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FOREWORD

Welcome to the first Annual Report from the Spongiform Encephalopathy Advisory Committee (SEAC). Previously, information about the Committee has been in the form of news releases issued by the Department of Health (DH) and the Ministry of Agriculture, Fisheries and Food (MAFF) and occasional reports. But the Committee and its sponsor departments, DH and MAFF considered that the time was now right for the Committee to issue a short annual report to summarise its work in the past year.

The 1997/98 year has seen considerable changes: the Membership has broadened and new terms of reference were set by the Minister following a wide-ranging review, which was published by MAFF and DH in July 1997.

I continue to be very grateful to my colleagues on the Committee for their valuable contributions during the year and their unreserved commitment to resolving the frequently difficult issues laid before the Committee. The same gratitude must be extended to the SEAC Secretariat and the support staff in MAFF and DH. I would also like to thank the many people who have helped the Committee through the provision of pre-publication research findings or technical briefings on particular issues

I hope that you find this report of interest. If you have any comments or suggestions on how it could be improved I would be grateful you could send these to the SEAC secretariat.

GRO-C

Professor Sir John Pattison

Chairman

Chapter One

INTRODUCTION

1. The Spongiform Encephalopathy Advisory Committee (SEAC) is an advisory non-departmental public body appointed by Ministers and sponsored jointly by the Ministry of Agriculture, Fisheries and Food (MAFF) and the Department of Health (DH) to provide independent, scientific advice to Government. It has the following terms of reference:

> "To provide scientifically based advice to the Ministry of Agriculture, Fisheries and Food, the Department of Health and territorial departments on matters relating to spongiform encephalopathies, taking account of the remits of other bodies with related responsibilities."

SEAC currently meets regularly and advises Ministers on any measures the Committee considers necessary to protect human and animal health. Ministers decide how to respond to these recommendations and announce their response and give details of the SEAC recommendations thereafter. To date, all advice given by SEAC has been accepted and acted upon by successive Governments.

History of the Committee

2. SEAC and its predecessors have been examining every aspect of spongiform encephalopathies since bovine spongiform encephalopathy (BSE) was first discovered, over 10 years ago.

BSE was discovered in November 1986. In May 1988 a Working Party was established to examine the implications of BSE in relation to both animal health and any possible human health hazards and advise the Government on any necessary measures. This Working Party on BSE, chaired by Sir Richard Southwood (Professor of Zoology, Oxford), produced some interim recommendations during 1988, all of which were acted upon, and reported finally in February 1989 ('The Southwood Report').

One of the recommendations of the Working Party was the establishment of a Consultative Committee on Research (CCR) into spongiform encephalopathies (SEs) and this was formed by MAFF in February 1989, under the Chairmanship of Dr David Tyrrell of the Medical Research Council. Its remit was to advise MAFF and DH on research on SEs, including the work in progress or proposed, additional research required and the priorities. An interim report ('The Tyrrell Report'), concentrating on research needs into BSE, was prepared in June 1989 and subsequently published.

In April 1990 the CCR was re-constituted as the **Spongiform Encephalopathy Advisory Committee (SEAC)** with a wider remit to advise MAFF and DH on matters related to SEs and effectively assuming the role of the Southwood Working Party *and* the CCR. A second interim report, published in April 1992 and prepared by SEAC, indicated that the funding agencies and the scientific community had responded positively to the first report by launching a substantial number of new research projects.

3. Between 1990 and 1996 SEAC met on average four times a year to consider the research findings and suggest where further work was needed. In 1994 they collated existing information and in 1995 published 'A Summary of Present Knowledge and Research into Transmissible Spongiform Encephalopathies (TSEs)'.

4. The work of SEAC increased considerably during 1996: scientific developments before the Secretary of State for Health's announcement on 20 March 1996 of the identification of a new variant of Creutzfeldt Jakob Disease (nvCJD) and the possibility of a link between this disease and BSE, and the ensuing BSE crisis, imposed a very heavy workload on the Committee. In the light of these new demands it was decided towards the end of that year to review the functioning of SEAC.

SEAC Review

5. The Review, which was presented to Ministers in the Department of Health and Ministry of Agriculture, Fisheries and Food in July 1997 was conducted by officials in those Departments and had the following terms of reference:

> "to review the terms of reference, structure, membership and operations of SEAC, having particular regard to the situation arising from the identification of new variant Creutzfeldt Jakob Disease (nvCJD)".

The Review made a number of recommendations and these are summarised in Annex I. With the completion of this Annual Report all of the recommendations contained within the Review will have been implemented.

6. This Annual Report therefore covers a period of considerable change in the history of SEAC, as it adapted in response to the current BSE/nvCJD situation. Full membership of SEAC is given in Annex II.

Sub-Groups and Working Groups

7. With the approval of Ministers the Chairman of SEAC can authorise the setting up of sub-groups to discharge specific tasks. Sub-groups are chaired by SEAC members, have clear terms of reference and are required to report to the main Committee. There is no established pattern for their structure, and there is considerable flexibility about how they are set up, depending on the issue in question.

During the year SEAC had sub-groups on epidemiology and on the risks associated with infectivity in dorsal root ganglia.

There is also a joint working group with the Advisory Committee on Dangerous Pathogens (ACDP), set up following the SEAC review, which is chaired by the Chairman of the ACDP. The terms of reference for this group are:

> "to consider the risks from exposure to the agents of transmissible spongiform encephalopathies that may arise as a result of work activities, to develop guidance to minimise such risk and to provide advice as requested by the parent committees (ACDP and SEAC)."

During the year of this report the epidemiology sub-group held one meeting on BSE and two meetings on nvCJD, the risk assessment sub-group met once before SEAC's December 1997 meeting, and the ACDP/SEAC working group met four times.

Full membership of the epidemiology sub-group and the ACDP/SEAC working group are given in Annex III (parts a,b and c).

Openness

8. The Committee, as part of a Government-wide initiative to increase the openness of advisory committees, considered ways in which it could improve the transparency of its deliberations. The SEAC Review recommended that the Committee publish a summary after each meeting. This has been done since September 1997 (see Annex IV). The Committee welcomed moves to greater openness and expressed a willingness to participate in them. However, it was also considered that a mechanism to safeguard confidential scientific, patient, veterinary and commercial information that was crucial to its work would need to be built into the process. Given the sensitive nature of much of the Committee's work, the Review recommended that agendas should not be published. Similarly, the minutes of each meeting were a record of a confidential process of decision-making and should continue not to be published. Throughout the year the Committee continued to give consideration to measures to promote further openness.

Chapter Two

MEMBERSHIP

Review recommendations

9. The SEAC Review recommended that membership of the Committee should be kept under review to ensure it includes expertise in the relevant fields. Epidemiology, microbiology, neurology, neuropathology, veterinary pathology, virology, genetics, veterinary medicine, public health practice, food toxicology/gastro-intestinal immunology and a representative of the public interest were identified as fields which should be represented on the Committee. However, it was emphasised that these should be constantly reviewed as more about TSEs becomes known. The Review recommended immediate expansion of the Committee's membership to include a representative of the Institute for Animal Health and a representative of the public interest.

10. In February 1998, in response to the Review, the Government announced that it had appointed six new members to the Committee, taking the total membership to 18.

11. The Review recommended that new appointments to the Committee should be made on a fixed term basis, usually for three years, with Members normally being asked to serve a maximum of two terms. All of the new appointments have been made on this basis. Appointments to the Committee made before December 1995 were not time limited. It was recommended that existing Members not already on fixed term appointments should be formally appointed on a fixed term basis, up to the end of the 3rd and 6th year respectively; and that those who had served more than 6 years should be put on a fixed appointment for one year, with the possibility of extension in individual cases. This has now been done.

Membership of SEAC at the end of the period covered by this report is given in Annex II.

Code of Conduct for Members

12. Following the Review, a Code of Conduct was drawn up by the Secretariat, written with regard to the seven principles of public life identified by the Nolan Committee in their report on Standards in Public Life. In the Code, guidance specific to SEAC is given on communications with Ministers and the media, handling of papers and operation of the Committee in general (e.g. clearing of minutes), publication of work by SEAC members, conflicts of interest and confidentiality.

Register of Members' Interests

13. In accordance with the principles of public life identified by the Nolan Committee, details of commercial and non-commercial interests of SEAC members, which may conflict with their responsibilities as Members of the Committee, are put into the public domain. This has been done by reply to a written Parliamentary Question. The register is at Annex V.

Chapter Three

THE WORK OF THE COMMITTEE DURING THE YEAR

14. As well as considering specific issues the Committee keeps abreast of current research. Research findings may be in the form of published papers, as pre-publication drafts, or presentation of key results.

15. The Committee met nine times between 15 April 1997 and 9 March 1998. During this period SEAC monitored the epidemiological information on BSE and nvCJD and noted that the number of BSE cases had continued to decline compared with the same period the previous year. The number of nvCJD cases had increased from 15 confirmed and one probable, to 22 confirmed and one probable. Throughout the year the Committee monitored the latest findings on nvCJD and in September members considered new research results which they concluded provided compelling evidence that nvCJD is caused by exposure to the same agent as causes BSE.

ISSUES ADDRESSED BY THE COMMITTEE DURING THE YEAR

A. Protection of human health:

- Human blood and blood products
- Routes of exposure
- Cattle and sheep audit trail
- Sheep and goat meat: specified risk material
- Risk of imported beef and sheep products
- Infectivity in dorsal root ganglia and safety of meat
- Gelatin
- Tallow
- Safety of Milk
- Water filtration

B. Protection of animal health and monitoring:

- Same species feeding
- Fishmeal
- Sub-Clinical BSE
- Maternal transmission
- Scrapie surveillance

C. Environmental issues

- Environment agency reports:
  - Incineration of meat and bone meal
  - Landfill of BSE carcases
- Spreading on land of rendering condensate
- Disposal of excreta
- Use and disposal of bovine blood

D. Alternative theories

- Organophosphates
- Autoimmunity

A. Protection of human health

HUMAN BLOOD AND BLOOD PRODUCTS

16. At their meeting in October 1997 SEAC recommended that the National Blood Authority adopt a precautionary policy of extending the leucodepletion of blood as far as practicable pending the results of an assessment of the risk of transmitting nvCJD by blood.

ROUTES OF EXPOSURE

17. In February 1998 the Committee considered a preliminary analysis of the possible ways by which BSE infectivity may have entered the human food chain over the course of the BSE epidemic. The Committee noted that this preliminary analysis required detailed review and substantial revision.

CATTLE AND SHEEP AUDIT TRAIL

18. In July 1997 the Committee considered the final report, prepared by Leatherhead Food Research Association (LFRA) for MAFF, on the potential routes of exposure to BSE through the historic sale of potentially infected tissue from bovines and sheep. The purpose of this audit was to provide an overview of the slaughtering, rendering and by-products industries for sheep and cattle in the period 1980-1995. Much of the report was based on anecdotal evidence, and the Committee was keen to validate the information it contained before publication.

SHEEP AND GOAT MEAT: SPECIFIED RISK MATERIAL (SRM)

19. During the year, the Committee concluded that all sheep and goat heads should continue to be treated as SRM. In addition, in May 1997, the Committee said that the spinal cord from sheep and goats with a first permanent incisor should be removed and treated as SRM and that the use of the vertebral column for mechanically recovered meat (MRM) should be banned. The Committee concluded however, that the production of tallow and gelatin, which involved a high degree of processing, could be permitted from sheep and goat vertebral column. The Committee recommended that these restrictions should also apply to imported sheep and goats (except those from scrapie-free countries).

RISKS ASSOCIATED WITH IMPORTS OF BEEF AND SHEEP PRODUCTS FROM OTHER MEMBER STATES

20. Also in May 1997 SEAC considered the issue of imports into the UK of material containing tissues from bovine central nervous system (CNS) in the light of existing controls on bovine risk materials in the UK and elsewhere. It took into account the EU Commission's assessment of surveillance and control in other Member States. SEAC concluded that action should be taken to extend, within the UK, controls on specified bovine material (SBM) to imports of CNS or bovine material containing CNS from the EU, and from third countries - other than those where there is no known risk of BSE. Again, it would be preferable if action could be taken on an EU wide basis but if agreement in Europe could not be achieved quickly, unilateral action by the UK was recommended.

INFECTIVITY IN DORSAL ROOT GANGLIA AND THE SAFETY OF MEAT

21. In December 1997 the Committee considered a report on the risk to consumers following the detection of infectivity in nervous tissue called the dorsal root ganglia (DRG). Under experimental conditions cattle were fed 100g of BSE-infected bovine brain. They later developed infectivity in the brain, spinal cord and DRG. The latter lie within the bones of the spinal column and would be left with the bone when meat is cut off the spine. The DRG were not at that time covered by the specified bovine material (SBM) restrictions. Preliminary findings indicated that infectivity might be found in the bone marrow of cattle at a very late stage of disease and showing clinical symptoms. The significance of the results on bone marrow was difficult to judge at the time and the Committee decided to consider this further when the experiment was complete.

Although the risk from infectivity in DRG was thought to be extremely small, SEAC recommended that the public should be informed immediately, and presented the Government with measures it could take if it felt such a risk was unacceptable. One option was to require that all beef from cattle over 6 months old should be sold with the bones removed, ensuring that DRG were not inadvertently eaten. This was the policy adopted by the Government and the Beef Bones Regulations 1997 came into force on 16 December 1997

GELATIN

22. The production and use of gelatin, which is used as a gelling agent in a variety of foods and cosmetics and is also used in the manufacture of pharmaceuticals, was reviewed by the Committee in October 1997. (Gelatin is manufactured either from hide material or bones.) The Committee noted that plants in the UK manufacturing gelatin for food, feed, cosmetic, medical or pharmaceutical use have been brought under official control. The Committee

also noted that all UK gelatin manufactured for these purposes from bovine raw material utilised only imported ingredients. They noted that implementation of Commission Decision 97/534/EC would exclude Specified Risk Materials from the source materials used for gelatin manufacture in all Member States. The Committee decided they needed to make no further recommendations on gelatin: UK controls were re-assuring.

TALLOW

23. As a by-product of the rendering industry, tallow is used in food and feed and for cosmetic, pharmaceutical or medicinal purposes. As with gelatin, it too was affected by the export ban. In October 1997 the Committee also reviewed the production and use of tallow. It noted the restrictions in the UK on the sources of raw material used in the production of tallow and was impressed by UK tallow production controls. The Committee noted that imported tallow was not subject to the same restrictions nor required to reach the same standards but that the implementation of Commission Decision 97/534/EC would result in the exclusion of Specified Risk Materials from the production of tallow across all Member States from January 1998.

SAFETY OF MILK

24. In the New Year the Committee reviewed the processing and use of milk. In particular, they considered the relevance of recent research publications implicating lymphocytes in the pathogenesis of TSEs. The Committee noted that there was no evidence of infectivity in spleen or lymph nodes of cattle infected with BSE. No changes were made to the previous advice on the safety of milk: SEAC confirmed that it considered current measures to protect the consumer to be appropriate.

WATER FILTRATION

25. The Committee considered the use of bovine bone charcoal for water filtration. They noted that the bones came from countries which had no reported cases of BSE, were sun-dried and bleached and that the production method included heating to 1000°C. Consequently they concluded in January 1998 that the practice could continue.

B. Protection of animal health and monitoring

SAME SPECIES FEEDING

26. The Minister of Agriculture, Fisheries and Food asked SEAC to review the practice of feeding animal by-products to animals of the same species. The Committee recommended in December 1997 that the Government develop a

strategy to remove the risk of TSE transmission from intraspecies recycling of pig and poultry waste at the earliest opportunity, in consultation with EU partners.

FISHMEAL

27. The Committee were asked to consider the feeding of fishmeal to farmed fish. It concluded in January 1998 that this was not strictly speaking intra-species recycling, since fish meal was sourced from different species to which it was fed. Also, farmed fish offal was excluded from fish feed. Consequently they saw no reason to change the practice.

SUB-CLINICAL BSE

28. At their meeting in March 1998 the Committee reviewed the theoretical possibility that, in certain circumstances, BSE infectivity could be present in cattle which do not show the signs of clinical disease at any time during their normal life-span. There was evidence from research in mice and hamsters that in certain conditions the TSE agent could persist in the animal without ever causing clinical disease within the natural lifespan. It would be important as the clinical disease in cattle declined to ensure that there was no such reservoir of latent BSE infection in the national herd. The Committee considered that the Government should initiate further research into this issue.

MATERNAL TRANSMISSION

29. In April 1997 SEAC concluded that the MAFF research into the possible risk of maternal transmission of BSE in cattle ('the cohort study') showed that there was some evidence of a low level of direct maternal transmission but that the inheritance of a genetic susceptibility to feed-borne infection could not be ruled out as a factor in determining the outcome. These findings were consistent with the interim results released in July 1996.

Having considered the evidence, SEAC recommended that the Government should consider the options for a cull of offspring based on the assumption that the cause of BSE cases born after 1 August 1996 was maternal transmission rather than exposure to contaminated feed. If any genetic susceptibility exists, the maternally based cull would contribute to the removal of these genes from the national herd.

SCRAPIE SURVEILLANCE

30. The Committee urged the Government to pursue its plans for improving the epidemiological surveillance of scrapie in sheep and goats and to screen as many cases as possible using newly developed techniques. In May 1997 it endorsed a three part strategy encompassing :

- compulsory slaughter of suspect cases with compensation and powers of veterinary investigation of cases and associated flocks;

- a survey of appropriate tissues from sheep and goats from abattoirs in the UK for signs of scrapie. This study was started in August 1997.

- a postal survey of sheep and goat farmers.

C. Environmental issues

ENVIRONMENT AGENCY REPORTS

31. SEAC were asked for their views on two reports prepared for the Environment Agency:

- Incineration of Meat and Bone Meal (MBM) in power stations

SEAC endorsed a risk assessment on the risks from burning rendered products containing BSE infectivity in power stations, which was subsequently published.

- BSE carcases in landfill

About 6,000 suspect cases were disposed of in 59 landfill sites in Great Britain between 1988 and 1991 (the current practice is to dispose of BSE suspect carcases by incineration). The Committee noted the methodology used in this risk assessment and were content with the conclusions of the report.

SPREADING ON LAND OF RENDERING CONDENSATE

32. The Committee considered in December 1997, at the request of the Environment Agency, whether the spreading of rendering condensate on farmland should be subject to controls. SEAC concluded that condensate posed no significant risk to human health, but wished to consider the results of further analyses of the protein content of condensate before finally deciding on the safety of the practice in relation to grazing animals.

DISPOSAL OF EXCRETA

33. The Committee considered options for disposal of excreta from experimentally infected cattle. They noted that project designs intended that for a period of one month experimental cattle were fed BSE-infected brain. All waste including bedding would be incinerated. The Committee agreed that other excreta could be composted and used as fertiliser on agricultural land at the experimental farms of the institutes concerned. They recommended that detailed records of disposal should be kept.

USE AND DISPOSAL OF BOVINE BLOOD

34. In January 1998 the Committee concluded that there was no significant risk associated with the disposal of bovine blood on agricultural land and saw no reason to change current advice. Such blood could only be derived from cattle under thirty months of age - all blood from older cattle has to be destroyed under the rules of the over thirty month scheme (OTMS).

D. Alternative theories

ORGANOPHOSPHATES

35. The Committee considered the theory that systematic use of 'Phosmet' triggered BSE. SEAC considered that the BSE epidemic was better accounted for by the contaminated feed theory and concluded that experimental evidence would be required to justify further consideration of the theory.

AUTOIMMUNITY

36. In January 1998 the Committee considered papers on the role of molecular mimicry and autoimmunity in BSE, CJD and Multiple Sclerosis. The Committee thought that the theory failed to explain certain aspects of TSE in general and BSE in particular and that the limited experimental data available were unconvincing.

Chapter Four

FUTURE WORK

37. The Government will continue to need advice on TSEs for the foreseeable future. Although the BSE epidemic in cattle is in decline, the identification of nvCJD and concerns about spongiform encephalopathies in other species, particularly sheep, means that there is no immediate prospect of the need for SEAC lessening.

38. Since 1996 the public profile of SEAC has grown. There has been enormous interest in the advice it gives to Ministers and the impact of this advice. The BSE crisis in 1996 fuelled calls from all political parties and the public for a more open, independent food safety structure. It is envisaged that the SEAC Secretariat will expand to include the Food Standards Agency in the forthcoming year.

39. During 1998/99 the Committee will continue to review the epidemiology of BSE and nvCJD and possible routes of exposure to SEs. The will also review key areas in the light of research findings and deal with any specific issues which are raised. The key areas are expected to include BSE in cattle and sheep, milk and human blood.

40. In addition to routine meetings, there will be occasional two-day meetings of the Committee and, in September 1998, SEAC met the Dormont Committee, which is the French equivalent of SEAC.

ANNEX I

REVIEW OF THE SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

SUMMARY OF RECOMMENDATIONS

Role of Committee

1. SEAC should report to territorial Ministers in addition to Ministers in the Ministry of Agriculture, Fisheries and Food (MAFF) and the Department of Health (DH), but, for administrative convenience, sponsorship and the secretariat should remain with MAFF and DH.

Terms of Reference

2. A joint Advisory Committee on Dangerous Pathogens (ACDP)/SEAC working group should consider areas of interest to both committees. Flexible, rather than standing arrangements should be adopted for the joint group, including for membership.

3. An official from the Health and Safety Executive's (HSE) ACDP Secretariat should be designated as observer to SEAC.

4. SEAC should have no formal responsibility in relation to research, but should point out gaps in scientific knowledge where further research is needed and refer these areas to the TSE Research and Development Funders' Co-ordination Group for consideration.

5. The terms of reference should be amended both to explain the purpose of the Committee and to clarify the overlap with other bodies with related interests:

> "to provide scientifically-based advice to the Ministry of Agriculture, Fisheries and Food, the Department of Health and territorial departments on matters relating to spongiform encephalopathies, taking account of the remits of other bodies with related responsibilities".

Membership

6. Membership of SEAC should not normally exceed 15.

7. The following appointments should be made to SEAC as soon as possible (even though this would exceed the recommended size of the committee for a short time):

- **a geneticist;**

- **an expert from the Institute for Animal Health;**
- **a neuropathologist;**
- **food toxicologist or gastro-intestinal immunologist;**
- **a representative of the public interest.**

8. When considering appointments to SEAC, the European pool of expertise should be actively considered alongside that in the UK. The principle should be to draw on the best expertise wherever it might lie.

9. As a guide, the following expertise should be included on SEAC: epidemiology, microbiology, neurology, neuropathology, veterinary pathology, virology, genetics, veterinary medicine, public health practice, food toxicology/gastro-intestinal immunology, representative of public interest.

10. An observer from the Central Veterinary Laboratory should be appointed to SEAC.

11. Appointments from industry should not be made.

12. The Chairman should be routinely consulted on appointments to SEAC.

13. Appointments to the Committee should be made on a fixed term basis, usually for three years, with Members normally being asked to serve a maximum of two terms. They should be made on a rolling programme to build continuity into the Committee's membership.

14. Existing members not already on fixed term appointments who have served less than three or six years should be formally appointed up to the end of the 3rd or 6th year respectively. Members who have served more than six years should be put on fixed 1 year appointments from the date of the review (with a possibility of extension in individual cases).

15. The Secretariat, in consultation with Members, should draw up a Code of Conduct for SEAC. This should be drawn to the attention of potential new members at the time appointment is offered.

16. Members appointed to the Committee should undergo an induction process to help them become effective as quickly as possible.

Openness

17. A statement summarising main topics discussed and any decisions reached should be issued after all SEAC meetings as a matter of routine. There should be a delay in publication to permit Ministers to note the content and take a view on handling, if necessary. The summary statement should normally be drafted by the Secretariat, and cleared with the Chairman.

18. A brief, factual Annual Report should be published, covering dates of meetings; a list of members and their interests; statements or advice to Ministers; summary statements; issues addressed; forthcoming work programme; subgroups and members; speakers; papers considered. The Report should be drafted by the Secretariat, and primary responsibility for clearing the content should rest with the Chairman.

19. It is not recommended that the agenda or minutes of meetings are published.

Secretariat and functioning of Committee

20. Occasional two day meetings of the committee should be scheduled. These meetings should ideally allow time for free discussion. Consideration should also be given to arranging SEAC meetings to tie in with visits, such as to the CJD Surveillance Unit.

21. The use of sub groups should be extended. They should:

- be chaired by SEAC members;
- have clear terms of reference;
- be required to report to the main Committee.

22. Appointments to sub groups should be approved by the Chairman and both departments.

23. Changes in secretariat support should be considered further when plans for the Food Standards Agency are finalised.

24. All papers put to the Committee should contain a one-page summary which specifically draws to the attention of the Chairman and Members the purpose of the paper, and the points on which advice or decisions are being sought. These should be prepared by the Secretariat.

25. For a trial period, the Secretariat should provide the Chairman with a written Chairman's brief.

27. The joint Secretariat should set up a routine mechanism for listing and following up action points.

28. The Committee should continue to observe defined procedures for clearing minutes.

29. The official observers from DH, MAFF (and CVL if appointed) should be renamed technical advisers to distinguish their role from that of other observers.

30. The TSE Research and Development Funders' Co-ordination Group should appoint one observer to represent the interests of all funders of research on TSEs, including the MRC and BBSRC, and to take back to that Group any suggestions on research emerging from SEAC.

31. Officials from outside the immediate Secretariat should not routinely attend SEAC meetings, but should be able to attend if the business of the committee makes this desirable.

ANNEX II

MEMBERSHIP OF SEAC AT 31 MARCH 1998

Chairman: Professor Sir John R Pattison

Vice-Provost and Professor of Medical Microbiology at the University College London. Honorary Consultant in Virology to UCL Hospitals NHS Trust and the Public Health Laboratory Service. He joined SEAC in February 1995 and became Chairman in May of that year.

Deputy Chairman: Professor Robert G Will

Consultant Neurologist at the Western General Hospital, Edinburgh, where he heads the National CJD Surveillance Unit which was set up in May 1990. Dr Will was a member of the former Consultative Committee on Research into Spongiform Encephalopathies and was appointed Deputy Chairman of SEAC in March 1994.

Members:

Professor Jeffrey W Almond

Virologist and Professor of Microbiology at the University of Reading.

Mr Ray Bradley CBE

Veterinary Pathologist and BSE co-ordinator for MAFF prior to his retirement in 1995. Mr Bradley has chaired/served on many TSE related sub-groups of the EC Scientific Veterinary Committee and Scientific Steering Committee.

Professor Fred Brown FRS

Virologist and Chemist -Formerly Deputy Director (Scientific) of the Animal Virus Research Institute (now known as the Biotechnology and Biological Sciences Research Council, Institute for Animal Health, Pirbright). Currently employed by the United States Department of Agriculture.

Professor John Collinge

Professor of Molecular Neurogenetics, Neurogenetics Unit incorporating the Prion Disease Group, Imperial College School of Medicine; Honorary Consultant Neurologist at St. Mary's Hospital and the National Hospital for Neurology and Neurosurgery, London.

Professor William D Hueston

Veterinary Epidemiologist and Professor of Veterinary Medicine at the University of Maryland, USA. Professor Hueston has held posts previously as clinical epidemiologist and clinical veterinarian, with consultantships in epidemiology, food animal production and bovine medicine. He also worked as an epidemiologist for the National Animal Health Monitoring system at the United States Department of Agriculture Animal and Plant Health Inspection Service.

Dr Richard H Kimberlin OBE

Independent Consultant on Scrapie and Related Diseases; Former Director of the Institute for Animal Health, Neuropathogenesis Unit, Edinburgh. Dr Kimberlin was a member on the former Consultative Committee on Research into Spongiform Encephalopathies. He also served on a number of TSE sub groups of the EC Scientific Steering Committee, the OIE and the WHO.

Dr Michael Painter

Consultant in Communicable Disease Control, City of Manchester.

Dr David B Pepper

Private Veterinary Surgeon (retired).

Professor Peter G Smith

Epidemiologist, Head of Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine.

Dr William A Watson CB

Former Director of the Central Veterinary Laboratory, Ministry of Agriculture, Fisheries and Food.

The six new members, who were all appointed on 1 January 1998 for three years are :

Professor Adriano Aguzzi

Professor Aguzzi is acting head of the Institute of Neuropathology at the University of Zurich; a clinician who now specialises in neurodegenerative disease research, including prion diseases.

Professor Roy Anderson FRS

Professor Anderson is Head of Zoology at the University of Oxford. He has been involved in epidemiological studies of the BSE epidemic for some years and has served on both epidemiology sub-groups of SEAC (1996-7 and 1997-8).

Professor Anne Ferguson

Professor Ferguson is a gastroenterologist at the Western General Hospital, Edinburgh. She advised SEAC in March 1996 on issues related to children and other special interest groups after the announcement of a probable link between BSE and new variant CJD. She has been President of the Society for Mucosal Immunology since 1996 and was a member of the Committee on Toxicity, the Committee on the Safety of Medicines and the Scottish Biomedical Research Committee. She is currently a member of the Committee on Food Intolerance.

Dr Peter Goodfellow FRS

Dr Goodfellow is a Senior Vice-President, Biopharmaceutical Research & Development, at SmithKline-Beecham Pharmaceuticals. He was previously Professor of Genetics at Cambridge University. He was a member of the first SEAC epidemiology sub-group.

Professor Harriet Kimbell

Appointed as a representative of the public interest, Professor Kimbell is an Associate Professor Lecturer at the Guildford College of Law; specialising in consumer law, civil litigation, personal injury, medical negligence and legal ethics. She is a Deputy Chairman of the Consumers' Association and was one of their nominees on MAFF's Consumer Panel. Professor Kimbell was a member of the Polkinghorne Committee on the Ethics of Genetic Modification and Food Use and the Banner Committee on the Ethics of Novel Breeding Techniques and Farm Animals.

Dr Christopher J Bostock

Appointed as an expert from of the Institute for Animal Health. Dr Bostock is the recently appointed Director of the Institute. He has led the TSE research work of the IAH for many years and has advised SEAC in the past.

No members resigned from SEAC during the year.

ANNEX IIIa

MEMBERSHIP OF THE SEAC EPIDEMIOLOGY SUB-GROUP ON nvCJD

Chairman:

Professor P G Smith
London School of Hygiene
& Tropical Medicine

Members:

Professor R G Will
National CJD Surveillance Unit
Edinburgh

Professor J Collinge
Prion Disease Group
Imperial College School of Medicine
St. Mary's Hospital, London

Professor N Day
Professor of Public Health & Director of the Institute of Public Health Service

Professor P Willeberg
Division of Ethology & Health
Denmark

Dr A Hall
London School of Hygiene & Tropical Medicine

Mr J W Wilesmith
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ANNEX IIIb

MEMBERS OF THE SEAC EPIDEMIOLOGY SUB GROUP ON BSE

Chairman:

Professor P G Smith
London School of Hygiene
& Tropical Medicine

Members:

Professor R Anderson
Department of Zoology
University of Oxford

Professor R N Curnow
University of Reading

Professor N Day
Professor of Public Health &
Director of the Institute of Public Health
University of Cambridge

Professor A Dijkhuizen
Wageningen Agricultural
University
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Dr P Goodfellow
SmithKline Beecham Pharmaceuticals

Professor W D Hueston
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Dr R Ridley
MRC Comparative Cognition Team
School of Clinical Veterinary Medicine
University of Cambridge

Dr R H Kimberlin
Scrapie and Related Diseases
Advisory Service (SARDAS)

Mr J W Wilesmith
Head of Epidemiology Department
Central Veterinary Laboratory
Veterinary Laboratories Agency

Dr J L Williams
Roslin Institute

ANNEX IIIc

MEMBERSHIP OF THE SEAC/ACDP SUB-GROUP

Chairman:

Dr M Crumpton

Members:

Dr M Painter
Consultant in Communicable Disease Control

Dr J Ironside
National CJD Surveillance Unit

Mr R Clare
Director
Bob Clare Associates

Professor D J Jeffries
The Medical College of St Bartholomew's Hospital, LONDON

Dr T Wyatt
Consultant Clinical Scientist

Dr R Owen
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Professor P G Smith
London School of Hygiene & Tropical Medicine

Mr R Bradley
Private BSE Consultant

Dr P Jones
Biological & Biochemical Sciences Research Council

Professor S Palmer
Communicable Disease Surveillance Centre Welsh Unit

Mrs T McGuire
General Manager
Lothian NHS Occupational Health Service

Dr D M Taylor
Institute for Animal Health Neuropathogenesis Unit

ANNEX IV

COMPLETE TEXTS OF SEAC STATEMENTS AND SUMMARIES (1997/1998)

SEAC STATEMENT ON MATERNAL TRANSMISSION OF BSE
16 April 1997

1. On 29 July 1996, the Spongiform Encephalopathy Advisory Committee (SEAC) issued a statement on maternal transmission of BSE following its consideration of an interim report on a study conducted by the Epidemiology Department, Central Veterinary Laboratory, Weybridge to investigate the occurrence and incidence of dam to calf transmission of BSE (the cohort study).

2. SEAC established an Epidemiology Subcommittee to consider the final results from the cohort study. The Subcommittee was chaired by Professor Peter Smith (London School of Hygiene and Tropical Medicine), a member of SEAC. It included two further members of SEAC, Dr Richard H Kimberlin (SARDAS) and Professor Will Hueston (University of Maryland). The Subcommittee also included Professor Roy Anderson (Oxford University), Professor Robert Curnow (Reading University), Dr Peter Goodfellow (SmithKline Beecham Pharmaceuticals), Professor Dr. Ir. Aalt Dijkhuizen (Wageningen Agricultural University, the Netherlands) Professor Nicholas Day (Medical Research Council Biostatistics Unit), Dr John Williams (Roslin Institute), Dr Rosalind Ridley (Cambridge University) and Mr John Wilesmith (Central Veterinary Laboratory). The Subcommittee was assisted by Dr Sheila Gore (Medical Research Council Biostatistics Unit), Dr Neil Ferguson (Oxford University), Dr Christl Donnelly (Oxford University), Dr John Woolliams (Roslin Institute), and Ms Judith Ryan (Central Veterinary Laboratory). The Subcommittee met on four occasions, and submitted its final report on maternal transmission of BSE to SEAC on 11 April 1997.

3. At its meeting on 15 April 1997, SEAC considered and accepted in full the report from the Epidemiology Subcommittee (attached).

4. SEAC noted that the results of the cohort study were not inconsistent with those of the case control study published in 1995 by Hoinville and others of the Epidemiology Department, CVL. That study, which involved cases of BSE born after the ruminant feed ban, did not identify significant evidence of maternal transmission, but the statistical confidence interval included a risk of up to 13 per cent (Veterinary Record (1995) 136, 312-318).

5. The cohort study provides no information on the mechanism of direct maternal transmission of BSE. We recommend that further research should be undertaken to shed light on the mechanism. Some research has already been carried out into potential routes of transmission from dam to calf, by testing the infectivity of tissues from BSE-affected animals, including placenta, embryos, blood and milk: no evidence of infectivity has been found. However, given that the rate of transmission is probably low, some of these negative results may be due to the practical difficulties of detecting low levels, or a low prevalence, of infectivity. SEAC recognises that a low level of transmission would make research on mechanisms difficult, and that it would be complemented by a better understanding of the mechanisms of scrapie transmission in sheep.

6. Any cull based upon the slaughter of calves born to cows in which BSE has been confirmed will have only a small effect on the incidence of BSE and the duration of the epidemic. Nevertheless, Government should consider the possibilities for such a cull, and its effects.

7. SEAC noted that, in its statement of 29 July 1996, it had concluded that the evidence on maternal transmission did not call into question existing measures to protect public health. In the light of the Subcommittee's report, SEAC reconsidered the existing measures.

8. With respect to consumption of bovine products the measures currently in place to protect the consumer are considered appropriate. In particular, the Committee considered the possibility of milk being a vehicle of transmission. SEAC concludes that no evidence has been found to suggest that milk from any species affected by transmissible spongiform encephalopathies is infectious. This concurs with the opinion of the Scientific Veterinary Committee, which advises the European Commission.

9. With respect to occupational exposure, responsibility for assessing whether any amendments are needed to the existing Health and Safety Executive guidance rests with the Advisory Committee on Dangerous Pathogens.

EPIDEMIOLOGY SUBCOMMITTEE STATEMENT TO SEAC ON MATERNAL TRANSMISSION

1. In July 1996 SEAC issued a statement on maternal transmission of BSE following an interim analysis of data from an ongoing study (called the "cohort study") being conducted by the Epidemiology Department, Central Veterinary Laboratory (CVL). The study was intended to determine whether maternal transmission occurred, and if so, to inform policy makers with respect to animal health implications.

2. The study involved over 300 "matched-pairs" of calves. One calf in each pair was the offspring of a confirmed case of BSE and the other an animal born in the same herd in the same calving season whose dam had reached the age of 6 years without developing clinical signs of BSE. The two groups of animals were born between August 1987 and November 1989, and were taken from their natal herds between July 1989 and February 1990, aged between 2 and 24 months. They were kept on one of three experimental farms until they reached the age of 7 years or were culled at an earlier age with BSE or another disease. All animals surviving to the age of 7 years were then slaughtered and their brains were examined pathologically for evidence of BSE.

3. The preliminary results of the study, when most but not all of the animals had been followed to the age of 7 years, suggested that the offspring of BSE cases had an incidence of BSE that was about 10% greater than that of control animals, with statistical confidence limits (95%) ranging from 5-15%, the range reflecting the limited numbers of animals that developed BSE in the study.

4. By November 1996 the last of the animals in the study had reached the age of 7 years, and by January 1997 the last of their brains had been examined. As had been anticipated, the final results were not markedly different from those on which the interim analysis had been based in 1996. Of the 301 offspring of BSE cases, 42 (14.0%) developed BSE. Among the 301 offspring of the "control" dams without BSE, 13 (4.3%) developed BSE. The difference between the two risks was thus 9.6%, and was highly statistically significant with a confidence interval ranging from 5.1% to 14.2%. A paper giving the results of the study will be published shortly in the Veterinary Record by the Epidemiology Department of CVL.

5. The cohort study was set up to investigate the occurrence of maternal transmission, but interpretation of the results was confounded by the likely exposure of some of the experimental animals to contaminated feed. The results could be explained by two hypotheses, acting alone or in combination, namely direct maternal transmission of infection or inherited genetic variation in susceptibility to BSE via contaminated feed. Although most of the animals involved in the study had been born after the ruminant feed ban in July 1988, feed-borne transmission is thought to have continued beyond that date. This is consistent with the observation that the BSE risk in both of the groups was greater among animals born before the introduction of the feed ban than among animals born later. However, the difference in risk between the two groups was also greater in those born earlier, and this would not be expected if direct maternal transmission was the sole route of infection of the calves in the study. Such an effect might be apparent if cattle vary in their susceptibility to contracting BSE from infected feed. It is possible that the offspring of BSE cases may inherit, from their dams, genes associated with increased susceptibility to disease and that at least some of the difference in BSE risk between the offspring of BSE affected and non-affected dams in the study may

be due to inherited factors, rather than because of direct transmission of BSE from dam to calf.

6. The subcommittee has reviewed the evidence for variation in genetic susceptibility to BSE in cattle. There is variation in the risk of TSEs according to genotype in some species. For example, polymorphisms of the PrP gene are associated with substantial variation in susceptibility to infection with the scrapie (and in incubation period) in sheep and mice and with differences in risk of CJD in humans. The subcommittee notes, however, that the limited research so far completed has failed to identify genetic factors as a major component in the epidemiology of BSE.

7. To assist the CVL Epidemiology Department in the interpretation of the results of the cohort study, independent analyses of the data were conducted by three additional groups with expertise in statistical analysis (based in the Wellcome Trust Centre for the Epidemiology of Infectious Disease, University of Oxford; the MRC Biostatistics Unit, Cambridge; and the Department of Applied Statistics, University of Reading). In so far as was possible, they tried to evaluate the contributions to the risk difference between the animals in the two groups from inherited differences in susceptibility to disease caused by infected feed and from direct transmission of BSE from dam to calf. In the absence of detailed information on the genetic make up of the animals in the study, the possible genetic contribution could only be assessed by statistical modelling.

8. The analyses by the three groups have been submitted for publication later this year. These analyses reached broadly the same conclusions. That there was a highly significant difference in risk between the two groups of animals was clear. The findings did not definitively establish direct maternal transmission as the sole explanation for the difference in risk. The statistical model which fitted the data best involved contributions from both direct maternal transmission and inherited susceptibility. The main evidence for direct maternal transmission is that the risk of BSE in the calf of an affected dam was greatest for calves born close to the onset of BSE in the dam. However, the power of the study to detect differences related to the time between BSE onset and the date of birth of a calf was limited by the design of the study which resulted in 83.4% of the calves being born within the six months prior to onset of clinical disease in the dam.

9. Further investigation was necessary of the possible variation in the risk of BSE associated with the time between the birth of an animal and the onset of BSE in the dam. This was undertaken mainly by the group from the Wellcome Centre for the Epidemiology of Infectious Diseases, University of Oxford through analyses of data on all cases of BSE born after the ruminant feed ban, which are recorded on the BSE database held by the Epidemiology Department at the CVL. The findings will be submitted for publication shortly. Evidence was found that the subsequent BSE-risk was greatest in calves born after the

date of BSE onset in the dam. For calves born before onset, the risk was lower, and diminished as the interval between birth and onset increased, and no risk was apparent more than two years before onset (see next paragraph). Thus, although possibly subject to some biases, these analyses also suggested that enhanced BSE-risk in the offspring of BSE dams involves a low level of direct maternal transmission in the late stages of the incubation period.

10. In view of the findings of the analyses that are summarised above, the subcommittee concludes that there is some evidence for direct maternal transmission of BSE at a low level, but some variation in genetic susceptibility to BSE following feed-borne exposure may occur. The risk of transmission of BSE from dam to calf is likely to be less than 10%, and appears to be confined to animals born after the onset of BSE in the dam or up to two years beforehand. This level of transmission is not sufficient, by itself, to perpetuate BSE in the cattle population and is likely to have only a minor effect on the rate at which the incidence of BSE declines. It is inevitable that cases infected via animal feed will continue to appear in diminishing numbers for several years. Therefore, although the number of cases infected maternally will be small, they may represent an increasing proportion of the remaining cases detected.

11. Given the evidence that variation in genetic susceptibility may have contributed to the results of the cohort study, and of the importance of genetic factors in TSEs in other species, the subcommittee considers that further research is necessary to clarify whether or not variations in the PrP gene or other genes may be influencing the transmission of, or susceptibility to, BSE in cattle. Research should seek to identify polymorphisms of the PrP gene which may be associated with BSE susceptibility, including stored samples from the cohort study. There should also be a search [AVMC1]for other genetic markers, outside the PrP gene, which may be associated with an increased BSE risk in cattle.

SEAC CONCLUSIONS OF 23 MAY 1997

The Committee reviewed the position since the advice it tendered to Government in July 1996 on the precautions necessary to protect the public from the theoretical risk of BSE in sheep. At that time it recommended action on brains, which was taken by the UK Government in September 1996, and that the issue be considered further with EU partners. The Committee noted that the EU Commission tried to introduce measures which would go beyond those adopted in the UK in that they would:

i) prohibit the use in human or animal feed of:

(a) the spinal cord from older sheep and goats (those with one or more permanent incisors);

(b) the spleen from all sheep and goats;

ii) prohibit the production of MRM from the vertebral column of all sheep and goats.

The EU measures were not adopted although SEAC notes that the Commission stated on 14 May 1997 that the case for these measures was stronger than ever and is insisting on their adoption.

SEAC agrees that these measures are prudent and that it has now been established that there are practical methods for removing the spinal cord of older sheep. It therefore advises the UK Government that early action should be taken to introduce these measures, preferably on an EU wide basis but if agreement in Europe is not achieved quickly, unilateral action by the UK is recommended.

The Committee also re-iterated its concerns that the surveillance of scrapie needs to be improved. It endorsed a three part strategy encompassing :

(a) compulsory slaughter of suspect cases with compensation and powers of veterinary investigation of cases and associated flocks;

(b) a survey of appropriate tissues from sheep and goats from abattoirs in the UK for signs of scrapie;

(c) a postal survey of sheep and goat farmers.

SEAC also considered the issue of imports into the UK of material containing tissues from bovine central nervous system (CNS) in the light of existing controls on cattle risk materials in the UK and elsewhere. It took into account the EU Commission s assessment of surveillance and control in other Member States. SEAC concluded that action should be taken to extend, within the UK, controls on specified bovine material (SBM) to imports of CNS or bovine material containing CNS from the EU, and from third countries - other then those where there is no known risk of BSE. Again, it would be preferable if action could be taken on an EU wide basis but if agreement in Europe is not achieved quickly, unilateral action by the UK is recommended.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING PUBLIC SUMMARY: 24 October 1997

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 24 October 1997 at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee conducted its regular review of the emerging experimental data and of the epidemiology of BSE and nvCJD.

The number of cases of BSE continues to be in line with predictions about the decay of the epidemic.

No new confirmed cases of nvCJD in the UK had been notified by the CJD Surveillance Unit since the last meeting. Subsequent to the meeting, however, a single case has been confirmed taking the total to twenty-two.

The Committee reviewed the safety of blood and blood products and has provided advice to Government on these matters (copy attached).

The Committee considered further papers relevant to the hypothesis that the organophosphate, Phosmet, is in some way causally linked to the BSE epidemic. It was noted that the epidemiological evidence is better accounted for by the view that the BSE epidemic is due to the widespread use of animal feed contaminated with the transmissible agent of BSE than by the OP theory. Central to the latter is the bio-accumulation of OP in treated animals however the available evidence does not support such accumulation. The Committee concluded that experimental evidence would be required to justify further consideration of a role for organophosphates in the epidemiology of BSE. Proponents of the theory were free to apply to funding agencies for resources to conduct such experiments. However, on the evidence to date the Committee did not feel that special priority should be given to this area of research.

The Committee reviewed the production and use of tallow. It noted the restrictions in the UK on the sources of raw material used in the production of tallow for food, feed, cosmetic, medical or pharmaceutical products and was impressed by UK tallow production controls. The Committee noted that imported tallow was not subject to the same restrictions nor required to reach the same standards but that the implementation of Commission Decision 97/534/EC would result in the exclusion of Specified Risk Materials from the production of tallow across all Member States from January 1998. The Committee also reviewed the production and use of gelatin. It noted that plants in the UK manufacturing gelatin for food, feed, cosmetic, medical or pharmaceutical use have been brought under official control. The Committee also noted that all UK gelatin manufactured for these purposes from bovine raw material utilised only imported ingredients. They noted that implementation of Commission Decision 97/534/EC would exclude Specified Risk Materials from the source materials used for gelatin manufacture in all Member States.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE - ADVICE TO MINISTERS

HUMAN BLOOD AND BLOOD PRODUCTS

The Committee have recently concluded that the transmissible agent of nvCJD is indistinguishable from that of BSE but distinctly different from any of the forms of classical CJD. Recent research (some unpublished) suggests that the pathogenesis of nvCJD differs from that of classical CJD and the former may have more involvement of lymphoreticular tissues possibly involving circulating lymphocytes. Therefore it is logical to seek to minimise any risk from blood or blood products by reducing the number of lymphocytes present.

SEAC recommends that the Government should consider a precautionary policy of extending the use of leucodepleted blood and blood products as far as is practicable. It will be for the National Blood Authority to devise a strategy to implement such a policy. It will take time to achieve full implementation and SEAC recommends that planning begins soon while the risk assessments suggested below are carried out. It is not possible at present to estimate accurately the risk of transmitting nvCJD by blood transfusion. The magnitude of the risk will depend, inter alia, on the number of blood donors who are incubating nvCJD and this is not known. However, SEAC recommends that risk assessments, making assumptions of various possible incidences of nvCJD, be carried out to inform decisions on any measures which may be necessary to protect recipients.

BEEF

SEAC reviewed the safety of beef in the light of its discussion on human blood and blood products. Transmission experiments in mice have not found infectivity in the spleen, tonsil, lymph nodes or white blood cells of BSE infected cattle.

The Committee conclude, therefore, that no further measures governing beef and beef products for human consumption, are necessary.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING PUBLIC SUMMARY: 2 December 1997

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 2 December 1997 at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee conducted its regular review of the emerging experimental data and of epidemiological information on BSE and nvCJD.

The number of cases of BSE continues to decline in line with predictions about the decay of the epidemic.

A further case of nvCJD had been confirmed, taking the total number of cases in the UK to 23.

The Committee reviewed the results from the long term "pathogenesis experiments" relating to dorsal root ganglia and provisional results on bone marrow and has provided advice to the Government on this matter. This was issued on 3 December.

The Committee considered the risks arising from eye tissue transplants from a donor with classical CJD. The Committee advised that, because of the possible risks of transmission via cornea, the patients concerned should be informed and counselled. The Committee were of the view that, providing the individual circumstances of the patients allowed, and they gave consent, the corneas and sclera should be explanted and further treatment provided at the discretion of the surgeons caring for them.

The Committee also provided advice to Government on the practice of intraspecies recycling of waste in the pig and poultry industries. A copy of the advice is enclosed.

The Committee reviewed a risk assessment, conducted on behalf of the Environment Agency, of the practice of spreading condensate from rendering plants on farmland. The Committee concluded that the risk to human health from this practice was negligible. However, before reaching a conclusion on the safety of this practice with regard to grazing animals, SEAC wished to see the results of additional analyses, which are being undertaken, of the possible protein content of condensate.

SEAC ADVICE TO MINISTERS ON DORSAL ROOT GANGLIA

1. Until recently BSE infectivity has been detected by mouse bio-assay only in terminal ileum, brain, eye (retina) and spinal cord of infected cattle. Up until now all tissues in which infectivity has been detected have been removed from the human food chain as specified bovine material (SBM).

2. In an on-going experiment conducted by MAFF, cattle deliberately infected with BSE have been killed at regular intervals as the disease develops. In this experiment infectivity has now been detected in the dorsal root ganglia (DRG), the trigeminal ganglia and in the bone marrow, though the bone marrow result is only provisional and requires further results before definite conclusions can be drawn. The trigeminal ganglion is in the skull and, as the whole head is now classified as SBM, no trigeminal ganglia enter the food chain.

3. In the experimental animals infected with a large dose of BSE by mouth at 4 months of age, clinical signs developed at 39 months of age i.e., 35 months post-infection. Infectivity has been demonstrated in dorsal root ganglia at 32 months post-infection but not at 26 months post-infection. Thus infectivity has been detected 3 months but not 9 months before clinical symptoms develop. To add a margin of safety in assessing risks to the human population it is assumed that infectivity may be present 7 months prior to the onset of clinical symptoms.

4. DRG are swellings on the sensory branches of the nerves near the spinal cord. They are surrounded by the bone of the vertebrae of the animal. Most beef is sold boneless and dorsal root ganglion tissue would normally be removed with the bone during the deboning process. That which is sold with the 'bone-in' is often in the form of rib or sirloin roasts and T-bone steaks. Risks are estimated on the basis that 5% of the DRG in these bone-in cuts may be eaten by the consumer.

5. With the Over Thirty Month Scheme (OTMS) in place the only DRG to pose a risk would be from animals which would have developed BSE before the age of 38 months. Using risk assessment techniques, and taking account of the 90% decline in the BSE epidemic since 1993, the numbers of such animals with BSE aged 30-38 months are shown to be very small. In 1997 it is estimated that there will be 6 animals in the latter category and 3 in 1998. Thus next year of the approximately 2.2 million cattle to be slaughtered for human food only 3 will be near enough to the end of the incubation period to raise the possibility of infectivity in their DRG. (Note in the worst year in the past the figure was many thousand times greater).

6. Using a series of pessimistic assumptions (published by the Environment Agency in other risk assessments earlier this year) concerning the various factors involved in the transmission of BSE to humans it is estimated that the risk from the DRG in food is now very small. On the basis of the risk assessment available to us it is estimated that there is a 95% chance of no cases and a 5% chance of one case of nvCJD arising as a result of this exposure in 1998.

Recommendations

7. We recommend that the new research findings from the pathogenesis experiment together with our assessment set out above be made public. If the Government decides that action is necessary to reduce this small risk further we recommend either:-

(a) no beef with the bone in from cattle over 6 months old should be sold to the consumer; or

(b) cattle slaughtered between 24 and 30 months of age for human consumption should be deboned under official control by the Meat Hygiene Service in licensed plants.

8. We realise that implementing (a) will mean that the regulations will have to depend on all butchery outlets removing the bone since we are informed that there is not the capacity to debone all beef in premises inspected by the Meat Hygiene Service. We accept this and think it is workable because the customer can monitor the efficiency of the process as bone is readily identifiable.

9. If (a) or (b) is pursued there is then a question of what to do with the bones. We think it would be impractical to have a scheme which distinguished between different types of bone and therefore recommend that all bovine bones which are required to be removed under option (a) or (b) be disposed of through routes which do not result in the use of this material for human food.

10. As evidence is also emerging of infectivity in bone marrow (albeit so far in animals with clinical disease which cannot be used for food) the measure we propose on the disposal of bones under either of the options would provide an additional margin of safety to deal with this finding.

11. It should be policy that imported beef should represent no greater risk than that from equivalent UK cattle under domestic control programs. If a decision is made that action is necessary and option (a) is chosen, then it would be difficult to ensure that meat with the bone in would be of non-UK origin. We therefore recommend that option (a) should apply to all beef to be consumed in the UK. If option (b) is chosen the risk from imported beef should be assessed against the risk from UK beef.

12. We recognise that our previous recommendations on sheep and goat SRMs were developed out of our understanding of BSE. As yet we have not found any evidence of BSE in UK sheep or goats but the surveillance is at a very early stage. Brain and spinal cord are to be banned and we believe that this is sufficient precaution at this stage. This will be reviewed whenever further experimental data are available.

ADVICE TO MINISTERS ON INTRASPECIES RECYCLING OF PIG AND POULTRY WASTE

Although the aetiology of sporadic CJD is not certain, it seems likely that it is an example of a random event leading to the spontaneous occurrence of transmissible spongiform encephalopathy which in theory could occur in any species with a PrP gene. Sporadic cases of pig or poultry transmissible spongiform encephalopathies could occur at similar low incidences and would

be difficult to detect even by active surveillance. Recycling of waste as feed within a species creates the potential for a major epidemic such as that seen with BSE.

Our assessment of current practice in the UK suggests that the likelihood of any problem arising is small but cannot be completely discounted.

Consequently the Committee recommend that the UK Government develop a strategy to remove the risk of TSE transmission from intraspecies recycling of pig and poultry waste at the earliest opportunity and that this is discussed with EC partners.

The strategy would need both to address enforcement issues and to ensure that appropriate utilisation or disposal systems were available.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING PUBLIC SUMMARY: 12 January 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 12 January 1998 at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee conducted its regular review of research findings and the epidemiological information on BSE and nvCJD.

The number of cases of BSE continues to decline in line with predictions about the decay of the epidemic.

The total number of nvCJD cases in the UK remains at 23.

The Committee reviewed the processing and use of milk. In particular they considered the relevance of recent research publications implicating lymphocytes in the pathogenesis of TSEs. The Committee noted that there was no evidence of infectivity in spleen or lymph nodes of cattle infected with BSE, that only low numbers of lymphocytes were left in milk after processing by the dairy and that the incidence of BSE in the UK continued to decline. No changes were made to the previous advice on the safety of milk.

The Committee examined the practice of feeding fishmeal to farmed fish. They concluded that the practice did not constitute intra-species recycling because there was more than one species involved and the material was not being sourced from farmed fish and therefore was not being recycled within the same population. They saw no reason to prohibit the practice.

The Committee considered the use and disposal of bovine blood. They concluded there was no significant risk associated with disposal of bovine blood on agricultural land and saw no reason to change current advice.

The Committee considered options for disposal of animal excreta from experimentally infected cattle. They noted that for a period of one month all waste from animals which had been orally challenged would be incinerated. They agreed that other excreta could be composted and used as fertiliser on agricultural land at the experimental farms of the institutes concerned. They recommended that detailed records of disposal should be kept.

The Committee considered the use of bovine bone charcoal for water filtration. They noted that the sources of the bone were countries which had no reported cases of BSE and that the production method included heating to 1000oC. Consequently they concluded that the practice could continue since it represented no risk to human health from TSEs.

The Committee considered a further draft of the guidance on TSE agents: safe working and the prevention of infection, prepared by the joint ACDP/SEAC working group.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING PUBLIC SUMMARY: 8 February 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 8 February 1998 at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee considered a preliminary analysis of the possible ways by which BSE infectivity may have entered the human food chain over the course of the BSE epidemic. The Committee noted:

- that this was a preliminary analysis that required detailed review and substantial revision;

- that the analysis was based on many assumptions, some of which were hypothetical and which were not supported by experimental or research data;

- that the analysis at this stage included only a single value for each of many factors which were unknown but where there was a range of possible values;

- that further work was necessary to determine ranges for these factors; the Committee planned to provide detailed input into this aspect of the analysis at a future meeting.

The Committee concurred with the point made in the summary of the preliminary analysis which states "There are many inputs to the study that are very uncertain, being based on judgement or limited data. Improvement would be desirable before decisions are made about public health implications of these results." The Committee also concluded that the preliminary analysis would not cause the Committee to call for changes in current measures to protect public health.

The views of the Committee will be provided to the appropriate sub-groups of the Commission's Scientific Steering Committee who have also considered the analysis.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING PUBLIC SUMMARY: 9 March 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 9 March 1998 at the offices of the Ministry of Agriculture, Fisheries and Food, Whitehall Place, London.

The Committee conducted its regular review of research findings and the epidemiological information on BSE and nvCJD. In particular the Committee reviewed an abstract of American research showing that scrapie infectivity had been detected in muscle in transgenic mice. The Committee noted that the mice used in this experiment had been genetically engineered to artificially produce more of the normal PrP protein in muscle cells than in normal brain cells. (PrP is the protein which adopts an abnormal conformation in TSEs). The Committee concluded that the results showed that muscle cells have the potential to produce abnormal protein and that the assays which were in progress for infectivity in muscle of BSE infected cattle which did not involve a species barrier were important. The Committee also noted research in another neurological condition, idiopathic brainstem neuronal chromatolysis, which had potential to be confused with BSE on clinical grounds.

The Committee was informed that a new case of nvCJD in the UK had recently been confirmed. The total now stood at 24 and would be reflected in the next monthly summary of CJD statistics to be issued by the Department of Health on 6 April. The Committee noted that the number of BSE cases continues to decline in line with predictions.

The Committee, as part of a Government-wide initiative to increase the openness of advisory committees, discussed ways in which it could improve the transparency of its deliberations. The Committee welcomed moves to greater openness and expressed a willingness to participate in such moves. However it was considered that a mechanism to safeguard confidential scientific, patient,

veterinary and commercial information that was crucial to its work would need to be built into the process.

The Committee noted the action being taken by Government following SEAC's previous advice on human blood. The Committee considered that it was not necessary to change or add to its previous advice at this stage and agreed to review the position when the risk assessment was completed.

The Committee confirmed its previous advice on the use of bovine blood in animal feeds and saw no need to go beyond the existing controls. The Committee noted the latest position with specified risk materials (SRM) in the EU and implementation of the SRM regulations in the UK especially with regard to controls on the spinal cord of sheep. They confirmed the previous advice; controls should prevent the use of sheep and goat vertebral column for production of mechanically recovered meat but production of tallow and gelatin, which involved a high degree of processing, could be permitted from sheep and goat vertebral column. The Committee went on to urge Government to pursue its plans for improving the epidemiological surveillance of scrapie in sheep and goats and to screen as many cases as possible using newly developed techniques, such as molecular strain typing using Western blot analysis of protease resistant PrP, to characterise the strains of TSE agent involved and to determine if any of these might be BSE.

The Committee reviewed the theoretical possibility that, in certain circumstances, BSE infectivity could be present in cattle which do not show the signs of clinical disease at any time during their normal life-span. Such a situation had not been detected in the UK cattle population, however there was evidence from experiments in mice that in certain conditions the TSE agent can persist in the animal without ever causing clinical disease. It will be important as the clinical disease in cattle declines to ensure that there is no such reservoir of latent BSE infection. The Committee considered that Government should initiate further research into this issue.

The Committee received data on BSE in imported cattle and, following discussions, asked to be kept informed about such cases on a regular basis.

The Committee noted that, in line with the recommendations of the SEAC review, an Annual Report of the Committee's business would be produced beginning with the period up to April 1998.

ANNEX V

REGISTER OF MEMBERS' INTERESTS

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Professor Sir John R Pattison (Chairman)	None	None	Medical Research Council	Senior Medical Adviser to the Chief Executive
Dr R G Will (Deputy Chairman)	Unilever	Share holding	Department of Health	Grant Holder
	SmithKline Beecham	Share holding	Scottish Home and Health Dept.	Grant Holder
	Marks and Spencer	Share holding	Medical Research Council	Grant Holder
			European Commission BIOMED	Programme Grant Holder
			Office International des Epizooties Expert Group on BSE and Related diseases (1990-present)	Adviser
			World Health Organisation	Adviser
			European Union	Member of the Multi-disciplinary Scientific Committee
Prof Dr A Aguzzi	Boehringer Ingelheim	Consultancies on an occasional basis	Swiss National Foundation No: 31-36059.92 3100-040827.94	Principal investigator
	Abbott Laboratories (Chicago)	Support of some laboratory costs e.g. care of mice, instrumentation	Cancer League of the Kanton Zûrich	Principal investigator
	Immuno A G (Vienna)	Support of some laboratory costs e.g. care of mice, instrumentation	European Union No. BMHI-CT93-1142	Co- investigator
			National Institutes of Health U.S.A. No 1-ROI-NS33377-01	Co-investigator
			Swiss National Research Program NFP38 & NFP38+	Principal investigator
Prof J W Almond	Medeva	Consultant	Society for General Microbiology	Member of Council
	Cobra Therapeutics	Consultant	Biotechnology and Biological Sciences Research Council	Chairman of the Working Group of the Biology of the Spongiform Encephalopathies Programme
	Arpex Biosciences Ltd	Consultant		
Professor R M Anderson	Scientific Advisory Boards: - Decode - IMS	 Member of Board Member of Board	The Wellcome Trust	Governor
	IBHSC Ltd	Director		
Dr C J Bostock (Appointed as an expert from the Institute for Animal Health (IAH), a Biotechnology and Biological Sciences Research Council sponsored institute)	Marks and Spencer plc	Share holding	The UK and some overseas Governments	Research contracts with the IAH
	J Sainsbury plc	Share holding	Non-governmental organisations and companies, spanning a wide range of interests including food, agriculture, chemicals and pharmaceuticals. Further details of the customers of IAH can be found on the Institute's Web Site (www.iah.bbsrc.ac.uk)	Research contracts with the IAH

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Mr R Bradley	Taylor By-Products	Adviser	Ministry of Agriculture, Fisheries and Food	Adviser
	European Natural Sausage Casings Association	Adviser	Veterinary Laboratories Agency	Adviser
	Meat and Livestock Commission	Adviser	World Health Organisation	Adviser
	National Dairy Council	Adviser	Office International des Epizooties	Adviser
	Jackson and Walker (Attorneys, Counsellors)	Adviser	European Agency for the Evaluation of Medicinal Products	Adviser
	Kraft, Jacobs, Suchard	Adviser	Food and Agriculture Organisation (UN)	Adviser
	National Renderers Association Inc	Adviser	European Commission	Adviser
	Fats and Proteins Research Foundation Inc.	Adviser	National Governments and individuals; especially in Africa, Europe and the Americas	Adviser
	Dr R Öberthur	Adviser		
	F D Bisplinghof and Associates Inc	Adviser		
Professor F Brown	None	None	None	None
Professor J Collinge	None	None	Wellcome Trust	Research Grant Holder
			Biotechnology and Biological Sciences Research Council	Research Grant Holder
			Dept. of Health	Research Grant Holder
			European Commission BIOMED programme	Research Grant Holder
			Medical Research Council	Research Grant holder
			Motor Neurone Disease Association	Chairman, Research Advisory Panel
			World Health Organisation	Adviser
Professor A Ferguson	None	None	Medical Research Council	Grant Holder
			Scottish Home and Health Dept	Grant Holder
			Wellcome Trust	Grant Holder
			Marlow Foods	Grant Holder re clinical research
			Norgine	adviser, collaborations re clinical research
			Astra Pharmaceuticals	adviser, collaborations re clinical research
			Nutricia	adviser, collaborations re clinical research
			Shering Plough	collaborations re clinical research
Dr P N Goodfellow	SmithKline Beecham Pharmaceuticals	Senior Vice President, Discovery Worldwide. (Head of research worldwide)		
	SmithKline Beecham	Share holding		
	Axys (an American Biotechnology Company)	Share holding		
	Hexagene (A UK Biotechnology Company)	Major share holding		
Professor W Hueston	Mullin, Hoard and Brown (solicitors)	Consultant	Food & Drug Administration (USA)	Adviser
	Cytotherapeutics	Consultant		
	Datascope	Consultant		
Professor H Kimbell	Bass plc	Small share holding		
	Tesco's plc	Small share holding		
Dr R H Kimberlin	Pharmaceutical Industry (world-wide)	Consultant	National Governments in Europe, the Americas and Australasia	Adviser
	Meat and Livestock Commission	Consultant		

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Dr M J Painter	None	None	None	None
Mr D B Pepper	The Veterinary Defence Society Ltd	Director and Claims Consultant	None	None
	Pfizer Animal Health (Pfizer Ltd)	Adviser		
	Intervet International BV (Netherlands)	Adviser		
	Intervet UK Ltd	Adviser		
Professor P G Smith	None	None	Department of Health	Grant Holder
Dr W A Watson		Farmer	None	None
	ADAS	Adviser		
	Pan Livestock	Adviser		
	Huntings plc	Adviser		
	Landell Mills plc	Adviser		

ANNEX VI

FINANCE

The cost of running the committee in 1997/98 was £55,595.92 The breakdown between departments is as follows:

Department of Health:

SEAC fees and expenses*	£11,128.35
Epidemiology Sub-Group fees and expenses	£2,068.00
Catering (incl. VAT @ 17.5%)	£239.98
DH Total	**£13,436.33**

Ministry of Agriculture, Fisheries and Food:

SEAC fees and expenses* (inc. travel)	£38,754.14
Miscellaneous expenditure	£1565.78
Catering (incl. VAT @ 17.5%)	£1431.77
Reimbursement of travel cost to Committee guests	£407.9
MAFF Total	**£42,159.59**

TOTAL COST OF SEAC 1997/98: £55,595.92

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* Member fees and entitlements (revised 1.1.98) =

	Chairman	**Members**
Basic fee per day	£148	£122
Exceptional circumstances allowance (currently payable currently to SEAC members)	£37	£31
Preparation time allowance		
For up to one day's preparatory work	£33	£33
For up to two days' preparatory work	£66	£66

ANNEX VII

REFERENCES

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SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE, TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES: A SUMMARY OF PRESENT KNOWLEDGE AND RESEARCH. (September 1994) London, HMSO.Published February 1995. ISBN 011 242 9874

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