progress in a number of research areas was limited by the lack of available funds and asked when funds were likely to be released. Dr Stephenson responded that it was presently unclear when further research funds would become available but funding for some areas could be prioritised.
44. A member asked if research on removable surfaces on surgical instruments that would trap TSE contamination had been

considered. Dr Stephenson explained that this approach had been considered but no studies had been commissioned.

#### **ITEM 8 – AOB**

45. The Deputy Chair noted that use of the terms “atypical scrapie” in sheep and “atypical BSE” in cattle may cause confusion over the nature of the disease agent involved, and the risk to consumers. Although it was not for SEAC to determine the nomenclature of TSEs, it is important that the committee is clear when discussing the science of these issues, particularly with the public.
46. A member noted that atypical scrapie is generally used to define TSE cases in sheep distinct from classical scrapie. As there are some differences in the phenotype of TSE cases in cattle that appear different from BSE, it is possible that more than one strain of TSE agent may be involved.
47. A member suggested that in the future when the genesis and molecular biology of TSEs are understood, a logical classification may be possible.
48. The committee concluded that the term “atypical scrapie” in sheep was not ideal, however as it was in common usage a change in nomenclature now would be confusing. However, it was important to clarify that, in contrast to classical scrapie, which appears benign, the human health implications of atypical scrapie are unknown. Use of the term “atypical BSE” in cattle should be strongly discouraged.