3. The Tyrrell Report

Rationale for an Interim Report

3.1 During its first meeting the Committee was told that a joint MRC/AFRC review of work on ‘slow viruses’ was scheduled for 8/9 June. At the Committee’s second meeting Dr Levy informed the members that the review agenda was not yet available, but it was still scheduled for June. The Committee therefore agreed to have its third meeting in May and endeavour to have an Interim Report available for consideration by the time of the MRC/AFRC review.106

3.2 This timetable led to confusion later over the exact role of the Committee. On 2 May 1989 Dr Pickles minuted Dr Jeremy Metters, Senior Principal Officer at DH, and sought guidance on the following:

The original rush to produce an ‘interim’ report was to be in time for MRC/AFRC discussion on the future of the NPU. I am not clear what sort of report the chairman had in mind for his ‘final’ report, or maybe he, like me, was unclear when he was expected to complete his work or perhaps whether indeed his committee was to continue for ever.107

3.3 In the end the proposed MRC/AFRC review was postponed because the Tyrrell Committee was covering similar ground.108

Development of the Report

Preparation for the second meeting

3.4 Dr Pickles sent Dr Tyrrell a draft research plan soon after the first meeting, which included everything on the existing CVL/NPU programme, everything suggested by the Southwood Working Party, and ‘a few more [projects] for good measure’. At this stage a total of 44 possible research projects had been identified, to which Dr Pickles suggested adding codes to indicate which projects were either in progress, actively being planned, or merely proposed.109

3.5 Dr Tyrrell suggested the ‘research questions document’ could be split into three categories: a statement of the role of the research being done; a summary of the questions to be asked in broad terms; and the third part along the lines of Dr Pickles’s draft. He too suggested inserting an index, or code numbers, into the third part to indicate whether the work had been or was being done; or was proposed (with the related documents seen by the Committee being set out); or was one of the ideas that the Committee had come up with. Further, the questions in section 2 could be coded to indicate which research projects they related to.110

106 YB89/4.11/2.1
107 YB89/5.2/1.1
108 YB89/5.8/2.2
109 YB89/03.20/1.1
110 YB89/3.29/1.1
Consideration during the second meeting

3.6 At its second meeting, the Committee considered the research questions and potential research programme as agreed by Dr Tyrrell and Dr Pickles beforehand. Dr Tyrrell suggested the document could form the basis of the final report, and that an introduction should stress that the number of questions identified by the Committee were far too numerous for them all to be answered, because of the shortage of skilled staff and facilities. Accordingly, the approach was to decide upon the most important ones.111

3.7 The draft document was split into three sections:

i. Section 1 discussed the role of the different sorts of research being done (as drafted by Dr Tyrrell);

ii. Section 2 covered in broad terms the questions that could be asked. At this stage, there were 17 questions with references to the studies that might be able to answer them (as drafted by Dr Tyrrell); and

iii. Section 3 set out the studies, with codes to indicate those already under active consideration and by whom (as drafted by Dr Pickles). At this stage, no attempt had been made to allocate priorities.112

3.8 During the Committee’s consideration, a number of comments and suggested amendments were made, with the result that the draft needed further expansion and recasting.113

Further development of the Report following the second meeting – discussion of priorities

3.9 Dr Pickles presented a revised draft copy of the Report to Dr Tyrrell on 19 April 1989. The draft reflected the changes decided upon during the Committee’s second meeting. The number of research questions had grown to 20, with sub-questions, and the research programmes now numbered 47.114

3.10 Dr Pickles explained to Dr Tyrrell that she was having difficulty deciding the right format, owing to the lack of guidance the Committee had been given as to whose perspective was relevant when deciding priorities. For example, it was not clear whether the perspective of the sponsoring Departments, the relevant Research Council, or industry should receive particular attention. It was also difficult to balance work to protect animals against work which might have a remote chance of benefiting humans. She pointed out the importance of these issues given that the Committee would need to indicate how the priorities had been allocated.

3.11 Dr Tyrrell told the Inquiry that such issues were not formally resolved. He said that when considering projects, the Committee tended to focus mostly on the understanding of the epidemic and the risks to human beings. When allocating priorities, it did not use set or explicit criteria, but rather worked on a consensus.
basis. Accordingly, if the Committee agreed upon something, it might not be explained in logical and consecutive terms.\textsuperscript{115}

\textbf{3.12} In her minute to Dr Metters of 2 May (see paragraph 3.2 above), Dr Pickles sought guidance on how priorities should be indicated.\textsuperscript{116} Dr Metters replied that ‘it would be helpful if the Committee could give an indication of priority and feasibility in the present state of knowledge’. He asked Dr Pickles to ‘manoeuvre members’ so that the report gave a clear indication of their views on priority.\textsuperscript{117}

\section*{Allocation of priorities}

\subsection*{The star ratings}

\textbf{3.13} The Committee drew up its star ratings as follows:

\begin{center}
\begin{tabular}{|c|c|}
\hline
\textbf{The Tyrrell Committee star ratings} &  \\
\hline
*** & highest priority projects  \\
**  & medium priority projects for immediate work  \\
* & lowest priority projects  \\
\hline
\end{tabular}
\end{center}

\textbf{3.14} The Committee recommended that all projects rated ** or *** be funded urgently.

\textbf{3.15} The day after the Committee’s final meeting, Dr Pickles sent a ‘clean version’ of the Report to Dr Tyrrell to help him with preparation of the final version. The recommendations on research appeared with their star ratings for the first time, which reflected consensus reached during the final meeting. In this draft, 28 research projects were recommended, compared with 47 in the previous one. Some of the projects had been merged; Table 3.2 lists those projects that were omitted completely. Of the 28 remaining, 14 were listed as high priority, 5 medium priority, 3 low and 6 unclassified.\textsuperscript{118}

\textbf{3.16} Dr Pickles circulated a further revised draft to Committee members on 24 May. It took into account redrafting of sections by Committee members subsequent to the third meeting. She suggested that if further significant changes were required, particularly to the priority ratings, another meeting might be necessary.\textsuperscript{119}

\textbf{3.17} On 27 May 1989, Dr Kimberlin expressed some concern over the lack of explanation of the priorities. He reviewed the ratings given to each of the projects and suggested a number of changes, of which all but two were taken up in the final report.\textsuperscript{120} He also suggested that they might like to include ‘an explanation of why the final ratings have been set as they are’.\textsuperscript{121}

\begin{footnotesize}
\begin{itemize}
\item \textsuperscript{115} T6 (Tyrrell) pp. 113–14
\item \textsuperscript{116} YB89/5.21/1
\item \textsuperscript{117} YB89/5.4/1–1.2
\item \textsuperscript{118} YB89/5.9/3.1–3.25
\item \textsuperscript{119} YB89/05.24/1.1
\item \textsuperscript{120} Dr Kimberlin gave project B1.a – study of the clinical features in cases of BSE with particular emphasis on methods of early diagnosis – a one-star rating. It was rated between two and three stars in the final report. He gave project D1.e – effect of PrP on neuronal function and gene regulation – a one-star rating. It was given two stars in the final report. See Table 3.1 below for full details of the final priority ratings
\item \textsuperscript{121} YB89/5.27/1.1–1.3
\end{itemize}
\end{footnotesize}
3.18 Dr Tyrrell conveyed these concerns to Dr Pickles, and explained that Dr Kimberlin was suggesting that the starring be explained by additional sentences after each section. Dr Tyrrell thought this might be very difficult to do well, and could substantially lengthen the text. Furthermore, another meeting would probably be required to sort the matter out.\footnote{YB89/6.2/1.1} As a result, this suggestion was not taken up.

The research projects

3.19 The full schedule of research projects recommended by the Committee is set out in Table 3.1. The recommendations included all of the research areas identified by the Southwood Working Party bar the feeding of the scrapie agent to cattle.

Table 3.1: Tyrrell Committee propositions for research into spongiform encephalopathies

<table>
<thead>
<tr>
<th>Code</th>
<th>Recommendation</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Epidemiology</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>Epidemiology of BSE</strong></td>
<td></td>
</tr>
<tr>
<td>A1.a</td>
<td>Monitoring the occurrence of cases, age, sex, pedigree, and geographical distribution and association with feeding practices and other possible risk factors.</td>
<td>***</td>
</tr>
<tr>
<td>A1.b</td>
<td>Formal controlled study on possible vertical transmission.</td>
<td>***</td>
</tr>
<tr>
<td>A1.c</td>
<td>More detailed examination of the source of meat and bone meal associated with high BSE infection rates and the processes in the relevant rendering plants.</td>
<td>***</td>
</tr>
<tr>
<td>A1.d</td>
<td>More detailed investigation into the fate of bovine (and ovine) tissues and products that could lead to infection being spread by as-yet-unrecognised routes.</td>
<td>***</td>
</tr>
<tr>
<td>A1.e</td>
<td>Mathematical modelling to help clarify the features of the epidemic and to predict likely scenarios for the future.</td>
<td>**</td>
</tr>
<tr>
<td>A1.f</td>
<td>Survey of the brains of cattle routinely sent for slaughter to monitor incidence of unrecognised infection.</td>
<td>*</td>
</tr>
<tr>
<td>A1.g</td>
<td>Further examination of the relative susceptibility of calves.</td>
<td>*</td>
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<tr>
<td></td>
<td><strong>Human</strong></td>
<td></td>
</tr>
<tr>
<td>A2.a</td>
<td>Surveillance of cases of CJD with particular reference to the overall incidence, the geographical distribution, the age and sex distribution, occupational history, association with medication; and any atypical clinical features.</td>
<td>***</td>
</tr>
<tr>
<td>A2.b</td>
<td>Prospective monitoring of groups with high exposure to bovine tissues such as slughtermen, veterinarians, and regular recipients of medicinal products of bovine origin.</td>
<td>*</td>
</tr>
<tr>
<td>A2.c</td>
<td>A study that may impinge on this research is that on recipients of hGH (human growth hormone).</td>
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</tr>
<tr>
<td></td>
<td><strong>Other animal spongiform encephalopathies</strong></td>
<td></td>
</tr>
<tr>
<td>A3.a</td>
<td>Monitoring the health of other species fed offal, carcasses or meat and bone meal; principally pigs, domestic cats and dogs and poultry.</td>
<td>***</td>
</tr>
<tr>
<td>A3.b</td>
<td>Continued surveillance of the incidence of spongiform encephalopathy (scrapie and transmissible mink encephalopathy) in species known to be susceptible (sheep, goats and mink) with particular emphasis on possible recent changes of scrapie in sheep.</td>
<td>*</td>
</tr>
</tbody>
</table>
### Table 3.1: Tyrrell Committee propositions for research into spongiform encephalopathies

<table>
<thead>
<tr>
<th>Code</th>
<th>Recommendation</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Clinico-pathological studies</strong></td>
<td></td>
</tr>
<tr>
<td>B1.a</td>
<td>Study of the clinical features in cases of BSE with particular emphasis on methods of early diagnosis.</td>
<td>**(*)</td>
</tr>
<tr>
<td>B1.b</td>
<td>Characterisation of vacuolation and other lesions found post-mortem and correlation with clinical features. Investigation of possible extra-neural lesions.</td>
<td>**</td>
</tr>
<tr>
<td></td>
<td><strong>Transmission of BSE</strong></td>
<td></td>
</tr>
<tr>
<td>C1.a</td>
<td>Primary titration of various tissues, organs, and secretions from BSE animals by inoculation into mice. To include colostrum, milk, semen, embryos, muscle, placenta, blood, buffy coat, spleen, lymph node, thymus, heart, liver, kidney, pancreas, lung, intestine.</td>
<td>***</td>
</tr>
<tr>
<td>C1.b</td>
<td>To investigate the susceptibility of different isolates of BSE agent to chemical and physical inactivation using bioassay in mice, in direct comparison with scrapie. Investigating:</td>
<td>**</td>
</tr>
<tr>
<td></td>
<td>Porous-load (surgical) autoclaving; gravity-displacement (laboratory) autoclaving; sodium hydroxide; Sodium hypochlorite.</td>
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<tr>
<td></td>
<td>Gamma irradiation; boiling; standard laboratory hot-air decontamination; formalin inactivation; Sodium dichloroisocyanurate and other oxidising agents; microbiologically-buffered glutaraldehyde.</td>
<td></td>
</tr>
<tr>
<td>C1.c</td>
<td>Transmission of BSE to other species such as:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pigs</td>
<td>**</td>
</tr>
<tr>
<td></td>
<td>Marmosets</td>
<td></td>
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<td></td>
<td>Chickens</td>
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<tr>
<td></td>
<td>Other primates</td>
<td></td>
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<tr>
<td></td>
<td>Sheep</td>
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<tr>
<td></td>
<td>Goats</td>
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<tr>
<td></td>
<td>Hamsters</td>
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<td></td>
<td>Cats and dogs</td>
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<td></td>
<td>Mink</td>
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<tr>
<td></td>
<td>Horses</td>
<td></td>
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<tr>
<td></td>
<td>Rabbits.</td>
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<tr>
<td>C1.d</td>
<td>Transmission to cattle: injection of various tissues from BSE animals; embryos from infected cows and semen from infected bulls into BSE-uninfected recipients, oral challenge with placenta, milk, colostrum.</td>
<td>**</td>
</tr>
<tr>
<td>C1.e</td>
<td>Clinical, histopathological, physio-chemical and biological studies of BSE isolates passaged in mice: application of strain typing techniques.</td>
<td>**</td>
</tr>
<tr>
<td>C1.f</td>
<td>Pharmacological manipulation of infectivity, effect of feed and feed additives, etc.</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td><strong>Pharmaceuticals</strong></td>
<td></td>
</tr>
<tr>
<td>C2.a</td>
<td>Bovine serum albumin and foetal calf serum and other common media that involve bovine material: intracerebral to mice.</td>
<td>***</td>
</tr>
<tr>
<td>C2.b</td>
<td>Additional transmission studies specifically relevant to pharmaceutical manufacture.</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Of meat and bone meal (MBM) made from scrapie-affected sheep</strong></td>
<td></td>
</tr>
<tr>
<td>C3.a</td>
<td>Transmission of meat and bone meal from scrapie-affected sheep to mice following modified practices in an experimental rendering plant to identify if any infection is still present and to help establish a process that can safely destroy infection.</td>
<td>**</td>
</tr>
</tbody>
</table>
**Table 3.1: Tyrrell Committee propositions for research into spongiform encephalopathies**

<table>
<thead>
<tr>
<th>Code</th>
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<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genetics/molecular biology/chemical pathology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D1.a</td>
<td>SAF morphology, distribution, quantitation and correlation with histopathology and PrP-BSE in cattle.</td>
<td>**</td>
</tr>
<tr>
<td>D1.b</td>
<td>Analysis of BSE fibril protein and its normal isoform and search for PrP (or its mRNA) in accessible peripheral tissues.</td>
<td>***</td>
</tr>
<tr>
<td>D1.c</td>
<td>Other attempts to find a diagnostic test for the subclinical state.</td>
<td>***</td>
</tr>
<tr>
<td>D1.d</td>
<td>RFLP linkage analysis to bovine PrP gene, its sequencing and cloning.</td>
<td>***</td>
</tr>
<tr>
<td>D1.e</td>
<td>Effect of PrP on neuronal function and gene regulation.</td>
<td>**</td>
</tr>
</tbody>
</table>

**Table 3.2: Propositions for research into TSEs omitted from final Report**

<table>
<thead>
<tr>
<th>Code</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epidemiology</strong></td>
<td></td>
</tr>
<tr>
<td>A1.h</td>
<td>Further examination of greater risk of infection in calfhood.</td>
</tr>
</tbody>
</table>

| **Clinico-pathology** | |
| **BSE** | |
| B1.c | Clinical and histopathological study of BSE in mice and comparison with scrapie in mice. |

| **Scrapie** | |
| B2.a | Comparison of the features of modern cases of scrapie with those described several years ago. |
| B2.b | Neuropathological and other work on natural and experimental scrapie in sheep and goats. |

| **CJD** | |
| B3.a | Detailed investigation (ante- and post-mortem) of any future cases of iatrogenic CJD since these may give valuable clues as to atypical spongiform encephalopathies in man. |

| **Transmission** | |
| **Pharmaceuticals** | |
| C2.c | Various final products (eg, bovine insulin) intracerebral to mice for complete reassurance. |

| **Of Scrapie** | |
| C3.a | For direct comparison with BSE agent in many experiments in C1 above. |
| C3.b | To mice to investigate whether current strains of natural scrapie are different from those isolated previously. |
| C3.c | Using mice to ascertain the susceptibility of scrapie (22A strain) to the procedures used in the rendering industry, including heat, solvent extraction and microwaves. |
| C3.d | Various scrapie strains orally to cattle. |
The recommendation to establish the Consultative Committee on Research (the Tyrrell Committee) was one of the first recommendations made by Sir Richard Southwood, in his letter to Ministers of 20 June 1988. Both he and Sir Donald Acheson had envisaged a joint committee of experts chosen by the MRC and AFRC from among scientists with appropriate experience. This concept was opposed by MAFF, who claimed that the CVL had discovered BSE and was already deeply involved in its investigation, and should therefore take a leading role in the committee and appoint its chairman.

A compromise was eventually reached between DH and MAFF by October 1988. Sir Donald Acheson’s nominee, Dr David Tyrrell, Director of the MRC Common Cold Unit and a distinguished virologist, was confirmed as chairman. Dr William Watson, Director of the CVL, and Professor John Bourne, Director of the Institute for Animal Health, both nominated by MAFF and the second DH nominee, Dr Robert Will, a clinical neurologist and expert in CJD, were duly accepted as members of the Committee. The fifth member to be appointed was Dr Richard Kimberlin, who had recently resigned from directorship of the NPU to become an independent adviser on TSEs. None of the members was actively engaged in scientific research on TSEs, although both Dr Watson and Professor Bourne were in charge of institutions in which such research was ongoing. The composition of the Committee was completed by the appointment of Dr Katherine Levy as MRC observer, and of Dr Hilary Pickles (DH) and Mr John Maslin (MAFF), who formed the secretariat.

### Table 3.2: Propositions for research into TSEs omitted from final Report*

<table>
<thead>
<tr>
<th>Code</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C4.b</td>
<td>Orally to cattle, to confirm the current hypothesis of the origin of BSE.</td>
</tr>
</tbody>
</table>

#### Genetics/molecular biology/chemical pathology

**Bovine**

- D1.e Immunohistochemistry.
- D1.g Structural analysis of bovine PrP gene.
- D1.h Cloning of bovine PrP gene.

**Ovine**

- D2.a Look for a scrapie genome.
- D2.b Continued work on *sip* in sheep.

**Murine**

- D3.a Continued work on *sinc*.

* "Propositions omitted" refers to projects that appeared in the draft considered during the Committee's final meeting, but which did not appear in the final report.

### Discussion

**3.20** The recommendation to establish the Consultative Committee on Research (the Tyrrell Committee) was one of the first recommendations made by Sir Richard Southwood, in his letter to Ministers of 20 June 1988. Both he and Sir Donald Acheson had envisaged a joint committee of experts chosen by the MRC and AFRC from among scientists with appropriate experience. This concept was opposed by MAFF, who claimed that the CVL had discovered BSE and was already deeply involved in its investigation, and should therefore take a leading role in the committee and appoint its chairman.

**3.21** A compromise was eventually reached between DH and MAFF by October 1988. Sir Donald Acheson’s nominee, Dr David Tyrrell, Director of the MRC Common Cold Unit and a distinguished virologist, was confirmed as chairman. Dr William Watson, Director of the CVL, and Professor John Bourne, Director of the Institute for Animal Health, both nominated by MAFF and the second DH nominee, Dr Robert Will, a clinical neurologist and expert in CJD, were duly accepted as members of the Committee. The fifth member to be appointed was Dr Richard Kimberlin, who had recently resigned from directorship of the NPU to become an independent adviser on TSEs. None of the members was actively engaged in scientific research on TSEs, although both Dr Watson and Professor Bourne were in charge of institutions in which such research was ongoing. The composition of the Committee was completed by the appointment of Dr Katherine Levy as MRC observer, and of Dr Hilary Pickles (DH) and Mr John Maslin (MAFF), who formed the secretariat.
3.22 The members of the Committee knew about current work on TSEs and were knowledgeable about the published literature. They did not see a need to organise workshops or seminars on the subject or consult more widely with universities, Research Councils and others to obtain new ideas about research into BSE and related issues. They relied on the suggestion of the Southwood Working Party and their review of ongoing research, largely at the CVL and NPU. This enabled them to proceed with speed. They completed an Interim Report after meeting on three occasions.

3.23 The 47 research projects described in the Interim Report of the Tyrrell Committee were prioritised, and a simple notation was used to indicate whether projects had been completed, were in progress, being planned, or simply suggested. The codes indicated where the work was being done, or where it was recommended that it might be done. The main institutes involved were the CVL and NPU. Three of the five members of the Committee were or had been closely associated with these two institutes. While they recommended that careful peer review be used to ensure quality, they did not seek external expert assistance in recommending projects or organisations to undertake them, or suggest an open call for proposals for unassigned projects.

3.24 We do not believe that it was totally satisfactory that the Committee set up to review research into BSE should have included members connected with institutions that were seeking to be involved in carrying out the majority of the research projects. Their priorities must have made it less easy to approach the task of according priority to the difficult projects with objectivity. They were well placed to argue the merits of the different projects, but we feel that it would have been better if they had not been involved in determining priorities. The independent committee envisaged by Sir Richard Southwood and Sir Donald Acheson would have been in a better position to review the current research work and advise on what further work was needed.

3.25 More generally we would observe that the process of recruitment of scientific advisers by MAFF and DH depended to a large extent on the consideration of individuals known to senior officials within the Departments. No attempt was made to consult more widely, and we believe that this limited the choice available. In such situations a wider range of suitable advisers is to be found within the biological sections of the Royal Society, the Royal College of Physicians, the Royal College of Pathologists, the Research Councils (BBSRC/AFRC and MRC), the Foresight Panels and the Wellcome Trust. The Royal Society has a Sectional Committee structure, which ensures a wide knowledge of top scientists in all scientific disciplines. The Royal Colleges have Scientific Advisory Committees for each speciality within their discipline. The Research Councils and the Wellcome Trust have Specialist Boards responsible for funding most of the research in the UK, and their granting and reporting procedures ensure that they have knowledge about the scientific merit of the research that they fund, including the quality of the investigators. This fund of knowledge about scientists and their work should be available to those charged with appointing scientific advisers to the Government.

3.26 The Committee met for the first time on 13 March 1989 and presented its ‘Interim Report’ on 10 June. It had set about its task with urgency. In a statement Dr Tyrrell explained to us how the Committee saw its task:
The members of the Committee believed that the role of the Committee was to follow up a specific recommendation of the Southwood Report [IBD2(IBD1 tab 2)] with a further report on research. As part of that, the Committee understood that their role was to identify areas of research which could be undertaken to better understand the nature of TSE’s, BSE in particular, and their epidemiology. [Governments departments and research funding agencies would use this information to make policy decisions and develop strategies for research.] The Committee members thought they were expected to very rapidly construct a framework against which research proposals could be considered and produce a graded list of projects.

It is important to recognise that the members believed that they were expected to produce a report quickly and we learned that the expectation was that we would focus on immediate research priorities.123

3.27 Further urgency was added by the fact that the joint MRC/AFRC review meeting was scheduled for June 1989, and the Committee understandably believed it important to produce its conclusions on research before that meeting. In the event that meeting was postponed.

3.28 The speed with which the Tyrrell Committee produced its Report was commendable, but it had its drawbacks. The Report did not identify the criteria which had been applied to determine the order of priority of the research projects, nor did it explain the reasoning behind the priorities accorded to the different projects. It was not part of the Tyrrell Committee’s remit to consider costs, although it was mindful of the resource implications of some proposals, notably those requiring experiments with cattle.124 Inevitably this meant that individual projects were not ranked on a cost/benefit basis. Had they been, we question whether the very expensive embryo transfer experiment would have received the priority that it did.

3.29 We believe that the Departments which received the Report would have wished to reassess its recommendations having regard to the cost/benefit of each project (see paragraph 3.46 below). This was difficult in the absence of any explanation as to why the Tyrrell Committee had accorded each project its particular priority. In the event, the Government decided to adopt a blanket response of putting in hand all the research in the top two categories of priority.

3.30 Dr Tyrrell gave us examples of the objectives of the research proposals:

(i) controlling the BSE epidemic

(ii) eradicating the BSE epidemic

(iii) protecting public and animal health

(iv) addressing basic scientific questions.125

3.31 We understand that it was the members of the Committee themselves who formulated these objectives, and they succeeded in identifying a sensible list. We
think, however, that it would have been desirable for the Committee to seek some input from those who were to be the ‘customers’ for whom the research would be carried out – those in MAFF and DH who had to handle the disease and take steps to deal with its implications.

3.32 For example, those who had just introduced the ruminant feed ban might then have told the Committee of their need for a test to identify the presence of ruminant protein in feed – an area of research which did not feature in the Tyrrell Report and which did not receive priority treatment.

3.33 In the same context, the practical importance of identifying the minimum amount of infective material capable of orally transmitting the disease might have been identified. Absence of knowledge about this was a recurrent problem when considering practical issues, eg:

- Was there any need to address the risk that ruminant feed might be contaminated with feed for non-ruminants?
- Was it safe to spread (i) MBM, (ii) blood or (iii) slaughterhouse waste on land as fertiliser?

3.34 The Tyrrell Committee did in fact give some consideration to whether it should recommend epidemiological research to attempt to identify just how small a pocket of contaminated material was sufficing to infect cattle through feed. Dr Tyrrell told us:

> The members of the Committee were aware of the importance of ascertaining the size of the dose that could transmit BSE by oral ingestion. The members of the Committee had thought about epidemiological calculations of the amount of infective material likely to have been included in a cow’s rations.

> The Committee could have recommended epidemiological calculations of the amount of infected material likely to have been included in a cow’s rations. This approach, however, fails to identify an important part of the question, which is that you are concerned with the concentration of infectivity and not just the amount of infected material. The practical or scientific value of such a calculation would have been severely limited by the large number of unknown factors to which a range of arbitrary values would have had to be assigned.\(^{126}\)

3.35 We were not persuaded by this reasoning. It seems to us that from the practical viewpoint the important question was the amount of material that was resulting in transmission of the disease rather than more sophisticated questions of titration.

3.36 Another practical need was a cheap and simple post-mortem test, such as the one that Dr Narang attempted to develop (see Chapter 5 below).

3.37 We mention these matters not by way of criticism but simply to draw attention to some of the consequences of having drawn up that Report under pressure. We

\(^{126}\) S488A Tyrrell Committee paras 96–9
consider that the Interim Report was a commendable piece of work in the limited time available.

3.38 The Southwood Working Party had recommended, as important research, the feeding to cattle of scrapie-infected meal in order to confirm that scrapie was indeed the source of BSE. The Tyrrell Report did not explain why this experiment had not been recommended by the Committee. These were the reasons given later:

(i) On 25th October 1988 Dr Watson reported to the Chief Veterinary Officer on evidence that scrapie had been transmitted to cattle in the United States of America. He provided information which had been obtained by one of his colleagues, Dr Wrathall, on a visit to America. On 17th November 1988 a BSE Research and Development meeting with the Chief Veterinary Officer was attended by representatives of MAFF and by Neuropathogenesis Unit scientists. The minutes of that meeting record:

‘There was a lower priority for the scrapie to cattle experiment since this had been done in the USA but not published. Professor Bourne stated that it was not anticipated that IAH (NPU) would be conducting experiments in cattle at Skedburg; it was agreed these would be done by CVL.’ [YB88/11.17/3.1-3.5 at 3.4–3.5]

(ii) The American study had been carried out, not by oral exposure, but intracerebral injection and the scrapie sources used would not have been representative of the strains of agent present in United Kingdom sheep. Collecting suitable sheep material was a major problem and strain typing methods were not available to show that BSE agent was not present as a contaminant.

(iii) Another obstacle was that the possible influence of the genetic make up on the susceptibility of cattle to these agents was not known. This was an important factor to resolve before attempting some of the further experiments on the transmission of BSE to cattle.

(iv) It was recognised that other experiments were being conducted on cattle at the Central Veterinary Laboratory and would either have to be abandoned or new accommodation would be required. A five-year development plan prepared by Dr Watson for the CVO on 9th September 1988 contained a section on transmission of scrapie to cattle [YB88/9.9/2.1–2.16] although it was noted that it was unlikely the experiment would commence in 1988/89. At this time a complete site redevelopment plan was being prepared for the Central Veterinary Laboratory and additional high security cattle accommodation was a first priority in the proposed construction work.

(v) Since BSE was a problem in cattle it made sense to work initially with the bovine agent in preference to scrapie. Although the origin of disease in cattle was of great scientific interest it was not of fundamental importance to the animal and pubic health consequences of BSE. Therefore, it was not given priority by the members of the Committee in the Report [IBD4(IBD1 tab 4)].

127 S488A Tyrrell Committee para. 103
3.39 We now understand why the Tyrrell Committee did not recommend this experiment, and make no criticism of their decision not to do so. It was, however, unfortunate that they did not explain their reasons at the time. In one sense it was true that the origin of BSE was not of fundamental importance to the animal and public health consequences of BSE. Whatever its origin, there was no guarantee that the virulence of the agent would not change upon transmission to the cow. Nonetheless, the belief that BSE was scrapie in cattle was the reason why many – Sir Donald Acheson is but one example – believed that BSE would be as innocuous as scrapie. In time the obstacles that the Tyrrell Committee saw in the way of the scrapie-to-cattle experiment were diminished. More became known on the question whether the susceptibility of cattle to infection was not influenced by their genetic makeup. Additional accommodation was constructed for cattle experiments. Unfortunately, the desirability of the scrapie-to-cattle experiment was lost sight of, and many continued to think that the scrapie theory was not seriously open to question.

3.40 The Tyrrell Committee rightly described its Report as ‘Interim’, and saw it as a first step:

... a framework that could be used by scientists to develop their own project proposals for research which could then be considered by the various funding bodies, that is MAFF, DoH, AFRC and MRC.\(^{128}\)

3.41 It also envisaged that the projects would be peer-reviewed.\(^{129}\) We now turn to see what occurred when, having succeeded in producing a Report within three months, the Committee handed that Report to Ministers.

Publication of the Report

Submission of the Interim Report

3.42 Dr Tyrrell presented Mr Andrews (MAFF) and Sir Donald Acheson (DH) with the Interim Report of the Tyrrell Committee on 10 June 1989. He remarked that the Committee felt that they should forward their immediate conclusions on BSE so that there should be no delay in the provision of resources for essential research and getting the projects under way. He stressed that ‘slow viruses’ lead to slow research, which made it all the more important to avoid unnecessary delays.\(^{130}\)

Subsequent handling of the Interim Report

3.43 On 13 June, the same day that MAFF and DH publicly announced their intention to introduce the SBO ban for human food,\(^{131}\) Mr Maslin prepared for the MAFF Minister, Mr John MacGregor, the reply to a Parliamentary Question which would announce, among other things, the receipt of the Report.\(^{132}\) The same day Dr Pickles informed Sir Donald Acheson that Mr MacGregor might want to

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\(^{128}\) S488A Tyrrell Committee para. 8

\(^{129}\) S488A para 14

\(^{130}\) YB89/6.10/3.1; YB89/6.10/2.1

\(^{131}\) YB89/6.13/5.1. The Specified Bovine Offal (SBO) ban prohibited certain bovine offal (brain, spinal cord, spleen, thymus, tonsils and intestines) from being used in any product intended for human consumption (see vol. 6: Human Health, 1989–96)

\(^{132}\) YB89/6.13/1.6
Scientists after Southwood

announce that he had received the Report when he made other BSE policy statements that week, so it was necessary to pass the Report on rapidly to the Health Ministers as well.133

3.44 Accordingly, Sir Donald forwarded the report to the Secretary of State for Health, Mr Kenneth Clarke. Sir Donald remarked that ‘a large number of research areas are allocated high priority and this work will be laborious, time consuming and expensive’. Since MAFF had the most difficult issues to deal with, Sir Donald suggested that the DH comply with whatever Mr MacGregor proposed about handling the Report, including publication if necessary.134

3.45 On 14 June 1989, Mr Cruickshank of MAFF minuted Mr Andrews, informing him that the Committee’s terms of reference were to advise Departments, meaning that there was no obligation to publish the Report. However, due to its high profile, demands for its publication were expected.135

3.46 Mr MacGregor also received Mr Cruickshank’s minute, and was struck by how much work was still to be done interdepartmentally before any decisions could be taken. In particular, some idea of costs was needed before an approach could be made to the Treasury. No work appeared to have been done on this. Mr MacGregor questioned whether mention of the Report needed to be made in an answer to a Parliamentary Question at that stage, and proposed that the announcement should be made a week or two later, by which time people would have had an opportunity to absorb it. Publication should certainly be postponed until such time as everyone internally had been able to read it.136

3.47 Mr Meldrum (the CVO) commented to Mr Andrews that it was not necessary to publish the Report since it did not ‘take us very much farther forward’. He was concerned that although the Report covered all aspects of research and development, it did not help with deciding which projects should be funded, since many of them were given high priority. Therefore, he thought funding should not be sought from the Treasury until the Report had been carefully scrutinised by the affected Departments.137

3.48 Mr Andrews told Mr Meldrum ‘to proceed in the way you suggest’. He thought it would be difficult to decide not to fund any of the research designated high priority. Further, a Parliamentary Question should not be inspired at that stage.138

Government handling of the recommendations

3.49 By 30 June 1989, MAFF had prepared a comprehensive document in response to the Interim Report, in accordance with Mr Andrews’s instructions.139 In addition to a submission to Ministers in relation to funding, the document included tables

133 YB89/6.13/9.2
134 YB89/6.13/10.1 (copy of the Report not attached)
135 YB89/6.14/9.1
136 YB89/6.15/4.1
137 YB89/6.19/7.1
138 YB89/6.19/6.1. For a short description of Parliamentary Questions, see vol. 15: Government and Public Administration
139 YB89/6.19/6.2
setting out MAFF’s response to each of the research projects detailed in the Interim Report. 140

3.50 The draft submission was discussed at a meeting chaired by Mr Andrews on 13 July, and it was agreed that:

- the two- and three-star projects in the report would be split into two categories. The first would list, with costings, projects which MAFF was responsible for funding, and the second would list projects MAFF regarded as falling to others;
- a draft letter would be prepared for the Minister to send to the Secretaries of State of Health and for Education and Science seeking agreement to MAFF’s approach to implementing the Interim Report;
- the letter would be copied to the Chief Secretary to the Treasury and would make clear how much extra funding the Minister would have to bid for to finance the extra research;
- the letter would enclose a draft statement for the Minister to make to Parliament announcing decisions on the implementation of the Report; and
- the letter would also seek agreement that there was no choice but to publish the Interim Report. 141

3.51 Mr Andrews later briefed the new Minister for Agriculture, Fisheries and Food, Mr John Gummer, on the decisions made at the meeting. 142 Mr Gummer in turn told Mr Kenneth Clarke and Mr John MacGregor, newly appointed Secretary of State for Education and Science, that the Tyrrell Report had to be published, though he did not say when. He provided them with a costed breakdown of high-priority projects, indicating whether MAFF, DH or the Research Councils would be responsible for their funding. 143

3.52 Mr Gummer thought that in view of the wide public concern about BSE, there was no option for the Government other than to ensure the projects in the top two priority categories were initiated. Not to do so would leave the Government open to criticism that it had failed to carry out research into any potential dangers associated with BSE. Mr Gummer wanted to announce urgently that the Government had accepted the findings about the higher priority projects, and that money was being made available so that work could begin on the most pressing recommendations considered by the Committee to be of primary importance. He sought Mr Clarke’s and Mr MacGregor’s agreement to his announcement, and asked them to confirm whether they wished to be associated with it. 144

3.53 Mr Roger Freeman, 145 instead of Mr Clarke, replied to Mr Gummer on 9 August 1989. He said he was ‘broadly content’ with the proposed arrangements, and agreed the Report should be published without delay ‘as a further indication of our intention to be entirely open about this disease and how the Government is responding to it’. He further commented that of the projects that fell solely to DH, work had begun on two, and the third had been given a one-star rating and would

140 YB89/6.30/3.1–3.23. Prepared by Dr David Shannon of the Chief Scientists Group, MAFF
141 YB89/7.14/1.1
142 YB89/7.28/5.1–5.11
143 YB89/8.1/3.1
144 YB89/8.1/3.1
145 DH Parliamentary Under-Secretary (Commons)
be considered by officials soon. Accordingly, funding for the DH projects could be contained within existing allocations. Mr Freeman concluded: ‘I recognise and support your need for more R&D funds for BSE research this year if we are to announce that the high priority studies identified by the Tyrrell Committee are being taken forward as a matter of urgency.’

3.54 Mr Gummer’s decision, made on the advice of his officials and proffered by Mr Andrews, and with the support of DH, that all projects recommended by the Tyrrell Committee as urgent should be put in hand, was creditable.

**Attempts to gain extra funding**

3.55 On 11 August 1989, Mr Norman Lamont told Mr Gummer that he had ‘some difficulty with your proposed funding arrangements and the content of your draft announcement’. In particular:

I am concerned that you have been unable to rearrange your priorities in order to accommodate research of such importance. I understand that your total provision for R&D is well over £100 million and, while the precise costings may not have been known until now, it has been known for a considerable amount of time that some research would be required into BSE. I should therefore like you to scrutinise your research programme in order to find savings which will balance the expenditure you propose in this area.

3.56 He further commented that his own predecessor had agreed to fund BSE measures introduced the previous year because of the possibility that the disease posed risks to human health. If BSE turned out not to be transmissible to humans, all funding should be borne by the industry. He continued:

Although I accept that it may not yet be possible to take a final view we have established that it is very unlikely that the disease can be passed on to humans. It is therefore disappointing that the attachment to your letter makes no mention of the possibility of industry funding. This would help avoid any claim on the Reserve in the present year.

3.57 On 18 August Mr MacGregor said in reply to Mr Gummer’s letter that although he agreed that the Report should be published, he could not agree with the terms of the draft announcement at this stage. This was because it was uncertain how the urgent work falling to the Department of Education and Science (DES) would be funded within the Science Budget. He, too, might need to approach Mr Lamont for extra funds, and was also consulting the relevant Research Councils on the appropriate allocation of the programme and the costs involved.

3.58 One month later the Management Board of DES met to discuss the Interim Report, and to determine which research projects would be appropriate for Science Budget funding. The next day, 19 September, Mr MacGregor told Mr Gummer...
that his agreement to the announcement was conditional on extra funds being made available in 1989/90 from the Reserve.\textsuperscript{152}

3.59 On 2 October 1989 Mr Lamont informed Mr MacGregor, as he had Mr Gummer, that he was not convinced that BSE research justified a claim on the Reserve. Indeed, he thought that, as with MAFF’s research budget, it would be possible to fund this expenditure from within the existing Science Budget through a reassessment of priorities.\textsuperscript{153}

3.60 Mr Andrews asked his Financial Guidance Division whether MAFF and DES had sufficient money in the current Public Expenditure Survey (PES) to fund the Tyrrell research.\textsuperscript{154} Mr Richard McIvor responded on 2 November that MAFF had sufficient money in the PES to fund in-house BSE research. The external research would be funded from available funds for commissioned research. Mr McIvor understood that DES had no specific allocation in the PES for BSE research, but did have unallocated money available. It would be for the Secretary of State to decide whether to allocate that money to BSE research.\textsuperscript{155}

3.61 On 7 November 1989 Mr Andrews told Mr Cruickshank that it was ‘very important that we now clear the way and deal with the publication of Tyrrell’. He claimed that DES had blocked it pending the PES outcome. Mr Andrews concluded: ‘We must now sort out exactly where matters rest and press ahead with an announcement.’\textsuperscript{156}

3.62 One month later Mr Robert Lowson of MAFF’s Animal Health Division wrote to Mr G J Mungeam of DES. He noted that it was 1 August 1989 when Mr Gummer wrote to Mr MacGregor seeking agreement on the terms of the announcement of the \textit{Tyrrell Report’s} publication. He continued:

Because of the need to ensure that adequate financial provision could be obtained to carry out the recommended research there have been inevitable delays while the PES process has been running. However, now that the major decisions on PES have been taken I am anxious for us to make progress on this issue as quickly as possible.\textsuperscript{157}

3.63 Mr Lowson noted that the only outstanding matter was the allocation of funds to the Research Councils for slow virus research. However, he understood that the Advisory Board for Research Councils would be advising Mr MacGregor that an allocation should be made. Although Mr MacGregor’s final decision would not be for some weeks, Mr Lowson hoped this would not prevent agreement to an announcement before then.\textsuperscript{158}

3.64 Dr Tyrrell expressed his frustration to Dr Levy on 14 December 1989:

I thought I should let you know that I did enquire what was to be done about the proposals in the report. I was told that the research proposals concerning

\textsuperscript{152} YB89/9.18/1.1
\textsuperscript{153} YB89/10.2/3.1
\textsuperscript{154} During the period covered by the Report, the amount of money for public expenditure was allocated to individual Departments each year after a formal Public Expenditure Survey, which took place in the autumn. Thus, for example, allocations for the 1988/89 financial year would have been decided in the ‘PES round’ of autumn 1987
\textsuperscript{155} YB89/11.2/6.1
\textsuperscript{156} YB89/11.7/6.1
\textsuperscript{157} YB89/12.7/1.1
\textsuperscript{158} YB89/12.7/1.1
MAFF were going to be implemented and that I should wait till November, by which time the funding would have been arranged, and the programme would be announced.

It is now clear that this was just a method of fobbing me off, and I see no point in going back to them for a repeat. I hope that the ideas sparked by the MRC meeting can and will be followed up in spite of the difficult financial climate. 159

3.65 On 20 December 1989 Mr Lowson informed Mrs Elizabeth Attridge (an Under Secretary at MAFF) that:

We are at last in a position to go ahead with publication of the Tyrrell Report into research priorities on BSE and the announcement of the Government’s reaction. This has been held up since we received the Report in the summer, first by the need to get agreement in the PES for the substantial extra spending required, and second, by the need then to await Management Board decisions on how funds received in the PES would actually be spent. 160

Final publication

3.66 Publication of the Interim Report was announced by way of an answer to a Parliamentary Question on 9 January 1990, and publicised by a press release the same day. Mr David Maclean’s161 written answer stated that:

The report recommends a comprehensive programme of research on the epidemiology, transmissibility and diagnosis of BSE with the aim of extending scientific knowledge about this new disease so that animal and human health can continue to be protected and the disease eventually eradicated.

The Government has considered the Report very carefully and accepts the recommendations of the Committee. A number of the projects are covered by the substantial programme of research that is already in progress, representing spending of some £1.3 million in the current financial year. Preparatory work is in hand on the other projects which the Tyrrell Committee recommended as urgent and of high priority. This represents additional funding from my Department’s Votes of some £2.2 million in 1990/91 and 1991/92, and £1.7 million in 1992/93. The Secretary of State for Health is setting in hand the high priority research that is within his Department’s responsibility and the Secretary of State for Education and Science is considering the advice of the Advisory Board for the Research Councils on what additional allocation would be appropriate from the Science Budget to the Agricultural and Food Research Council in support of its proposed programme of research, including research on slow viruses. 162

159 YB89/12.14/1.1
160 YB89/12.20/3.1
161 Minister of Food at MAFF
162 YB90/1.97.1–7.3
3.67 The reference to additional funding in the written answer makes it clear that the Departments responsible for the Tyrrell research were required to make funds available from existing Votes (ie, money already voted to them by Parliament). The Treasury did not provide additional funds specifically for the research projects recommended by the Tyrrell Committee.

Discussion

3.68 On 5 January 1990 Dr Pickles minuted Mr Roger Freeman and pointed out that time had not been wasted between completion of the Report and its publication. Although it had not been published, those who needed to act upon its recommendations, such as the Research Councils, had access to pre-publication copies. Accordingly, much of the high-priority work was already in progress at the time of final publication.\footnote{YB90/1.5/3.1}

3.69 Professor Bourne reiterated this view during his evidence to the Inquiry. He said that the delay in publication made very little difference to the implementation of the research, particularly with respect to the IAH and the NPU. He explained: ‘There may have been some small delay, but I do not think that is significant.’\footnote{T6 (Bourne) p. 127} Similarly, Dr Will did not think the delay in publication had affected his work on CJD surveillance, as it was something originally recommended by the Southwood Working Party.\footnote{T6 (Will) p. 130} Dr Watson added that most of the work at the CVL was in progress, and was not particularly influenced by funding.\footnote{T6 (Watson) p. 129}

3.70 It may be that no time was lost as a result of the delay in publishing the Tyrrell Report, although we are not convinced of this. Publication of the Report would have acted as a spur to the speedy identification of how the recommended research was to be funded. Whether or not delayed publication resulted in delayed research, we believe that the better course would have been to publish the Report promptly after it had been delivered. This would have accorded with the policy of openness which Mr Gummer was to introduce when he became Minister of Agriculture, Fisheries and Food. It would also have informed the outside world, and in particular the scientific world, of the likelihood of research opportunities, which could have led to a degree of competition for some of the projects. As it was, the CVL and the NPU proceeded to prepare to implement most of the high-priority projects without the peer review that the Tyrrell Committee had advised they should receive.