SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

Minutes of the 65th meeting held on 28 February 2001 at the Methodist Central Hall, London

Members:	**Professor P Smith (Chairman)** **Dr C Bostock** **Mr R Bradley** **Professor H Kimbell** **Professor A Aguzzi** **Professor J Ironside** **Professor C Masters** **Mr P Jinman** **Professor R Anderson** **Professor I McConnell**
Technical Advisors:	**Mr P Soul (MAFF)** **Dr M Dawson (FSA)** **Dr J Stephenson (DH)** **Dr N Connor (DH)** **Dr P Edwards (DH)** **Dr M Bailey (TSE R&S U.)**
Observers:	**Dr K Finney (MRC)** **Dr M Wilson (BBSRC)** **Dr M McMurray (DARD-NI)** **Dr M Simmons (NAW)** **Dr D Shannon (MAFF- CSG- Morning only)** **Dr J Neilson (HSE)** **Dr A Leigh (DH)**
Secretariat:	**Dr P Nash (MAFF)** **Mr A Harvey (DH)** **Ms B Richards (FSA)** **Dr L Harbron (MAFF)** **Mr D Carruthers (FSA)** **Mr M Hall (DH)**
Also in attendance:	**Dr C Lister (DH- Item 5 only)** **Mr I Davidson (MAFF- Item 4 only)** **Mr P Comer (DNV-Item 4 only)** **Dr G Barnard (Item 7 only)** **Dr D Cunningham** **Dr C Donnelly (Imperial College- Morning only)** **Dr S Baxter (MAFF)**

Item 1- Introduction

1.1 Apologies were received from Professor Collinge and Dr Safar. The Chairman welcomed Deirdre Cunningham, the Director of Public Health Services for Lambeth & Lewisham Health Authority, who was attending the meeting to provide public health expertise to the Committee. The Committee also welcomed Barbara Richards who was attending her first meeting as the FSA secretary to SEAC. Martin Hall was also attending his first meeting as a member of the DH secretariat.

1.2 It was reported that the position of Chair of the Committee remained unresolved though it was hoped that a decision would be reached in the near future. The three outstanding Membership positions had been advertised and a number of applications have been received for the positions of protein chemist and public health expert, and the selection process was underway for the two posts. However there had been few applications for the position of geneticist and Members were again invited to submit suggestions for possible candidates to the secretariat.

Action: Members

1.3 Members welcomed the opportunity to suggest possible agenda items in advance of the meeting. Several topics had been included in the current agenda and further suggestions would be welcomed.

Item 2- Council decisions and imports

Epidemiology and testing (SEAC 65/1)

2.1 Dr Nash noted that since the last SEAC meeting, there had been greatly increased numbers of BSE cases in several Member States. This had resulted from the implementation of large scale surveillance throughout the EC, and the EU-wide requirement to screen all cattle over thirty months age for the presence of BSE before being passed fit for human consumption.

2.2 Members considered current BSE surveillance of UK cattle. Under the new EU regulations, the UK is required to test 9,000 fallen stock (casualty animals that are not subject to veterinary inspection and hence are not allowed to enter the food chain) and this began in January 2001. In addition, a further survey of five year old cattle slaughtered under the OTMS (over thirty month scheme) would begin in August 2001. Dr Nash also reported that the EC Standing Veterinary Committee had also recently agreed a proposal which would require the removal of vertebral column from all bovines over 12 months of age in the majority of Member states. This would require the re-introduction of the beef on the bone ban. However, because of existing control measures, the

UK had been exempted on the proviso it implements additional large scale surveillance of 275,000 OTM and casualty animals in GB, and an equivalent figure in NI.

2.3 Members considered the reliability of current BSE diagnostic tests. The Committee agreed that the tests were useful tools for epidemiological surveillance, but expressed concern that although the tests were being used to screen cattle in continental abattoirs, the tests had only been validated for use on brain material derived from animals with clinical BSE. Although it was likely that the diagnostic tests are able to detect BSE infection in the late pre-clinical phase of disease, infected cattle early in the incubation period may not be detected by current testing regimes. Members recommended that further work to assess the sensitivity of BSE diagnostic tests during the incubation phase of disease should be carried out.

Action: MAFF/FSA

2.4 Five tests were currently being assessed in the second EC BSE diagnostic test evaluation programme. In addition to measuring test specificity in NZ cattle, the programme would also examine sensitivity using a serial dilution. Members considered that although this was an important process, experiments should also be conducted to examine the sensitivity of putative tests using brain tissue collected throughout the incubation period. If the time in the incubation period when the test was able to detect infectivity was known, it would not only give clear guidelines to the efficacy of the test, but using data on the age structure of the whole UK herd, it would also allow an assessment of the overall number of sub-clinically infected animals in the UK. It was noted that although a research project has been specifically set up to collect and store tissues from cattle killed throughout the incubation period to aid test development, the resource was limited and care was needed to ensure that tissue was released appropriately. It was suggested that an independent panel to judge the merit of each request for archive tissue for test development should be considered.

2.5 Members noted that the UK BSE epidemic continues to fall, with approximately 20 cases per week currently being reported. However, the rising number of BSE cases in other EC Members States continued to be a cause for concern, particularly the small number of BSE cases with relatively late dates of birth (1996 and after), which may imply continuing exposure in some countries. It was noted that replacement animals for beef and dairy herds are still imported into the UK from Member states, and this would only increase because of the foot and mouth epidemic. There was some concern that if imported animals subsequently display clinical signs of BSE, it could jeopardise the UK's strong public health assurances and prolong the UK epidemic. If such animals also display clinical signs at a young age, it could

also inhibit the removal of existing control measures, particularly the OTM - rule.

2.6 SEAC expressed concern about results from a recent epidemiological survey of casualty animals over thirty months of age in Northern Ireland which indicated evidence of BSE infection in 2% of the 2546 animals sampled. Although these samples were taken from a high risk group of old, sick cattle which would not have entered the food chain, Members thought that the results were not fully consistent with the low incidence of clinical BSE in Northern Ireland and requested further information at the next meeting.

Action: Secretariat

SRM including Pithing (SEAC 65/2)

2.7 Members were updated on progress in implementing the EU legislation on specified risk material. They were informed that the extension of the EU controls to include the entire intestine of all bovines had been implemented in the UK from 01 January 2001 and that implementing legislation was in place to ban pithing of cattle, sheep and goats whose meat is intended for human or animal consumption from 01 April 2001.

2.8 In relation to this agenda item, Members asked for information about the use of catgut, which is manufactured from cattle intestines and used for surgical stitches in human and veterinary medicine. In terms of human health, it was recognised that the medical use of catgut sutures was being reviewed by the Medical Devices Agency (MDA), an Executive Agency of the Department of Health. SEAC welcomed the news that the MDA were in the process of informing the NHS about the decision of the manufacturers to stop supplying catgut sutures to the UK market. SEAC acknowledged that the decision to cease supply of catgut sutures in the UK was facilitated by the adequate supply of acceptable, alternative synthetic sutures.

2.9 Members requested clarification of whether current EU legislation classifying cattle ileum as a specified risk material prevented its use for cat gut and asked that further information on its use in veterinary surgery should be provided at the next meeting.

Action: Secretariat

Animal feed ban (SEAC 65/3)

2.10 Members considered a number of EU-wide animal feed regulations which had been temporarily adopted in light of the emerging BSE epidemic on the Continent. The temporary regulations prohibited the feeding of processed animal protein to all farmed livestock, as opposed to merely ruminants. This brought Members States broadly in line with current UK legislation adopted in

1996. SEAC strongly agreed that widening the EU feed ban was beneficial to the protection of animal health and should be made permanent.

2.11 On specific animal feed issues, Members were asked to consider a recent SSC opinion which stated that peptides and amino acids derived from animals where TSEs have not been identified did not need to comply with established processing standards provided appropriate microbiological standards are respected. In terms of feather meal, although ostrich have been reported to display TSE like symptoms, histological studies have not shown that this was due to a novel TSE in this species, and no other TSE's have been reported in avians. In general, Members concurred with the SSC opinion and agreed that hydrolysed protein could be included in non-ruminant animal feed in the UK without established processing standards, provided it was derived from animals where experimental or natural TSEs had not been identified.

2.12 Members also agreed that fishmeal could also remain exempt from the feed ban and be fed to all farmed livestock, although their interim conclusion was that fishmeal derived from wild fish was preferable to material derived from farmed fish.

2.13 In subsequent discussion with the Chairman, the conclusion was clarified in that, because of concerns about intra-species recycling, material from farmed fish should only be allowed if it could be assured that farmed fish had not been exposed to material derived from other farmed livestock, including other fish. If this could not be guaranteed then it should not be used.

Imports (SEAC 65/4)

2.13 The Committee was informed of the conclusions of a sub-group of SEAC which had met on 05 December 2000 to consider the risk from imported beef and beef products. The sub-group had welcomed the introduction of an EU requirement that from 01 January 2001 cattle aged over thirty months would not be allowed to enter the food chain unless they had tested negative for BSE using one of the EU-approved rapid tests. It had, however, expressed concern that, because of the limitations of these tests, a negative result would not necessarily mean that the animal was free of infection. The sub-group therefore considered that the UK's over-thirty-month (OTM) rule should continue to apply to imported meat until questions concerning the efficacy of the tests had been resolved. The sub-group had also expressed concern that the OTM rule did not apply to imports of processed meat products.

2.14 The FSA reported on the statements it had subsequently made, recommending retention in the UK of the existing controls, including the OTM rule, and advising that legally-sold imported French beef posed no significantly greater risk than UK beef. The latter statement had, however, made clear that

processed meat products from countries where BSE had been recorded might pose a slightly higher risk than legally-sold carcase meat, because they might contain beef from OTM animals. The FSA also informed the Committee that the EU SRM rules would permit trade in bovine head meat from all EU Member States except UK and Portugal.

2.15 In discussion, the Committee endorsed the conclusion of the sub-group that the OTM rule should continue to apply to imported carcase meat and confirmed that it continued to have a particular concern about the safety of imported meat products, given that they were not covered by the OTM rule. The Committee noted the FSA's statement on the safety of imported beef, but suggested that the position on French beef would need to be kept under review and that the assessment of the risks from imports should be made more comprehensive and include live animals. On bovine head meat, the Committee expressed concern about the possibility of contamination by brain material and recommended that a case for extending the SRM rules to include the whole head be made to the European Commission.

Action: FSA

Results of modelling work on BSE in Ireland and France

2.16 Dr Christl Donnelly from Imperial College outlined epidemiological modelling work on the BSE epidemic in Ireland and France. Estimates based on the number of reported cases during the previous year suggests that in 2000, 150 infected animals were slaughtered for human consumption in Ireland, of which 72 were within 12 months of clinical onset of the disease. Comparable estimates for France indicate 52 animals within 12 months of clinical onset were consumed. Both estimates assumed some level of underreporting. Because of UK protection measures, primarily the OTM rule, the UK figure was 1.2 animals.

2.17 Allowing for relative cattle herd sizes in the UK, France and Ireland (10m, 21m and 7m respectively), and assuming that 25% of Irish and French cattle consumed were over 30 months, the relative risks were roughly 25 times greater in Ireland than Great Britain, compared with roughly 6 times greater in France than Great Britain.

2.18 Members noted that if the OTM rule were fully enforced, the risk of consuming Irish meat in the UK would be essentially zero, as none of the cattle within 12 months of developing clinical disease would be consumed in the UK. But if enforcement fell short, then the relative risk would rise in proportion to the level of deficiency of enforcement. Overall, however, the relative risk from Irish beef, even if no account were taken of the OTM rule, was much lower than that from consumption of British cattle before the OTM rule came into force in March 1996.

2.19 Dr Donnelly noted that the epidemiological modelling was based only on clinically confirmed BSE cases and assumed full reporting of all cases. However, because reporting rates had increased during the later part of 2000, Dr Donnelly thought that the predictions may be revised upwards when additional data on BSE incidence in late 2000 became available.

2.20 Members considered current data on BSE cases in the UK and in other EU Member States. The rising number of infected animals in other Member States was a cause for concern, particularly the high proportion of 1996 (and possibly 1998) born cases in Germany, which may imply continuing transmission.

Item 3- Sheep

SEAC sheep sub-group report (SEAC 65/5)

3.1 At the meeting in November 2000, SEAC agreed to set up a small sub group to consider the basic principles underlying the national scrapie eradication plan. Members considered the subgroup's conclusions, which noted that there was increasing evidence to suggest that animals carrying the ARR allele were not sub-clinical reservoirs for prion infectivity. Therefore implementing an eradication plan based on selective breeding, both to eliminate susceptible genotypes – focusing particularly on the VRQ allele in the first stages – and to increase the prevalence of the ARR allele in the national flock, was a valid and important approach.

3.2 The sub-group recommended that the breeding program should proceed and in parallel, work should continue to determine if experimentally infected sheep carrying resistant alleles develop clinical disease or sub-clinical infection. It may be appropriate to assay tissues in transgenic mice or sheep to fully verify that tissues are not carrying infectivity. The sub-group considered that if new results came to light that implied that apparently resistant sheep were able to incubate disease, the National Scrapie Plan should be reviewed. SEAC accepted the conclusions of the sub-group and endorsed their recommendations.

ACTION: MAFF

Consideration of Phase III of the National Scrapie Plan (SEAC 65/19)

3.3 Dr Baxter outlined the proposals for phase III of the national scrapie plan which concerned scrapie affected flocks. The proposals had been drawn up by MAFF in consultation with the scrapie information group (SIG) and other interested parties, but were still at an early stage. SEAC were asked to consider both on the overall approach and a number of specific points raised in the paper.

3.4 SEAC agreed that targeting scrapie infected flocks and introducing appropriate measures such as breeding from fully resistant rams and lamb genotyping were important elements of the eradication plan. By increasing resistant alleles in flocks known to be infected with scrapie, it would impact on infection at the point of source.

3.5 There was a fine balance between pressure to take action to remove all scrapie affected animals, and encouraging farmers to report scrapie. In order to address the first concern, the proposals included the possibility of taking compulsory action on scrapie affected flocks at some point in the future. However in the first instance it was envisaged that the scheme would be voluntary, and incentives such as free genotyping and possible compensation would be provided to encourage farmers to join the scheme. As a further incentive, farmers who did not take advantage may then be forced to pay for genotyping and slaughtering costs if the scheme became compulsory.

3.6 Like the earlier discussion on selective breeding, Members agreed that the scheme should be introduced on a voluntary basis until further work had demonstrated that scrapie resistant animals, which would be used as replacement stock in scrapie infected flocks, are not capable of being latent carriers of infectivity.

3.7 Due to limited time, Members were not able to consider many of the specific aspects on the proposals for phase III of the NSP. It was suggested that a sub-group should convene to further consider the issues, but it was agreed that in the first instance, Members should comment via correspondence to the secretariat.

Action: Members

3.8 Subsequent to the meeting, it was agreed with the Chairman that a SEAC sub-group should consider phase III of the NSP in more detail. Their conclusions would then be fed back to the main Committee.

Action: Secretariat

Item 4- Risk assessment on small incinerators (SEAC 65/7)

4.1 The Chairman welcomed Mr Davidson from MAFF and Mr Comer from DNV. In September 2000, Members agreed the terms of reference for an independent study by DNV on the potential risks to human health from small incinerators burning SRM. A draft version of the report was tabled which indicated that the risk from such incinerators was negligible. However, Members agreed to convene a small working group to discuss the risk assessment in detail and report back to the full Committee at the next meeting.

Action: Secretariat

Item 5- Current Health Issues

vCJD update (SEAC 65/8A)

5.1 The Committee was informed that the total number of definite or probable vCJD cases now stood at 95. Of the 95 cases, the mean age at death was 29, with a range from 14 to 74 years of age; the mean age at onset was 28, with a range from 12 to 74 years of age. This meant that the mean ages at onset and death had remained approximately constant for the last 4 years. The median duration of illness was 13 months with a range from 5 to 39 months. Of the 95 cases, 53 were male and 42 female. It remained the position that of the 87 cases genetically tested, all were methionine/methionine at codon 129 of the PrP gene. 10 of the 95 were probable cases, with 6 out of the 10 still alive and 4 dead. The National CJD Surveillance Unit still awaited the results of autopsy investigations on these.

5.2 The Committee was referred to paper SEAC 65/8A that showed the PHLS quarterly analysis of the incidents of vCJD onsets and deaths. The analysis reviewed the data to the end of December 2000. With 4 new cases diagnosed in the quarter September to December 2000, the trend in deaths and onsets had increased to a rate of a 23 per cent increase per year for onsets and 35 per cent per year for deaths. On the evidence of the number of deaths observed so far, if the current trend continued, the short-term prediction for the total of number of deaths for 2001 was 36. Comparison of those potentially exposed when young to those exposed when older showed that the trends did not significantly differ.

5.3 The Committee commended the use of diagnostic tests for vCJD, and considered it was important that the clinical and histopathological criteria were categorised to ensure that the same criteria were used worldwide. The Committee heard that the National CJD Surveillance Unit did not identify vCJD by just one set of criteria such as glycotype. The National CJD Surveillance Unit encouraged ongoing collaboration so that any unusual strain of CJD was investigated. It was agreed that disease transmission tests e.g. into RIII mice should be employed in establishing whether cases were vCJD.

5.4 The Committee appraised the web atlas of images of vCJD that the National CJD Surveillance Unit had compiled and was informed that it had circulated microscopic slides of vCJD cases to researchers. The Surveillance Unit's microscopic slides were freely available to any interested researchers and the Unit was keen to examine the casework and results from other researchers to widen its experience base.

Action: DH

5.5 The Committee was advised that the French and Irish cases of vCJD had similar characteristics as the UK cases. It was reported that one case of sporadic CJD in a Dutch patient who was valine homozygous at codon 129 in the prion protein gene showed PrP isotype which resembled that of variant CJD. However, additional investigations had concluded that this case represented an unusual form of sporadic CJD. As part of the National Retrospective Review of CJD and Related Disorders, any cases of atypical dementia in the elderly showing amyloid plaques in the brain were subject to further review. One case in Edinburgh previously thought to be an atypical case of Alzheimer's disease had been shown to be an example of a rare familial form of CJD, and no cases of variant CJD in the elderly had so far been identified in this study.

Action: Members

5.6 The Committee was informed about a European Union funded project called QAMRIC that had used pattern recognition software to examine MRI scans of the brain. The software had compared and identified differences between vCJD and other types of CJD and could define sets of variation and be used as a point of reference tool for other clinical studies. It could help identify cases of greater concern and place them within a spectrum of the disease. Some of this data had already been placed on the Unit's website.

5.7 The Committee heard about the progress of the Surveillance Unit's research activity. The Unit had extensively sampled various regions of the brain and showed that in vCJD cases the glycotyping patterns did not vary significantly from one region of the brain to another or between different parts of the nervous system such as the spinal cord. However with sporadic CJD, there was sometimes quite a marked variation from one part of the brain to another. One of the NCJDSU's research priorities had entailed identifying human BSE infection where it did not display the customary characteristics of classical variant CJD. A World Health Organisation working group on TSEs chaired by Dr Phil Minor was assembling reference samples and standardising nomenclature associated with different glycotypes.

5.8 The Committee noted that the Unit's atypical cases had been genotyped.

<u>Geographically Associated Cases (SEAC 65/8b)</u>

5.9 The Committee was told that there were 9 geographically associated areas around the country with 2 or more cases of probable or definite vCJD. Three of these areas, including Leicestershire, were the subject of detailed local investigation in collaboration with the CJDSU, the London School of Hygiene and Tropical Medicine (LSHTM), the Public Health Laboratory Service (PHLS) the Communicable Disease Surveillance Centre (CDSC) and the Department of Health (DH).

5.10 The Committee noted that a national protocol to identify geographically associated cases, to decide which cases to investigate, to ensure consistency of the investigation process and to report feedback was near completion. The steering group that was composing the national protocol was comprised of representatives from CJDSU, LSHTM, CDSC, DH and the Public Health Medicine Environmental Group.

5.11 A final report on the Leicestershire cluster was due to be published soon by Leicestershire Health Authority. The draft report would be presented to the SEAC Epidemiology sub-group on 12 March. The Committee heard about some of the characteristics of the cases in these 9 areas: The *Leicestershire* cluster consisted of 4 definite and 1 probable case; in GRO-A there were 2 definite and 1 probable case, with two having attended the same dentist (earlier fears that they had both attended this dentist on the same day on one occasion proved incorrect), they had attended the same secondary school and two of them had lived in the same street; although the third case lived in GRO-A he had stayed in GRO-A in GRO-A there were 2 definite cases that had lived in the same street, possibly at the same time and had both attended the same special school for children with learning difficulties, although not at the same time, the investigation had looked at the two families involved; in GRO-A GRO-A a local investigation had been looking at the cases of 1 definite and 1 probable patient who was still alive, they had lived in adjacent streets for several years and had attended the same primary school; in *Wales* the investigation concerned one confirmed fatality and one probable case that had lived within 4 kilometres of one another and had attended the same comprehensive school for a year; in GRO-A investigators still had to look further into one fatality and one probable case; they had an age difference of 26 years although they had lived at the same time in the same street; in GRO-A an investigation was still awaited into one fatality and one probable case who was still alive who had lived in close proximity for a number of years; in *Surrey* an investigation had started into 3 definite cases who had lived within six kilometres of each other; in *Strathclyde* there were 8 cases. It had been noted that the Strathclyde cases had come from an urban and rural mix of a highly populated conurbation which reduced the epidemiological and statistical likelihood that this represented more than just a geographical connection. Therefore, no decision had been taken on whether an investigation should take place.

5.12 The Committee was informed that it would be premature to speculate in advance of the findings of the local investigations currently underway. It was clear that some geographical links were more tenuous than others. The Committee agreed that it would be helpful to investigate these geographical connections further but considered that it was too early to draw any conclusions from the findings so far.

5.13 The Surveillance Unit had noted that in some of the investigations, cases had attended the same school and had been about the same age, but that in at least one other case there had been a 26-year age difference which suggested that they had not had any educational or social commonality. The Committee was advised that the investigations of the geographically associated cases had included inspection of their medical and surgical histories. The investigations had not yet revealed any connection with surgical interventions, most particularly between patients in the same hospital at the same time and who had undergone the same procedure. However, the investigations were ongoing and the information collected was not yet sufficient to draw conclusions from.

5.14 The Committee agreed that it might be helpful to compare the geographical incidence of sporadic CJD cases with vCJD cases. It appeared that there were not so many geographically connected sporadic CJD cases as there were amongst vCJD cases. In addition, the analyses of the investigations were still ongoing. A report of the results would be published shortly.

Action: DH

Safety Of Human Blood- Fresh Frozen Plasma (FFP) (SEAC 65/9)

5.15 The Committee was told that last year the Department of Health's Blood Advisory Committee, MSBT, asked the Blood Policy Unit in DH to take a fresh look at whether to continue using fresh frozen plasma (FFP) from UK donors. This was the last remaining form of plasma used from UK donations. The National Blood Service had examined possible alternative sources of plasma and the sustainability of the supplies. The issue had been addressed when the UK had started to use US plasma blood products and it had seemed appropriate to take a fresh and more in-depth look at the situation.

5.16 Consequently the risk assessment had looked at the potential risk of person to person transmission of vCJD from fresh frozen plasma. The risk assessment described the risks quantified relative to a range of scenarios compared to the use of USA derived sources.

5.17 The Committee was told that last year the Department of Health had asked for an examination of the case for withdrawing UK derived plasma. It took account of issues such as increased viral risk and the sustainability of supplies. MSBT had discussed these issues at their last meeting in January and intended to return to them in April when there would be more information about the sources of plasma supplied from the USA. The Committee was asked to consider the assumptions in the risk assessment undertaken. It was hoped that SEAC could bring its knowledge of the various assumptions to bear, particularly on the size of the future epidemic. The Department of Health explained that MSBT would also appreciate knowing the Committee's view on

the assumptions that had been made in reaching the conclusion that, if alternatives to UK plasma could be found, it would be sensible to use them.

5.18 The Committee was advised that the Department of Health had considered various options, one of which was to use blood from US sources. In particular, the Department had looked at unpooled voluntary donated plasma collected by the US Red Cross. It was unclear whether these supplies would be sufficient to meet UK needs. Another possibility was a pooled product made from voluntary donated plasma that was currently under examination by the MCA for licence application in the UK. In the event that there was insufficient supply to meet the demand for unpooled plasmas, the Department had discussed the possibility of using it for infants and neonates as a priority and to recommend the use of pooled plasma for adults.

5.19 The Committee commented that the range of risk assumptions as presented should be widened. They considered that there was considerable uncertainty in a number of the parameters used, and that it was important to generate a range of options because the range of possible infectivity issues was unknown. The Committee pointed out that there was uncertainty surrounding the infectivity of plasma with some infectivity in leukocytes and some in the plasma fraction and yet there was a fixed result. Several current research programmes aimed to answer these questions.

Action: DH

5.20 The Committee asked for clarification on the incidence of white blood cells in plasma. The Committee commented that they understood from the CJD Research Strategy Group of the National Blood Service that filters reduced the leukocytes by 4 to 5 logs. The Committee expressed concern that although processing by filters could reduce leukocytes by 4 to 5 logs, despite this reduction, a pessimistic assumption was that there was still a real risk of infection from the damage and breakage of cells and possibly an increase in particulate infectivity in plasma. The Department of Health explained that research was in progress to examine these fragmentation concerns. The results so far were pessimistic/they showed no or only one log reduction or even an increase in infectivity. It was uncertain how many leukocytes remained in the plasma. The National Blood Service had done tests that showed that leukocyte depletion removed 30 to 40 per cent of infectivity in leukocytes. The Committee enquired about the effect on the risk assessment if leucodepletion had no effect e.g. depending on what was assumed about when the blood was drawn during the incubation period and what was assumed from the typical incubation period distribution of vCJD. The Committee postulated that the filters might not eliminate all the platelets, and that it was unfortunate that there were no alternative sources for investigating platelets. They asked if further research into platelets could be included in the research programme.

5.21 The Committee accepted that if FFP was sourced from outside the UK, the risk of vCJD transmission could be minimised further, but possibly at the expense of an increased risk from other infectious agents such as HIV and hepatitis C. It was explained that the Microbiological Safety of Blood and Tissues for Transplantation (MSBT) Committee would shortly be examining the risk assessment in the light of SEAC views and would be interested in examining the possible risks from these other infectious agents.

5.22 As the risk assessment was complex, the Committee recommended that Dr Azra Ghani, who had experience of these kinds of studies, should be asked to examine the risk assessment especially as the Committee considered that there were major uncertainties and variables that the risk assessment ought to reflect more strongly.

Action: DH

Safety Of Human Blood- Minimising potential vCJD risk (SEAC 65/10)

5.23. Members considered paper 65/10 on minimising potential of vCJD transmission via blood components. The Department of Health told the Committee about measures underway, in addition to alternatives to fresh frozen plasma derived from UK sources, to make blood safer. The Committee was told about the key vCJD risk reduction measures for blood already in place. One was that all fresh blood components were leucodepleted and that no plasma from UK donors was used in the manufacture of fractionated blood products.

5.24 The Department of Health had also commissioned a risk assessment to consider the impact of excluding blood transfusion recipients from donating blood. However, the National Blood Service had established that there would be a significant reduction in blood supply if this group were excluded. The service had to work hard to maintain adequate blood supplies from current sources. It would be difficult to recruit up to 30 or 40 per cent new donors every year which would be needed if this group of donors were excluded from giving blood. However, the Committee was advised that the results of this risk assessment would be available at the next meeting of the Microbiological Safety of Blood and Tissues for Transplantation Committee in April. The preliminary results suggested that the likely benefits would be fairly small compared to the disadvantage of a fairly significant reduction in blood supply. The Committee welcomed the review to consider possible alternatives to the plasma component of platelets and red cell concentrates. SEAC heard that the Advisory Committee on the Microbiological Safety of Blood and Tissues would consider the implications of this research on transplantation practice.

5.25 SEAC heard that there were three manufacturers worldwide producing a synthetic alternative to blood, known as synthetic clotting factor. It was in short

supply and because it contained some human albumin it was not free from the risk of transmitted infection. The Department of Health had been considering whether all haemophiliac patients should receive only synthetic products. As clinical trials of synthetic clotting factor had started it should be available in 2 to 3 years. The Committee was informed that over the next few months it was intended to set up a working group with the UK blood services to look at the feasibility of replacing all of the current blood products by synthetic compounds and the sort of research programme necessary to implement that.

5.26 The Committee was informed that there was a significant amount of research in this area and that there were products on the market and other products under development but that experience of their effects had met with mixed enthusiasm and success thus far. The Committee welcomed the research programme engaged on replacing all blood products with synthetic alternatives. The Committee supported the working group's study of the feasibility of implementing this and endorsed the move to transfer haemophiliacs to synthetic blood alternatives.

5.27 More generally, SEAC noted and welcomed efforts being made to secure the better use of blood including persuasion of clinicians to use less blood, to reduce the need for transfusion and to promote autologus blood transfusion where possible for elective surgery. This was part of a NHS-wide initiative that involved education of clinicians, audit and other medical strategies to reduce blood use. At the request of the Department of Health, the National Blood Service had established a National Blood Transfusion Committee. This would have a key role influencing the promotion of reduced blood use. A Better Blood Transfusion Conference planned for July would identify initiatives and strategies. This would be followed by detailed guidance to NHS Trusts.

Update On Decontamination Of Surgical Instruments And Introduction Of Single-Use Instruments (SEAC 65/21)

5.28 The Committee was referred to tabled paper SEAC 65/21. At SEAC's meeting last November the Department of Health had described the strategy it intended to announce to take forward decontamination of single use instruments. The Committee was advised that the announcement had appeared in a press release dated the 4th January 2001. It described the measures adopted to take forward work on decontamination and the introduction of single-use instruments. The Health Minister, John Denham, had announced the investment of £200 million to underpin a major drive on raising standards of decontamination to ensure that surgical equipment was cleaned and sterilised to the highest standards. This included modernising sterile service departments, providing new fully automated state-of-the-art sterilisers and washer disinfectors. All hospitals had been asked to review their services and, at the

direction of the NHS Chief Executive, each NHS Trust/hospital had appointed a person to draw up plans to implement these measures. Each NHS region had appointed one person charged with implementing procedures to deliver this programme of action.

5.29 The Department of Health confirmed that it had followed the advice of SEAC and introduced single-use instruments for tonsillectomy. The Committee noted that at its last meeting they had welcomed the launch of a pilot study looking into the practical options for introducing single-use instruments in other types of surgery.

5.30 SEAC heard about recent advice issued by the British Association of Otorhinolaryngologists, Head and Neck (ear, nose and throat) surgeons, following a meeting with the Deputy Chief Medical Officer. This had followed SEAC's advice to introduce single-use tonsillectomy surgery. As a result the Association had since instructed their members not to carry out routine tonsil surgery until single-use instruments were available unless it was an emergency involving, for instance, malignancy or airway blockage. The first 3,000 single-use instruments should be available in hospitals by March and by late summer all surgical units should have sufficient supplies of instruments.

5.31 At the meeting with the representatives of the ear, nose and throat surgeons it had been agreed that the introduction of single-use instruments would be closely monitored to learn any lessons and to analyse what other steps might be advisable. It had been estimated initially that the cost of single-use tonsillectomy instruments would be £25 million a year, but early indications were that this amount might be lower largely because of savings associated with mass production.

5.32 The advice that the British Association of Otorhinolaryngologists had issued to their members, included information about anaesthetic procedures following which the Department of Health had started discussions with the Royal College of Anaesthetists. Agreement was close on drawing up guidance about single-use anaesthetic equipment associated with tonsillectomy procedures that included equipment such as endotracheal tubes and laryngoscope covers.

5.33 The Committee was informed that the British Association of Otorhinolaryngologists had advised their members to try to ensure that instruments used in neurosurgery that were not single-use or were not currently practicable for single use, should be decontaminated to a particularly high standard using sterile service units that met the highest possible decontamination standards.

5.34 The Department had employed an independent operating theatre consultant to look at neurosurgery in practice (in clinical settings) and to try and identify a core list of instruments that were used for entering the dura mater. In the next two months, 6 trial core kits would be piloted at a number of neurosurgery units to evaluate whether surgeons could use these instruments and whether they constituted a kit that could be developed for single use and manufactured on that basis. A theatre nurse consultant had been engaged to provide a written evaluation of how this had worked at the 6 trial units. The Department undertook to keep the Committee informed of developments. In addition, the Department intended to hold further talks with ophthalmologists to identify the level of risk associated with back of the eye procedures and to explore the possibilities of adopting single-use instruments for these procedures.

5.35 The Department reassured the Committee that it had consulted fully with representatives of the professional bodies concerned and had consulted health authorities about the timing and feasibility of implementing these changes whilst ensuring that patient care was not impaired.

Update On Incident Panel (SEAC 65/18)

5.36 The Committee was informed about the CJD Incident Panel, which was an independent panel of experts chaired by Reverend Professor Michael Banner, Professor of Moral and Social Theology at Kings College, London. The panel was a subgroup of the ACDP/SEAC Joint Working Group. The membership of the panel came from various professional bodies, scientists, doctors, nurses, ethicists, lay people and lawyers. The panel's main role was to deal with possible exposures to CJD in healthcare settings. These generally came to light where there was a patient who was suspected or diagnosed of having vCJD or other forms of CJD and found to have a past history of surgery or blood transfusion, possibly having given an organ or tissue for transplantation.

5.37 The panel's task was to assess the risk and manage (where possible) the risk to other patients, for instance, where instruments had been used on patients after being used on patients who had then developed CJD. The panel provided advice to clinicians, other health professionals, trusts, health authorities and regional health authorities on deciding the most appropriate action to take to handle incidents that involved potential transmission of CJD and vCJD between patients through clinical interventions, including via surgical instruments, tissues and blood. The panel was launched in August 2000, had met the previous week and might meet in November.

5.38 The Department was engaged in preparing draft guidance on how the panel should respond when an incident was reported and had used the findings

of the risk assessment on surgical instruments, endorsed by SEAC, to inform this guidance. The Department of Health's Economics and Operational Research Division that introduced that risk assessment had also been working closely with the panel to assess how the panel could offer assistance to these more personal public health incidents. At the panel's meeting in the previous week the panel had agreed the general principles behind this guidance, namely public openness when these local incidents occurred, the panel's duty to increase knowledge about the actual risk of transmission through surgery and other invasive medical interventions and the wider protection of public health. The Committee was informed that the panel's advice would include the quarantine or disposal of instruments, if necessary.

5.39 The panel was also considering whether to authorise the establishment of a confidential public health database of people who may have been exposed through surgery or other medical procedures. Where it was considered that there was a particular public health need, the panel might recommend informing individuals who had been exposed.

5.40 The panel was considering what advice it should give in the case of blood and organs that had been donated by patients who had been exposed and what other precautionary measures were appropriate if these individuals had surgery in the future. Following last week's meeting this guidance was being redrafted for presentation to the panel in June and presentation to the parent body, the SEAC/ACDP Joint Working Group, in July. The panel had looked at incidents concerning 41 patients with CJD. These patients had received invasive medical procedures before symptoms of CJD had been identified. The panel was considering what advice they should give. That advice would reflect the guidance currently being drafted.

5.41 The Committee was informed that it was expected that a member of the dental profession would be added to the membership of the panel.

SEAC/ACDP TSE Joint working group

5.42 Due to lack of time, this item was deferred until the next meeting in April.

Item 6- DH Research Update (SEAC 65/12)

6.1 The Department of Health advised the Committee that the initial studies to detect infectivity in tissues from vCJD patients were nearly complete. Preliminary results indicated that the highest titres were to be found, as expected, in brain; the levels of infectivity in tonsils and spleen were 100 to 1,000 times lower than in brain. No infectivity had been found in whole blood

samples, serum or buffy coat. Further studies were due to start shortly and samples of spinal cord, appendix, CSF, lymph nodes, peripheral nerve, dorsal ganglia, trigeminal ganglia and bone marrow were to be tested. In addition, it was planned to examine samples of ocular tissue, dental pulp, placenta, thymus, and colostrum if and when these tissues became available.

Update on sheep transfusion study

6.2 The Institute for Animal Health had been commissioned to conduct a research programme designed to test whether infectivity could be transferred through blood transfusions. These experiments were carried out in sheep as procedures adopted by the National Blood Service could be copied closely. Of the two series of experiments, one used blood from sheep naturally infected with scrapie and the other transfused blood from animals fed BSE-contaminated material. Blood from an experimentally BSE-infected sheep in the preclinical phase of disease had been shown to transmit infectivity to a recipient animal. This work had been published in the Lancet in September 2000. The results of tests on blood from the complete set of other BSE-infected sheep, to find out if they transmitted disease, would not become available for several years nor would the results from the complete set of blood transfusions from naturally infected scrapie cases become available for at least as long. Although the estimate of the reduction in leucocytes through filters was clear, it was not known if that process eliminated infectivity. However, because sheep blood cells were considerably more fragile than human blood cells and their particulate characteristics were very different. Care would need to be taken in relating any results from work on sheep blood to the efficacy of leukodepletion of human blood in reducing levels of TSE agent infectivity.

6.3 The Committee was told that the retrospective surveys of archived tonsil and appendix tissue carried out in Plymouth and Edinburgh had gone well. It had been agreed by the DH/MRC steering group that further results would not be discussed until the Edinburgh arm of the study had been completed, and that group was expected to report in December 2001. The Steering Group had also recommended that a larger, possibly nation-wide, survey should be carried out, and to that end two subgroups had been set up. The first, chaired by Professor Boryseiwicz, was examining the technical and logistical problems associated with such a survey and this group had met for the first time earlier this month. The second subgroup chaired by Dr. John Saunders would examine ethical and associated issues. It was hoped that this group would hold its first meeting in the near future. The Department intended to set up a management committee to ensure that tissues collected by DH funded groups would be readily available, properly collected and managed and available to validate potential diagnostic tests. A group managed by the Department and the MRC oversaw the collection and use of tissue.

UK joint Funders TSE diagnostic meeting (12-13 Feb 2001)

6.4 The Committee heard that a meeting of various academics and commercial companies engaged in research work had taken place in February 2001 at Hinxton Hall Conference Centre on the Wellcome Trust Genome Campus outside Cambridge. Delegates had been able to share information and hear about various research projects. Between 130 to 140 delegates had attended with speakers from major industrial companies and the media. Feedback arising from the meeting had generally been favourable and members of the Committee congratulated the organisers of the meeting who had assembled such a large group of experts in the field.

6.5 The Department was currently discussing additional projects to develop and evaluate new diagnostic tests with 5 research groups. Two of these proposals involved an evaluation of the ICE technology developed by Dr Mary-Jo Schmerr and her colleagues in the USA.

Item 7- MAFF R&D update

7.1 The Committee conducted its regular review of research findings and epidemiological information on BSE. SEAC noted that in ongoing experiments to examine the pathogenesis of experimental BSE in sheep, Romney, Suffolk and Cheviot sheep of susceptible genotype had shown evidence of infectivity in their tissues early in the incubation period. However, encouragingly, no tissues from sheep carrying the ARR allele had yet been found to be positive.

DELFIA results

7.2 Dr Barnard from Southampton General Hospital presented an overview of the technology underlying the time resolved dissociation-enhanced fluoroimmunoassay (DELFIA) diagnostic test for BSE. Initial technical problems related to sample preparation which gave rise to an unexpectedly high number of positive results had been resolved and the test was now giving results which were consistent with those from histopathological examination, which is considered to be the most reliable standard against which tests such as DELFIA are compared. The test is being applied to samples collected from OTM animals.

Progress on the new study on bovine Milk

7.3 Members considered the protocol of a new FSA funded experiment to examine milk for evidence of BSE infectivity. Mr Dawson explained that milk taken from 10 cattle experimentally infected with BSE would be collected at eight time points over two lactations. Both somatic cell fractions and bulk samples would be concentrated and examined using a validated diagnostic test.

7.4 Members agreed that bioassaying samples in cattle or mice would be a more sensitive test for infectivity than current immunologically-based diagnostic techniques, and should be considered. However it was noted that all previous work, including mouse bioassay, had found no detectable infectivity in milk.

Action: FSA

Novel changes in red blood cell progenitors in TSEs

7.4 Discussion of this pre-publication paper was deferred because of lack of time

Item 8- Internal Committee Items

8.1 Dr Nash reminded Members of their commitment to hold an open meeting in September 2001. Members briefly considered possible approaches to the meeting (SEAC 64/14), but in view of the limited time available, it was agreed to convene a small SEAC working group to consider the arrangements in more detail.

Action: Secretariat

8.2 All other Internal Committee items were deferred because of a lack of time.

Item 9- Matters arising

9.1 These items was deferred because of a lack of time.

Item 10- Any other business

10.1 This item was deferred because of a lack of time.

SEAC Secretariat- March 2001

Working Notes

1. Feb 2002- Circulated to Chair and secretaries for comment
2. 23 April 02- Comments for the Peter Smith incorporated