



**SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE**  
Draft minutes of reserved business of the 78<sup>th</sup> meeting held on 24<sup>th</sup> June  
2003

At

The Department of Trade and Industry  
Conference Centre  
1 Victoria Street  
London

Members: Professor P. Smith (Chairman)  
Professor J. Ironside (Deputy Chairman)  
Professor A. Aguzzi  
Professor G. Bostock  
Professor R. Carrell  
Mr P. Jinman  
Prof H. Kimbell  
Dr C. Lasmezas  
Professor C. Masters  
Professor I. McConnell  
Dr J. Safar

Technical Advisors: Dr P. Barrowman (Defra)  
Ms A. Conroy (FSA)  
Dr S. Dixon (FSA)  
Mr P. Soul (Defra)  
Dr J. Stephenson (DH)  
Prof J. Wilesmith (VLA)

Assessors: Mr A. Harvey (FSA)  
Dr R. Jecock (DH)

SEAC Secretary: Dr C. Boyle

Observers: Dr S. Baxter (SERAD)  
Ms Y. Boyd  
Dr P. Crook (EA)

Mr B. Harris	(BBSRC)
Dr I. Hill	(FSA)
Dr J. Neilson	(HSE)
Dr M. Pitman	(MRC)
Dr D. Reynolds	(FSA)
Dr M. Simmons	(NAWAD)
Dr H. Tyson	(BBSRC)

Secretariat: Mr M. Pemberton  
Dr B. Jeffery  
Dr P. Keep  
Dr C. Ravirajan  
Ms T. Dale

Also in attendance: Professor N. Ferguson (Paper 78/7)  
Dr G. Wells (Paper 78/8)  
Ms S. Goligher (Paper 78/9)

**Item 1 – Chair’s introduction**

1. The Chair welcomed Professor Neil Ferguson (Imperial College London), Dr Mark Pitman (Medical Research Council), Mr Gerald Wells (formerly VLA) and Ms Sue Goligher (Defra) who were in attendance to present agenda items.

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2. The Chair asked the SEAC secretary to outline the criteria that had been used to include items in the reserved business meeting rather than in the open part of the meeting. Dr Boyle explained that the secretariat have put together draft criteria for including items in the closed session. These are still subject to refinement and discussion but the criteria used so far had been discussed and agreed with the Chair of SEAC and government departments. The committee was informed that the revised SEAC Code of Practice, terms of reference and the criteria for the reserved business session were at an advanced stage of drafting and would be presented to the committee for discussion at an early date.

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3. Pre-published scientific data will be considered in closed session unless the author gives permission for the information to be released in the public domain. With respect to the agenda for this meeting, most of the items included in the closed session fell under the category of pre-publication results. Item 78/9 on the Defra BSE contingency plan had been included in the closed session as discussion of this was likely to rely substantially on consideration of unpublished data that were being presented in another item in the reserved session.

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**Item 2 – Approval of 11<sup>th</sup> February 2003 confidential draft minutes (Paper SEAC 78/6)**

4. Members considered the minutes of the previous meeting on 11<sup>th</sup> February 2003, which had been circulated to members in draft form.

5. The Chair referred members to paragraph 3.9, of item 3 - Revision of ACDP/SEAC Guidance on “Transmissible Spongiform Encephalopathy Agents: Safe, Working and Prevention of Infection”. At the last SEAC meeting members queried about the transport requirements for TSE infected cell lines and whether this material should be treated as equivalent to tissue transported for diagnostic or investigation purposes. The Chair drew members' attention to the Health and Safety Executive's (HSE) response on this issue. Members noted the response and the draft minutes were agreed without any changes.

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**Item 3 – FSA Review of the Over Thirty Month Rule - preliminary results from an assessment of the risk posed to human health by BSE in cattle in the Republic of Ireland (Paper SEAC 78/7)**

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6. Professor Ferguson from Imperial College London presented this item.

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7. The aims of the assessment were to i) estimate past and current BSE infection levels in the Republic of Ireland (RoI) cattle population, ii) estimate exposure to infectivity in the human food supply, and iii) assess the risk from [this exposure](#) relative to the risk from BSE in UK cattle. [The assessment had been conducted as part of the work relating to the review of the Over Thirty Months Scheme and was relevant with respect to the risks associated with beef products imported to the UK, for which RoI was the largest supplier.](#)
8. Members were informed that the data available from RoI [were](#) less detailed than data available for the Great Britain (GB) and Northern Ireland (NI) risk modelling work. As with the risk modelling for NI, the incubation period and age dependent exposure / susceptibility parameters for RoI were assumed to be the same as estimated for GB. Deleted: was
9. It was estimated that 19,000 to 30,000 cattle [had been](#) infected [with BSE](#) in RoI during the epidemic, assuming a single increase in case reporting occurring in 2000. Infection incidence increased to a peak in 1996. A significant reduction in infection levels occurred in 1997 following the introduction of tighter controls, as reflected in the data [on BSE-testing of](#) apparently healthy [animals](#) and [fallen stock and casualty](#) animals. Deleted: were  
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10. An estimate of the number of infected cattle entering the food supply in the last 12 months of incubation [of BSE](#) was presented. The estimate was based on a test sensitivity profile, which [assumed high sensitivity only](#) in the last three months of the incubation period and a differential mortality [of animals incubating BSE](#) in the last three months before onset. It was predicted that exposure to infectivity peaked in 1998 with approximately 250 animals in the last year of BSE incubation entering the food supply. This was approximately 1,000 fold less [than](#) the peak exposure seen in GB. As a consequence of the drop in BSE incidence and the introduction of OTM screening, [the](#) number of infected animals in the last year of incubation that entered the food supply in 2003 was estimated at less than 25 animals. Deleted: of 100%, which assumed sensitivity  
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11. The total amount of infectivity entering the human food supply [was](#) predicted to have peaked in 1994 at approximately 20,000 bovine ID<sub>50</sub> oral units. In 2003, the amount of infectivity entering the human food supply is estimated at less than 100 bovine ID<sub>50</sub> oral units. Historically, the peak exposure level in GB was estimated as ~1,000 fold greater than in RoI. However at present, the current risk level in GB is estimated to be lower than in RoI due to the effect of the OTM rule. For the future, however, should any of the proposed birth-date options for changing the OTM rule be adopted, it is predicted that the risk in GB will increase to ~4 fold higher than in the RoI. Deleted: is
12. Based on a pessimistic scenario of 5,000 vCJD deaths from the cumulative exposure to BSE in GB cattle, the risk of exposure from RoI infected material entering the food supply between 2004 -2009 [was](#) Deleted: is

predicted to result in 0.0055 extra deaths over the next 60 years. This is about four times less than the equivalent GB figure. Using the worst-case parameter set, which assumes a test sensitivity profile of 3 months and a differential mortality over the last 12 months of the incubation period, it was estimated that it would increase the absolute risk to 0.016 extra vCJD deaths over the next 60 years.

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13. The uncertainty in the existing and predicted levels of infection in cattle was highlighted and the impact on the risk estimates was discussed. Allowing for a pessimistic scenario this would translate into a ~10 fold uncertainty in exposure during 2004-2009. When combined with the 3-fold higher risk in the worst case parameter set, the overall worst case risk estimate is predicted to be ~30 fold greater than the baseline results *i.e.* 0.15 extra vCJD deaths over the next 60 years. This compares with an equivalent GB estimate of 1.6 extra vCJD deaths.

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14. Members noted that compared with any likely date-based replacement to the OTM rule, the risk levels in Rol are predicted to be much lower than in GB.

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15. The Chair informed members that the Rol risk modelling work had been presented to the joint SEAC / FSA Risk Assessment Group (RAG) on 20<sup>th</sup> June 2003; RAG accepted that the analysis provided a sound basis for assessing the relative risk of bovine material originating from the Rol.

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16. Members queried the lack of reported BSE cases in Rol, as it was important to establish that cases were not being missed. They asked whether the Rol slaughter policy for infected farms could have impacted on the analysis. Members were informed that whilst the Rol slaughter policy would have removed some infected animals, it would not make a significant difference to the estimates. In considering the under-reporting of clinical cases, the historic and current movement of animals from the Rol to GB and NI was discussed. Although these movements were not taken into account as part of the modelling, and may explain some under-reporting of clinical cases, it was unlikely to account for the ~6 -10 fold under-reporting as estimated.

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17. Professor Ferguson noted that a full screening programme for Rol OTM animals is in place, and the infection prevalence levels for fallen stock, which are more problematic to test than apparently healthy animals, are comparable to those of GB.

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18. The Chair concluded that under any of the options proposed for replacing the OTM rule, inclusive of a testing programme, the predicted risk of animals imported from Rol is less than that for UK animals. It was acknowledged that members had only seen the data for the first time at the meeting, and it was therefore difficult for members to expect detailed comment on a relatively complex analysis. The Chair suggested that if members had further comments on further consideration of the analyses presented they should provide comments to the secretariat before 10<sup>th</sup>

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July when the FSA board are due to consider [potential revision of the OTM rule](#).

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**Note:** the final results for the risk assessment for RoI, which updates many of the figures given above, is now available online at <http://www.food.gov.uk/multimedia/pdfs/lsaotmroi0703.pdf>

**Item 4 – Update on cattle pathogenesis studies (Paper SEAC78/8)**

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19. The [committee](#) was updated [by Dr Gerald Wells](#) on ongoing research on the cattle pathogenesis studies at the Veterinary Laboratory Agency (VLA).

20. The initial pathogenesis study demonstrated the presence of BSE infectivity, [using the mouse bioassay](#), in a number of tissues (brain, cervical spinal cord, terminal spinal cord and retina) from naturally infected BSE clinical cases.

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21. A further study was commissioned to determine the temporal and spatial development of infectivity and pathology following oral exposure of calves to a single dose (100g) of naturally BSE infected cattle brain homogenate. In this study, clinical signs of BSE [in challenged animals](#) first occurred at 35 months post inoculation (p.i.). Infectivity was detected in the distal ileum of cattle at 6-18 months and 36-40 months p.i. Infectivity was also found in CNS and dorsal root ganglia at 32-40 months p.i. and in trigeminal ganglion at 36-40 months p.i. [by](#) the mouse bioassay. The detection of the PrP<sup>Sc</sup> in CNS at 32 months p.i. was followed by visible pathological changes at 36 months p.i. A large number of other tissues examined [by](#) the mouse bioassay did not show any evidence of infectivity, including tonsils.

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22. Comparative titration has shown that the [bioassay in cattle](#) is approximately 500-fold more sensitive than the [bioassay in mice](#). Therefore [infectivity studies had been repeated for](#) a range of tissues [by](#) [cattle bioassay](#). Groups of five calves from herds with no history of BSE or MBM feeding were inoculated i.c. with tissue homogenates. The results from this study had shown infectivity in caudal medulla and spinal cord collected at 32 months p.i. The recipient cattle had a mean incubation period of 23 months. The distal ileum from 6, 10 and 18 months p.i. in the pathogenesis study was also positive by cattle bioassay, with mean incubations of 27, 22 and 24 months respectively. A single animal inoculated with a pooled sample of palatine tonsil from the 10-month post exposure time in the pathogenesis study developed BSE with an incubation period of 45 months. The other four animals in this group were still alive at 58 months p.i. with no definite clinical signs of BSE.

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23. The [level](#) of BSE [infectivity](#) in tissues was estimated using a regression curve of incubation/dose from BSE affected cattle brain tissue. The estimates of the titre of BSE infectivity in CNS and the distal ileum with [an](#) approximate [two-year](#) incubation period suggests 10<sup>2</sup> cattle i.c. ID50/g.

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Tonsil samples with a 45-month incubation period suggest a low level of infectivity between  $10^0$  -  $10^1$  cattle i.c. ID<sub>50</sub>/g.

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24. To date, infectivity has not been detected in pooled lymph nodes and spleen (lymphoreticular tissues) from clinical cases of BSE using the mouse bioassay (at 700 days p.i.) or the cattle bioassay (at 86 months p.i.). Therefore, if any infectivity were present in spleen or lymph nodes the estimated potential titre of infectivity would be less than  $10^{-1}$  cattle i.c. ID<sub>50</sub>/g.

25. Further results from the ongoing cattle bioassay studies showed one of five animals inoculated i.c. with a pooled homogenate of lymphoid tissue from the nictitating membranes of 10 naturally infected BSE cases, succumbed to disease at 33 months p.i., 12 months shorter than the tonsil results previously reported. The shorter incubation period with nictitating membrane indicates a higher potential infectivity titre than tonsillar tissue. The estimated potential infectivity titre of nictitating membrane would be between  $10^1$  and  $10^2$  cattle i.c. ID<sub>50</sub>/g, which was higher than the tonsillar tissue but lower than CNS. However, nictitating membrane is not included in the human food chain.

26. One member suggested that end point titration studies conducted with CNS tissues gave the most accuracy and precision because of the homogeneous nature of infectivity distribution in CNS. The same is probably not true for lymphoid tissues because infectivity may be distributed more focally, i.e. concentrated in germinal centres. The possible heterogeneity of the inoculum was proposed as a possible explanation for single inoculated animals succumbing to disease in groups, which received tonsillar tissue and nictitating membrane. A histoblot of tonsils and nictitating membrane may help confirm any correlation between the anatomical distribution of infectivity in inoculated tissues and the number of animals infected. Members noted that a titration to establish a dose response curve for distal ileum was proposed.

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27. Members noted that the PrP<sup>Sc</sup> accumulation in tissues could be altered by proinflammatory cytokines following infections. As the experimental animals in the pathogenesis study and the cattle bioassay experiments had been reared in a near conventional environment (not germ free), the results could be influenced by intercurrent infections and/or parasitism. However, no specific intercurrent disease with which correlations might be made, has been noted in the studies. Members noted further that the nature of the PrP<sup>Sc</sup> in the tissue samples (whether complexed or dissociated) and the nature of the biological matrix in which it was found can alter the PrP<sup>Sc</sup> titration.

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28. The committee was informed that the cattle bioassay studies, which had been planned to continue for 15 years p.i., would be subject to review soon. SEAC's advice would be sought on making any decision on terminating the experiments.

**Item 5 – Update on Defra funded research on experimental BSE in sheep, and key pathogenesis research (Paper SEAC 78/9)**

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29. The Chair welcomed Dr Peter Barrowman from Defra to present the first part of this item. Dr Barrowman presented a summary of Defra-funded research on experimental BSE in sheep. One major component of this work aims to examine the pathogenesis of the disease and thus identify tissues which might present a risk to public or animal health or to the environment if BSE is found in sheep. The SEAC secretariat had requested an update on this work. Dr Barrowman emphasised that much of the research was in progress and preliminary findings should be regarded as confidential.

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30. Research from the Institute for Animal Health (IAH) first showed that BSE could be experimentally transmitted to sheep. Following this report, further research was commissioned to examine a range of questions including the pathogenesis of BSE in sheep, how BSE might present in sheep and how it might differ from the clinical manifestation of scrapie. Interim results from nine ongoing Defra-funded projects on experimental BSE in sheep were presented to the committee.

31. Dr Barrowman presented data that showed that the incubation period of BSE in ARQ/ARQ sheep was in the range of 495-671 days after intracerebral (i.c.) challenge with a dose of 0.5mL of a 10% bovine BSE brain homogenate. The incubation time was longer in all other genotypes studied, with the longest, notably, in ARR/ARR sheep with an incubation period after i.c. challenge which was approximately double that reported in ARQ/ARQ sheep. To date, only ARQ/ARQ sheep have developed disease after oral challenge with BSE (5g BSE infected bovine brain) with an incubation period of 628-1132 days. In these animals, PrP<sup>Sc</sup> was detected in lymphoid tissues from as early as 4 months post inoculation.

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32. No vertical transmission of BSE in sheep has been observed in one research project (SE1424) over 7 years, which includes 6 lamb crops. Dr Barrowman noted that it was important to pursue this project as following the withdrawal of MBM from ruminant rations, BSE could theoretically only be maintained in the sheep population through vertical transmission or environmental contamination.

33. Sheep imported from New Zealand were used in many of these projects to ensure a clean TSE background. Various genotypes of imported New Zealand sheep were challenged with BSE or scrapie to check if they were susceptible to infection (project SE1432). The most notable result to date is the finding that 3/19 ARR/ARR sheep developed BSE following i.c. challenge. The average incubation period in the ARR/ARR sheep was twice as long as that observed in ARQ/ARQ sheep.

34. Research is also in progress to examine if the BSE strain phenotype is stable following first and second sub-passage in sheep (SE1435, SE1945). Preliminary results from SE1435 indicate that glycoform patterns

of the prion protein remain “BSE-like” on passage in sheep, with SE1945 results pending.

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35. A study to examine the titration of experimental BSE in-sheep homogenate in sheep and across the species barrier in mice has started (SE1842). This research aims to determine the homogenate dilution required for infection post i.c. inoculation. To date, all ARQ/ARQ sheep challenged with a homogenate with a dilution of  $10^{-4}$  have succumbed to disease with an incubation period of 483 to 667 days. In addition, 3 out of 5 sheep challenged with homogenate dilution  $10^{-5}$  have succumbed between 644 to 734 days post inoculation. All mice in the  $10^{-1}$  to the  $10^{-3}$  dilution groups and some in the  $10^{-4}$  dilution group have shown clinical disease. This study should provide a measure of the underestimation of infectivity of sheep BSE when titrated in mice.

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36. Work to examine the effective minimum oral dose of BSE in scrapie-susceptible ARQ/ARQ UK Romney and New Zealand Suffolk sheep breeds challenged at 3 and 6 months old respectively is still at an early stage as sheep were inoculated in June and September 2002 (SE1846).

37. Research is underway (SE1946) to examine whether experimental BSE can be transmitted and sustained within a sheep flock. Unchallenged (control) sheep have been introduced to a flock containing sheep orally infected with BSE. This study will also provide a future archive of tissues from BSE-infected sheep.

38. Two pathogenesis studies, one at IAH (SE1428) and a larger one at VLA (SE1929) were outlined. Both studies aim to examine the distribution of BSE infectivity in sheep, particularly in the peripheral tissues. Tables summarising the findings from these studies were made available to inform the committee.

39. The pathogenesis study at IAH (SE1428) is examining UK Cheviot sheep. Although the challenged animals were ARQ/ARQ, which in this flock do not succumb to natural scrapie, it cannot be guaranteed that they were from a scrapie free environment. This needs to be borne in mind when interpreting the results. In view of this potential complication, another pathogenesis study (SE1929) was commissioned at VLA with a slightly different experimental design. UK Romney sheep were challenged orally with BSE at 6 months of age. Two years later NZ Suffolk sheep were orally dosed with BSE to verify that results obtained previously were typical and not breed dependent.

40. Dr Matthews described the pathogenesis study at VLA but stressed that at present this study can only give a qualitative rather than quantitative view of disease progression in the early months after exposure. A combination of IHC and bioassay is being used in the VLA pathogenesis study on the tissues of highest priority. In the early months in the challenged ARQ/ARQ sheep evidence of infectivity in limited lymphoreticular tissues has been detected. It progresses towards clinical onset with widespread distribution

of infectivity within the gastrointestinal tract, lymphoreticular tissues and central nervous system (CNS). Infectivity was detected in the CNS of Suffolks 10 months post challenge but not in the Romneys. In a number of the groups only one animal out of four was positive. This may be a sampling issue and be not significant, as closer to clinical onset it is more likely that more animals will develop disease.

41. Dr Matthews noted that sheep in the vertical transmission study at the IAH (SE1424) had not succumbed to BSE as the sheep at VLA had in SE1929. It was suggested that this might reflect age related susceptibility, as sheep in the IAH study were older at the time of challenge than in either of the pathogenesis studies.

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42. To date, no evidence of TSEs has been reported in ARR/ARR and ARR/ARQ Romney sheep up to 5.75 years after oral challenge with BSE. In ARR/ARR and ARR/ARQ Suffolk sheep, the animals are still healthy 3.75 years post-oral challenge. The bioassay results to date have not detected infectivity or immunostaining in the ARR/ARQ and ARR/ARR sheep tissues up to 22 months in the Romneys and 10 months in the Suffolks.

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43. Dr Matthews indicated that a paper had been submitted for publication and that once the full experimental design was in the public domain, it would be an appropriate time to consider the data from the mouse bioassay. Dr Matthews stressed that at present the research only included an initial screen for infectivity rather than estimations of tissue titre. For a risk assessment discussion, data would have to be considered including the number of mice that have died per assay and their incubation period. Therefore any infectivity estimates could only be derived via relative incubation periods and extrapolation from CNS results.

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44. Members asked if the Western blot (WB) and glyco-type analyses had shown any atypical results. Dr Matthews replied that WB analysis was limited to the CNS and was not being carried out on a full range of tissues.

45. Members asked if the second passage of BSE to sheep maintained all the biochemical characteristics of the original BSE. Dr Matthews replied that the Western blot pattern of the original BSE had been maintained but emphasised this was in ARQ/ARQ sheep. VRQ homozygotes were orally challenged last summer with no sign of clinical disease yet.

46. Dr Matthews noted that as evidence of infectivity in sheep liver had been reported, archive tissue from sheep liver was examined and found positive by immunostaining. Dr Matthews suggested it may be appropriate to include all tissue destined for food consumption in a risk assessment. Members agreed but it was pointed out that the tissue consumed most in sheep was muscle and members asked if there were plans to examine this by IHC. Dr Matthews suggested that other assays could be applied that may be more sensitive than immunostaining. Members commented that if

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BSE was found in sheep the data for the liver and muscle would be extremely important, as it would help prioritise formation of a SRM policy.

47. Dr Barrowman informed members that tissue from both pathogenesis studies had been collected and placed in a large archive. A selection process was required to help prioritise tissues for future testing and recommendations from SEAC would be very helpful in this respect.

48. Dr Gerald Wells commented on the differences between the VLA pathogenesis study (SE1929) and data published by Hadlow in that the latter detected traces of infectivity in spleen between 34 and 57 months in clinically affected animals. The current pathogenesis study found infectivity in Romney ARQ/ARQ sheep from 10 months post oral challenge.

49. Members asked Dr Matthews about the positive result in thymus in the bioassay. Dr Matthews replied that the first phase of the bioassay study was carried out on pooled tissues, partly due to costs involved. At interval culls, tissue was collected from 3 challenged animals, pooled and inoculated into mice. It had been subsequently shown that this approach compromises sensitivity, so some one-to-one assays using non-pooled challenges were performed. Dr Matthews commented that pooling of tissues might have influenced some earlier results where it might have been expected that thymus was positive, but he could not be absolutely sure.

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50. Members voiced surprise at the relative insensitivity of the VRQ homozygotes to BSE challenge. The incubation period was almost twice that of the ARQ homozygotes. Members asked if it was breed specific. Members were informed that this stemmed from an IAH parenteral challenge study, and all the VLA (SE1929) challenges reported on so far had been in ARQ/ARQ, ARQ/ARR or ARR/ARR sheep. At VLA, VRQ animals had only been challenged with BSE orally 8 to 9 months ago. Dr Matthews believed that BSE in the VRQ challenged at the IAH retained its pathological phenotype and glycoform, but this would need to be verified directly with the IAH.

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51. Dr Barrowman added that work on BSE challenge of VRQ/VRQ genotype is limited to a small number of UK breeds, which is ongoing so a complete set of information was not available.

52. Members noted that, although not part of the Defra-funded pathogenesis project at IAH, the positive transmission of BSE by blood transfusion could usefully be noted in the tabulated results to indicate the presence of BSE infectivity in sheep blood at different times in the incubation period.

Scrapie strain typing programme

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53. Dr Matthews updated the committee on progress with the scrapie strain typing programme using the modified Western blot procedure. The

prospective testing of samples from scrapie suspects started from November 2001. To date, the VLA has tested 1124 animals of which 770 were positive for a TSE. For retrospective testing (1998 to Nov 2001), 1062 samples have been tested with 1041 positive for a TSE; the remainder will need to be retested, as the signals were weak or negative. None of the results for the positive samples suggested that the isolate was behaving like BSE in ARQ/ARQ sheep.

54. The relatively small number of flocks of origin represented in the study, limited the value of these results in terms of whether BSE is in the national flock. With this caveat, the Chair concluded that to date, about 1800 sheep have been strain-typed with no indication of a BSE-like pattern. The Committee agreed this was a significant advance and despite the limitations of the test system these results were reassuring.

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#### Item 6 – Defra BSE contingency plan (Paper SEAC 78/9)

55. The Chair welcomed Ms Sue Goligher to present this item. Ms Goligher explained that Defra aimed to finalise a Sheep BSE contingency plan for submission to the EC this summer.

56. The EC has recently produced guidelines, which suggest that if BSE is found in sheep member states should consider a worst-case scenario where sheep meat would be excluded from the food chain. These guidelines are based on an opinion from the EU Scientific Steering Committee (SSC) in April 2002 on the safe sourcing of small ruminant materials.

57. The SSC opinion states that if BSE was found in sheep only the following animals would be allowed into the food chain:

- ARR homozygous sheep under 18 months of age
- ARR heterozygous sheep under 6 months of age

58. The SSC opinion also states that sheep and goat milk from suspect BSE cases should be excluded from the food chain. The SEAC secretary clarified this explaining that the detail on this point is slightly different between the draft EC Contingency plan and the SSC opinion. The guidelines represent the risk management view based on the scientific assessment of the SSC opinion. The contingency plan states that sheep and goat milk should be excluded from the food chain unless derived from sheep carrying at least one ARR allele, or unless derived from holdings certified TSE resistant or TSE free on the basis of solid criteria. The SSC opinion states that sheep and goat milk from suspect BSE cases should be excluded from the food chain.

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59. Ms Goligher reminded the committee that SEAC had advised on this issue on a number of occasions, most recently in March 2002. The most recent SEAC view concluded that if BSE were found in sheep only animals carrying the ARR allele should enter the food chain. A 12-month cut-off was appropriate for ARR heterozygotes, but in view of the SRM

requirements there was no justification for an age cut off in ARR homozygotes.

60. The SEAC sheep subgroup agreed in March 2002 that although the pathogenesis data had shown no TSE infectivity up to 34 months post infection, the 12 month cut off was appropriate for ARR heterozygote animals on a precautionary basis. In March 2002, an age cut off for ARR homozygotes was not warranted on the basis of experimental data as no ARR homozygous animals had been confirmed as TSE positive.

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61. In terms of safety of milk, SEAC advised in 2002 that only milk from ARR homozygote sheep should be considered as highly unlikely to contain the infectious agent if BSE were found in sheep.

62. It is important that the BSE contingency plan is based on the most recent evidence and risk assessments. The committee was asked to advise if the recent scientific developments indicate any change in the risk associated with consumption of the following

- 1) ARR heterozygous sheep over or under 12 months
- 2) ARR homozygous sheep of all ages
- 3) milk from ARR homozygous sheep

63. The Chair noted that the SSC contingency plan suggests that only homozygous ARR sheep under the age of 18 months should go into the food chain. This differs from SEAC previous opinion and the Chair asked members if the new scientific data required a revision of this opinion.

64. Members queried the scientific basis of the SSC opinion for an 18-month cut off for ARR/ARR sheep. They asked if infectivity had been demonstrated in any tissues of ARR/ARR sheep, (apart from those inoculated intracerebrally). The Chair replied that the cut off may have been a pragmatic view based on a convenient time when the third molar erupts.

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65. Members noted that as yet there is no evidence of BSE in experimentally challenged sheep at 18 months of age following peripheral challenge in ARR homozygotes or heterozygotes. Members noted that heterozygous ARR Romney sheep challenged with BSE are still free from infection five and three quarter years post challenge, and heterozygous ARR Suffolk sheep for three and three quarter years. On the basis of this the committee agreed there was no need to change previous advice with respect to ARR homozygous or ARR heterozygous sheep entering the food chain.

66. Extending this point, the committee was asked if the restriction of a 12 months cut off for ARR heterozygous sheep was still appropriate. Members noted that oral BSE challenge of defined genotypes in particular breeds has not indicated signs of infection in ARR homozygous or heterozygous sheep thus far, though there are recorded cases of natural TSE disease in ARR carrying heterozygous sheep. This indicates that

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ARR heterozygous animals are susceptible to TSEs. The Chair surmised that this would tend towards a more cautious approach maintaining the age cut off at 12 months until more information on the issue of general susceptibility to TSEs becomes available.

67. Dr Matthews asked SEAC to confirm that their recommendation was based on the experimental BSE research in sheep or if it was based on the lack of evidence for scrapie in ARR homozygous animals. The Chair indicated that the judgements are based not only on the experimental evidence of BSE in sheep but also knowledge of pathogenesis and distribution of scrapie in sheep. However if scrapie were reported in ARR homozygous animals, the committee would need to review their recommendation.

68. Dr Matthews informed members of the suspect scrapie case in an ARR homozygous sheep reported in Germany. The animal has tested positive by ELISA and Western blot however final confirmation is required as the sample was autolysed. The result is being treated as "inconclusive" until verified. Dr Matthews agreed to keep the committee informed on this issue.

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69. With regard to sheep milk, the Chair stated SEAC's previous advice of March 2002 that only homozygous ARR sheep should be used for milk production in the event BSE was found in sheep. The SSC opinion suggests that only milk from suspect BSE cases should be banned from the food chain.

70. Members considered that in view of the widespread infectivity throughout the lymphoreticular system in sheep post infection with TSEs, lymphocytes in milk could not be ruled out as a possible source of infectivity. Dairy sheep are kept to an older age than sheep reared for meat and some could be incubating disease in the event BSE was in the sheep population. Members expressed surprise that from the SSC opinion milk would only be excluded from sheep known to be suffering from BSE and not necessarily from those incubating it. There was concern that infants would represent a special at risk group.

71. The committee agreed there was no change in the risk associated with consumption of milk from ARR homozygous sheep, and endorsed their previous advice of March 2002.

#### **Item 7 – Joint Funders Group strategy for TSE research (Paper SEAC 78/10)**

72. Dr Mark Pitman (MRC) introduced the item and explained the background to the Joint Funders Group (JFG) strategy for research and development in TSEs. The JFG asked Professor Bostock to provide a scientific review of current knowledge on TSEs. Forty to fifty international experts in the TSE field were also asked to identify 5 key TSE issues that had been resolved in the last 5 years, 5 key publications to support the scientific

findings and 5 key questions about issues science may solve in the next 5-10 years.

73. The committee was asked to comment on the scientific review to ensure it covered all necessary topics.

74. The Chair and members welcomed the review and congratulated Professor Bostock on the quality of the review. Members noted that no priority had been indicated within the review. Dr Pitman replied that the JFG are currently considering all the topics and will identify key strategic priorities in due course. The strategy document will go out for public consultation, and SEAC will be included. Members commented that important research areas include structure and function of prions, the mechanism of neurodegeneration and therapeutic strategies, development and validation of further in vitro rapid tests and faster bioassays in transgenic animals.

75. Members highlighted a need to attract new scientists to the TSE field and give them sufficient lead time to establish themselves. Dr Pitman indicated that the research councils have the mechanism to offer such support.

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