2. The Tyrrell Consultative Committee

The establishment of the Tyrrell Consultative Committee

2.1 The establishment of the Consultative Committee on Research (‘the Tyrrell Committee’) was publicly announced by way of a press release on 17 February 1989. However, its genesis was a Southwood Working Party recommendation made eight months earlier. During its first meeting on 20 June 1988, the Southwood Working Party agreed ‘that an expert Working Party on Research should be established – possibly jointly between the MRC [Medical Research Council] and AFRC [Agriculture and Food Research Council] – to advise on research in hand and that which is required, to answer the questions identified by the BSE Working Party’. This recommendation was conveyed the next day by letter from Sir Richard Southwood to Mr Derek Andrews, the Permanent Secretary at the Ministry of Agriculture, Fisheries and Food (MAFF), and Sir Donald Acheson, the Chief Medical Officer (CMO) at the Department of Health (DH).

2.2 After receiving Sir Richard Southwood’s letter, Sir Donald discussed its implications with Mr Andrews. Sir Donald said he might copy the letter to the Secretary of the MRC. He would suggest that the MRC Secretary meet with his AFRC colleagues to draw up some research and development proposals. Mr Andrews pointed out that MAFF was heavily involved in animal research and development, and that BSE research would not be a matter for the MRC and AFRC alone.

2.3 On 29 June 1988, Sir Donald advised Mr Kenneth Clarke, the Secretary of State for Health that ‘Sir Richard Southwood’s committee also recommends that an urgent review of research in this field is undertaken jointly by MRC and AFRC’. Sir Donald recommended that this advice be followed.

2.4 Meanwhile, after the receipt of Sir Richard Southwood’s recommendation, the following steps were taken by MAFF:

- on 7 July 1988 the Animal Health Division drafted a submission to the Minister, stating that MAFF should play a leading role in the proposed working group, given its major stake in BSE research work, and should put forward a bid for chairmanship of the working party;
- on the same day Mr Keith Meldrum, Mr Alistair Cruickshank and Dr William Watson met Mr Donald Thompson MP to discuss BSE...
research projects. Mr Thompson said that MAFF should take the lead on
BSE research and development, and that the proposed working party should
report to MAFF. Mr Meldrum informed Mr Thompson that Dr Watson of the
Central Veterinary Laboratory (CVL) was MAFF officials’ preferred choice
to chair the new working party;12

- Mr Andrews reiterated these views to Sir Donald Acheson the next day,
stating that it might make sense for the Director of the CVL to chair the
group,13 and

- on 12 July 1988, Mr Andrews wrote to Sir Richard Southwood to say that he
and Sir Donald Acheson agreed that a new body to coordinate research on
BSE could be set up. Mr Andrews said that he wanted MAFF to play a
leading part, and that he himself and Sir Donald were in touch about the
detailed arrangements.14

Appointment of the chairman

2.5 To help make quick and efficient progress in solving outstanding research
issues, Sir Donald Acheson favoured the appointment of a distinguished
microbiologist of international reputation as chairman. On 21 July he suggested
Sir Michael Stoker and Dr David Tyrrell as candidates to Mr Andrews (and later to
Sir Richard Southwood15), and commented that:

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\text{With people of this quality, if and when the unfortunate time comes where a}
\text{human health hazard becomes painfully evident, we will all be able to justify}
\text{what we have done in that we will have obtained advice at the very highest}
\text{possible level.16}
\]

2.6 Sir Richard Southwood favoured Sir Michael Stoker, a virologist, as
chairman,17 which prompted Sir Donald Acheson’s subsequent suggestion to
Mr Andrews that Sir Michael be invited to chair the new group.18 However,
Mr Andrews was not persuaded that a microbiologist was the best option since
much of the BSE research would focus on animals, and MAFF would have to
provide the bulk of funding. He therefore preferred as chairperson ‘someone with a
veterinary background who has experience of research in this area’. Mr Andrews
now suggested Dr William Martin, a member of the Southwood Working Party and
former Director of the Moredun Institute, as ‘a name on which we could all agree’.19
Sir Donald later noted this suggestion but suspected Sir Richard Southwood would
feel it best to have a chairperson with a microbiological background.20

2.7 The issue was still unresolved on 6 October 1988, when a meeting of senior
MAFF staff determined that Dr Martin, who had overseen much work on scrapie,
was MAFF’s preferred chairman. Professor Peter Biggs, recently retired Director of
the Institute for Animal Health and ‘another vet of international reputation’, was

12 YB88/7:14/2.1
13 YB88/7:8/8.1
14 YB88/7:12/2.1
15 YB88/08:11/2.1
16 YB88/7:21/1.1
17 YB88/5:30/3.1
18 YB88/9:6/1.1
19 YB88/9:16/1.1
20 YB88/10:03/3.1
their second choice. If neither of them was appointed chairman, then one of them should at least be a member of the Committee.21

2.8 The matter was decided towards the end of October. In the light of Sir Richard Southwood’s view that a virologist should be appointed to chair the Committee, in order to help secure public confidence in it, and of Sir Donald Acheson’s opinions, Mr Andrews concluded that MAFF would not succeed in having a veterinarian appointed as chairperson. Sir Richard and Mr Andrews agreed that since Sir Michael Stoker was no longer as active as he used to be, Dr David Tyrrell, Director of the MRC Common Cold Unit, or Professor Anthony Epstein, a distinguished virologist and member of the Southwood Working Party, were viable options. Mr Andrews agreed to the appointment of Dr Tyrrell.22

2.9 On 3 November Mr Andrews confirmed that MAFF and its Ministers had agreed to the appointment, and suggested that Sir Donald formally approach Dr Tyrrell.23 Sir Donald did so on 23 November,24 and Dr Tyrrell accepted the invitation to be chairman on 29 November 1988.25

Appointment of the other Committee members

2.10 Sir Richard Southwood had told Mr Andrews on 19 July 1988 that it was important a ‘small and very expert group of those involved in the subject’ make up the Committee. This would help ensure the maximum coordination of the research, and that the appropriate research was carried out to answer the questions raised by his own Working Party.26

2.11 The meeting of senior MAFF staff on 6 October (see paragraph 2.7 above) decided that the Committee should have four members in addition to the chair, including two medics chosen by Sir Donald Acheson and Sir Richard Southwood, and two vets chosen by MAFF.27 Sir Donald and Sir Richard subsequently agreed to this.28

2.12 By 3 November 1988 MAFF had decided Dr Watson of the CVL was a definite candidate, and they were ‘inclined to suggest’ Professor John Bourne, Director of the Institute for Animal Health (IAH), as their other veterinary member. When Mr Andrews so informed Sir Donald Acheson, he suggested Dr Richard Kimberlin of the Neuropathogenesis Unit would be suitable as a fifth member because, though being neither a medic nor a vet, he would ‘bring an independent view to bear’.29 Dr Kimberlin was subsequently appointed to the Committee and, upon Sir Donald’s recommendation, Dr Robert Will (a neurologist) filled the vacant DH post – the other having been taken by Dr Tyrrell.

2.13 Sir Donald and Mr Andrews acknowledged that the MRC and AFRC might wish to have input into the work of the Committee.30 Further, at a meeting with

21 YB88/10.10/2.1. The meeting was between Mr Andrews, Mr Cruickshank, Mr Meldrum and Mr E Smith (a Deputy Secretary at MAFF)
22 YB88/10.24/6.1
23 YB88/11.03/1.1
24 YB88/11/23/1/1
25 YB88/11.29/2.1
26 YB88/7/19/1.1
27 YB88/10.10/2.1
28 YB88/10.24/6.1
29 YB88/11.03/1.1–1.3
30 YB88/10.24/6.1
MAFF officials and Ministers in late November 1988, Sir Richard asked for AFRC and MRC involvement in the Committee, to help ensure it had a full picture of all work in progress.\(^{31}\) Dr Katherine Levy was subsequently appointed as MRC observer, and attended the Committee’s meetings.\(^{32}\) Although an AFRC observer was not officially appointed, Professor Bourne, as Director of the IAH, was in a position to liaise between the Committee and the AFRC because the IAH was an institute within the Research Council. Moreover, according to Dr Tyrrell, on occasions the Committee ‘had a representative’ from the AFRC.\(^{33}\)

2.14 The full committee membership was therefore as follows:

- **Dr David Tyrrell** – Director of the MRC Common Cold Unit (Chairman);
- **Dr William Watson** – Director of the Central Veterinary Laboratory, MAFF;
- **Professor John Bourne** – Director of the Institute for Animal Health;
- **Dr Robert Will** – Consultant Neurologist at the Western General Hospital, Edinburgh;
- **Dr Richard Kimberlin** – ex-Director of the Neuropathogenesis Unit (NPU), Edinburgh, and Head of the Scrapie and Related Diseases Advisory Service (SARDAS), an independent consultancy advising on all transmissible spongiform encephalopathies (TSEs), but mainly BSE.

### Terms of reference

2.15 The Tyrrell Committee (Consultative Committee on Research) was established to advise on TSE research, and its terms of reference were:

To advise the Ministry of Agriculture, Fisheries and Food and Department of Health on research on transmissible spongiform encephalopathies including:

(a) work already in progress or proposed;

(b) any additional work required;

(c) priorities for future relevant research.

In the context of these terms of reference, transmissible spongiform encephalopathies includes those affecting both domestic and wild ruminants and man.\(^{34}\)

2.16 These terms had been amended a number of times. The original draft terms by Mr Alan Lawrence of MAFF’s Animal Health Division were simply:

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\(^{31}\) YB88/11.29/4.1

\(^{32}\) YB89/1.31/4.1

\(^{33}\) T6 p. 25 (Tyrrell)

\(^{34}\) IBD1 tab 4 p. 2. These terms were first proposed by Sir Donald Acheson on 24 November 1988 (YB88/11.24/2.2)
To advise on coordination of the research work which is being carried out in relation to all aspects of Bovine Spongiform Encephalopathy (BSE) and to advise on any further research which may be required, in particular to answer the questions identified by Sir Richard Southwood’s expert Working Party.\textsuperscript{35}

\textbf{2.17} Mr Lawrence’s draft terms related only to BSE. Mr Meldrum, the Chief Veterinary Officer (CVO), first suggested that the terms of reference should be extended to include any animal encephalopathy,\textsuperscript{36} and subsequently changed the terms of reference to include domestic and wild ruminants.\textsuperscript{37} However, Professor Ronald Bell of MAFF’s Chief Scientist’s Group went further and pointed out to Mr Andrews that the draft terms made no reference to humans,\textsuperscript{38} which resulted in another amendment.

\textbf{2.18} The terms of reference gave the Committee an advisory role only, and ensured that the Central Veterinary Laboratory (CVL) and the Veterinary Investigation Service (VIS) would not be formally subject to the coordinating control of an outside working party.\textsuperscript{39}

\textbf{2.19} Mr Meldrum suggested the Committee should report to himself and Sir Donald Acheson.\textsuperscript{40} Sir Donald drafted the final terms, which duly required the Committee to report jointly to MAFF and DH.

\textbf{2.20} On 24 January 1989 Sir Richard Southwood expressed his regret to Mr Andrews that the terms excluded animals other than ruminants and man, and pointed out that a ‘watching brief’ on domestic pets and pigs was also needed.\textsuperscript{41} Indeed, in its report, the Southwood Working Party recommended that the Consultative Committee should consider the possibility of formal monitoring of the health of pigs and domestic animals, and said that:

\textit{We assume that there is no intention to exclude these animals from the Committee’s terms of reference, and believe that the departments concerned will recognise the dangers of excluding these potential infective pathways.}\textsuperscript{42}

\textbf{2.21} In response to Sir Richard’s intervention, Sir Donald said to Mr Andrews that ‘I think we can reassure [Sir Richard] that Dr Tyrrell’s group could consider any animal species that might be relevant, including those such as pigs and domestic pets’.\textsuperscript{43}

\textbf{Interpretation of the remit by the Tyrrell Committee}

\textbf{2.22} During their first meeting, the Committee members agreed that they would interpret the terms of reference widely, and reserved the right to consider research directed at species beyond ruminants and humans.\textsuperscript{44} Dr Tyrrell, however, told the Inquiry that although the Committee was asked to make its advice wide enough to cover all TSEs, it was decided that that would take too long, and that it would be...
more useful to produce quick answers on BSE, which was to be the focus. He thought the Committee’s objective was to review what had happened and what was known about BSE in as wide a context as possible, and then produce a refined list of research that would be useful to MAFF and DH.

2.23 Other members of the Committee also told the Inquiry what they perceived their role to be. Dr Watson said he saw the Committee’s role as initially to review and approve work undertaken by the CVL, and to devise a research programme that was capable of being supported by adequate resources and of being carried out expeditiously. Dr Kimberlin suggested the Committee’s aim was to review the NPU’s and CVL’s BSE research programmes, fill in gaps, ensure the programmes were coherent, and prioritise the list of projects. Professor Bourne thought the Committee needed to promote more epidemiological work, and to establish a stronger science base on the understanding that BSE’s pathogenesis was similar to the existing scrapie model.

The secretariat

2.24 Sir Donald Acheson and Mr Andrews agreed that MAFF and DH should jointly service the Committee. Dr Pickles, a Principal Medical Officer in DH, explained to the Inquiry that the secretariat, comprising herself and Mr John Maslin of MAFF’s Animal Health Division, was responsible for preparing and agreeing meeting agendas and minutes, and collating relevant papers. She also said that she played a key role in drafting the final report, as she wrote most of it, and devised its layout.

2.25 According to Dr Tyrrell, the meetings of the Committee ran smoothly, and were well organised and coordinated, with MAFF and DH tending to take turns in organising them. Dr Kimberlin reiterated this view, and suggested that both the MAFF and DH limbs of the secretariat served the Committee very well.

The first meeting

2.26 The first meeting of the Committee was held on 13 March 1989, at the CVL in Weybridge. All members of the Committee attended, as did Dr Levy (the MRC observer) and other representatives from the CVL and NPU.

2.27 Once its role under the terms of reference was established, the Committee considered the actual and proposed programme of research and development by the CVL and NPU, discussed the research areas listed in the Southwood Report (see paragraphs 2.31ff below), and considered the contribution made by bovine ingredients to pharmaceuticals.
2.28 There were a number of presentations of work in progress and planned. Mr John Wilesmith of the CVL’s Epidemiology Department outlined his modelling studies thus far. Mr Gerald Wells of the CVL reported on the progress of clinical and neuropathological studies, and his colleague, Mr Michael Dawson, gave a progress report on transmission experiments in calves and hamsters and on one about to be set up in pigs. Dr Hugh Fraser of the NPU presented recent data from transmission experiments in mice, and Dr Watson gave a presentation on the maternal transmission study (see paragraphs 2.42ff below).

2.29 Other items on the agenda included a discussion of which centres might assist in research work, and consideration of a paper on the thermal analysis of DNA and RNA in relation to inactivation of infective agents in food.52

2.30 At the end of the meeting it was agreed that Dr Tyrrell, Dr Pickles and Mr Maslin would prepare a draft list of research questions to be considered at the next meeting.53

**Consideration of research identified in the *Southwood Report***

2.31 During the first meeting Dr Pickles told the Committee that although key research areas had been identified in the *Southwood Report*, the Working Party had not had time to go into detail.54 Instead, they listed the following areas of research which they thought the Consultative Committee should consider in detail:

- epidemiological studies – in particular to examine further the role of meat and bone meal as the source of BSE and to determine whether maternal and horizontal transmission could take place;
- transmission studies in a variety of possible host species;
- transmission experiments using muscle and milk;
- the formal monitoring of the health of pigs and domestic pets, with possible transmission studies;
- studies to determine whether the BSE agent was identical in its molecular structure to scrapie, and to determine whether there were single or multiple strains;
- the determination of the nature of the infectious agent;
- studies to determine whether genetic factors were involved in the incidence of the disease in cattle; and
- the surveillance of humans at particular risk, and formal monitoring of CJD cases.55

2.32 The Tyrrell Committee undertook a wide-ranging discussion covering all of these research areas at the meeting. It concluded that in relation to animal epidemiology it ‘felt the need for access to supporting data and a detailed presentation from Mr Wilesmith’ (see paragraphs 2.60–2.61 below). The
epidemiology would then need to be reassessed in the light of the new information. Other questions that would need to be addressed included:

- why there were geographical differences in incidence of the disease;
- whether the scrapie agent had changed and, if so, whether that change was before or after it had crossed the species barrier; and
- whether BSE was already a transmissible disease in cattle and whether it would become endemic in cattle.

**Views on the Southwood Report**

2.33 Although the members of the Committee agreed that the *Southwood Report* was a good document, and was a fair reflection of the state of the BSE epidemic, their evidence suggests that they did not treat it as infallible. Dr Kimberlin, for example, said:

> I think what Southwood did in the short space of time that he had available to him was admirable, and he did the obvious easy things, and that was fine. But it became very clear to some of us anyway that that would not be enough.  

2.34 The following paragraphs consider particular conclusions in the *Southwood Report* that were questioned by Tyrrell Committee members.

**Human health concerns**

2.35 The *Southwood Report* had concluded that:

> From present evidence, it is likely that cattle will prove to be a ‘dead-end host’ for the disease agent and most unlikely that BSE will have any implications for human health. Nevertheless, if our assessments of these likelihoods are incorrect, the implications would be extremely serious.

2.36 The term ‘dead-end host’ has caused some confusion. Volume 4: *The Southwood Working Party, 1988–89* discusses the Working Party’s use of this term. It is apparent that they took it to mean that BSE would not be naturally transmitted between cattle to a degree to make the disease endemic. They did not, however, discount the possibility that maternal transmission could occur. While Tyrrell Committee members did not dispute the ‘dead-end host’ conclusion, Dr Kimberlin referred to the Working Party’s proviso that, if their assumptions were incorrect, the implications for human health would be very serious, and suggested that it weighed heavily on the Tyrrell Committee members’ minds:

> This concern about BSE not being a dead-end infection, that it might possibly become a naturally endemic infection in cattle, not only had tremendous implications to animal health, the future of the epidemic, but it had implications to public health, because if the disease was not going to go away, then it would obviously present much more of a public health problem.
than if it were to go away in due course. So the two things are extremely important, and I think were of major significance to us in focusing on quite a lot of the research programme, to anticipate that.  

2.37 It is apparent that, like the Southwood Working Party, Tyrrell Committee members did not discount the possibility of maternal transmission. At the time Dr Watson felt that the placenta as a route of infection was very likely,\(^59\) and Professor Bourne believed it was assumed that maternal transmission would occur.\(^60\)

2.38 During oral evidence Dr Kimberlin expressed further reservations about the Southwood Report. He referred to the ‘enormous difficulty’ the Southwood Working Party had encountered in making projections of the number of cases of BSE there would be, and said the Tyrrell Committee was aware that the epidemic was going to be bigger than the Southwood Report anticipated. This was because the Southwood Working Party had based their assessment on constant exposure to infective material, while the Tyrrell Committee knew that there was recycling of bovine material in the food chain, so that it was impossible to make accurate predictions of the number of cases. This realisation raised questions as to whether the Southwood recommendations were an adequate response to the public health issues.\(^61\)

2.39 Dr Tyrrell endorsed Dr Kimberlin’s comments, and added that he was concerned about how the Southwood Report had dealt with public health issues in relation to subclinically affected animals.\(^62\) In particular he told us that, in relation to the Report, he:

. . . would have given more emphasis to the probable large numbers of [subclinically] infected cattle which would be by now around, and what we were going to do about them, and something ought to be done, because that is where risks for the human population would mainly arise.\(^63\)

Scrapie as the origin of BSE

2.40 The Southwood Report had concluded that scrapie in sheep was the origin of the BSE epidemic.\(^64\) This conclusion provided an element of reassurance to Tyrrell Committee members that BSE would not transmit to humans, since it was known then that scrapie was not transmissible to humans. However, it did not mean there was no problem. Dr Kimberlin summarised the situation as follows:

There definitely was some good scientific data that said that sometimes, when you cross a species barrier, you create a situation in which the agent will change. You actually exercise or impose a selective pressure, the consequence of which is that the agent can change. So the ethos of scrapie not being transmissible to man that we knew about, and BSE probably
having a scrapie origin, did give grounds for optimism, but by itself, it really was not enough to say that there would be no problem from BSE.65

2.41 The fact that the scrapie agent had infected cattle suggested that it was possible that it could infect humans also. Dr Tyrrell told us that the Committee treated this threat as a ‘distinct possibility and not just a hypothetical idea’.66 Professor Bourne likewise commented that although the assumption that a scrapie agent was the origin of BSE was important, ‘no one working in this field would ever suggest that BSE could not transmit to man’.67

The maternal transmission study

2.42 The request to the Tyrrell Committee in relation to the maternal transmission study was in effect to peer-review this. As such it fell outside its principal task of advising on the needs and priorities in research on TSEs.

Origin of the study

2.43 Prior to the formation of the Southwood Working Party, MAFF had been monitoring over 300 offspring of cows in which BSE had been confirmed, along with the same number of control animals (offspring of cows not infected with BSE). The Working Party believed it was ‘essential that enough offspring of cows known to have had or to have subsequently developed BSE are monitored to enable evidence for or against vertical transmission to be obtained’. They also urged that all necessary resources be used to ensure those animals being monitored were not destroyed before they were old enough to display the disease.68

2.44 MAFF’s existing monitoring was done with the agreement of the owners of the animals, which meant that the study could be invalidated if the owners decided to slaughter the cattle. While there were a number of options to help ensure the study ‘cohort’ remained intact, the purchase of animals was the only method by which MAFF could obtain complete control over the cattle concerned. On 24 January 1989 Mr Lawrence of MAFF distributed a draft submission intended for the Parliamentary Secretary to Mr Meldrum, Dr Watson, and Mr Wilesmith, among others. This recommended the purchase of 600 calves (300 offspring of BSE affected animals and 300 controls) for monitoring, followed by slaughter and histopathological examination at four years of age.69

2.45 On 14 February a joint MAFF and DH meeting was held to discuss the implications of the Southwood Report recommendations. It was agreed that the monitoring of offspring of affected animals was an important point, and it was noted that Mr John MacGregor, the MAFF Minister, had already acknowledged this. MAFF would seek advice from independent experts to ensure that what they were doing was technically sound. Ministers would decide how to proceed once that advice had been received.70
2.46 Dr Watson subsequently had a meeting with Dr Kimberlin and Dr Rosalind Ridley of the MRC on 28 February 1989, and their ‘firm conclusion’ was that it was essential that the study cohort be under the complete control of MAFF. They also thought 400 offspring of affected animals and 400 control animals would be required to allow for mortality throughout the duration of the experiment. Dr Watson sent a note to the Permanent Secretary that day, based on Mr Lawrence’s draft submission, but also informing him of the conclusions drawn at the meeting held that morning, particularly that it was now thought that 800 animals were required to make the study successful.71

2.47 The next day Mr Andrews met senior MAFF officials and agreed that the proposed study should be commissioned, and that the Ministry should purchase the whole study group of 800 cattle. Dr Watson was to coordinate the preparation of a properly costed research proposition that would set out the scientific design of the experiment, and this would be put to the Tyrrell Committee for comments and advice.72

2.48 The research proposal was prepared by Mr Wilesmith, and was considered at a meeting of MAFF officials on 3 March 1989.73 The objective of the study was to examine maternal transmission under natural conditions, and its main features were:

- the comparison of the incidence of BSE in the offspring of animals confirmed as having the disease (cases) with that in the offspring of unaffected animals (controls);
- cases were defined as female offspring of confirmed BSE-affected animals born six months or less before the onset of clinical signs in their dam or after the onset of clinical signs;
- controls were defined as female offspring of cows in affected herds from which the cases were selected, born in the same calving season as the cases. The dam should have survived to at least six years of age without clinical signs of BSE;
- a sample size of 300 cases and 300 controls (it appears that a late decision was made to settle for this number of animals, which was the statistical minimum required for the study to be successful);
- cases and controls would be purchased and maintained on MAFF or other property; and
- a maximum period of seven years for the experiment.74

**The Committee’s consideration of the proposed study**

2.49 Dr Watson presented Mr Wilesmith’s paper to the Tyrrell Committee during its first meeting on 13 March 1989. The minute records that the Committee was told the Minister had already accepted the need for this study,75 so their role was to advise on the most effective way of implementing it.76
2.50 Following its discussion of the proposal, the Committee decided that Dr Tyrrell would write to Mr Andrews outlining its views on the maternal transmission study.\textsuperscript{77} Dr Tyrrell’s letter of 21 March 1989 summarised the main points raised by the Committee:

- the clearest experiment would involve separating the calves from their dam shortly after birth and maintaining them under supervision on Ministry premises;
- ensuring that the study cohort received no suspect feed supplements would involve restricting the study to calves born some time after the ruminant feed ban (ie, long enough to allow any residual meat and bone meal (MBM) in animal feed to be withdrawn or used up beforehand), and could delay the experiment by up to two years;
- the opportunity to use the Agricultural Development and Advisory Service (ADAS) experimental husbandry farms to accommodate the study cohort could be lost if not taken up at once; and
- the proposed experiment would therefore run the risk that the calves had been fed contaminated feed, but would still show whether calves from affected dams had significantly more disease incidence than the herd in general.\textsuperscript{78}

2.51 Mr Wilesmith pointed out later that the Tyrrell Committee’s recommendation that calves should be separated from their dam shortly after birth rested on the false assumption that one could tell whether or not the dam had BSE at that time. In only a few cases would the dam exhibit symptoms prior to calving.\textsuperscript{79}

Discussion

2.52 The maternal transmission study has been criticised by Professor Roy Anderson of the University of Oxford as a ‘badly designed experiment’. In particular, the decision to proceed with a cohort exposed to contaminated feed was the ‘flaw’ in the study.\textsuperscript{80} Members of the Tyrrell Committee agreed that the method employed by the study was not ideal, as indicated in Dr Tyrrell’s letter of 21 March 1989 to Mr Andrews (see above).

2.53 Dr Tyrrell explained to the Inquiry that the central issues for the Committee’s consideration were how urgent it was to do the experiment, and how important it was that it be refined and precise. The main problem was that if the experiment was undertaken quickly, there was a risk that the calves used would have been exposed to contaminated feed, necessitating the use of a large number of animals to obtain a reliable result. If the experiment was delayed until the risk of contaminated feed had passed, it could produce a clear-cut result with fewer animals.\textsuperscript{81}

2.54 The eventual decision to proceed quickly with a large number of animals was based on the need to get information on maternal transmission as soon as possible. In oral evidence Dr Tyrrell said:

\textsuperscript{77} YB89/3.13/3.4
\textsuperscript{78} YB89/3.21/9.1–9.2. ADAS was MAFF’s Agricultural Development and Advisory Service, which has since been privatised
\textsuperscript{79} S91A Wilesmith para. 19
\textsuperscript{80} T4 p. 38 (Anderson)
\textsuperscript{81} T6 pp. 65–6
Although a clean experiment would have been possible if we had waited until all the contaminated feed was out of the way, it would have meant the answer coming much later. If the answer had been that there was a lot of maternal transmission, it would be better to have that information sooner rather than later.  

2.55 The Tyrrell Committee appears to have proceeded on the assumption that if a significantly greater number of cattle born of BSE-infected dams developed BSE than the controls, this would demonstrate that maternal transmission had occurred. They overlooked the fact that an alternative explanation for such a disparity would be a genetic susceptibility to infection from feed inherited by the calves of the BSE dams. This was the most significant weakness in the design of the experiment.

2.56 Whatever the weaknesses in design, however, the Tyrrell Committee rightly concluded that while the experiment was not ideal, it was worth doing. With hindsight, it was as well that the experiment proceeded without delay. Had the experiment been delayed until feed was presumed to be free of ruminant protein, that presumption would subsequently have been confounded when it became apparent that cattle feed had continued to be contaminated by ruminant protein.

2.57 Volume 2: Science can be consulted for an account of the implementation of the maternal transmission experiment, and the results obtained.

The second meeting

2.58 The Tyrrell Committee met for the second time on 11 April 1989 at the NPU in Edinburgh.

2.59 At this meeting the Committee:

- discussed an epidemiology paper prepared by Mr Wilesmith;
- considered a paper on CJD monitoring; and
- considered BSE and medicinal products in more detail.

There was also a presentation by Dr James Hope on the work of the NPU, and the Committee considered the draft research plan prepared by Dr Pickles.

Epidemiology

2.60 At its first meeting the Committee had decided that it needed access to accurate and up-to-date epidemiological data to help it identify relevant areas of research.
Mr Wilesmith’s epidemiology paper

2.61 Accordingly, during the Committee’s second meeting, Dr Watson introduced an epidemiology paper prepared by Mr Wilesmith. The paper was prepared on 28 March 1989, and:

- provided an updated summary of the number of reported cases and their geographical distribution;
- gave information on general epidemiological features including herd type, within-herd incidence, age- and sex-specific incidence, and breed incidence;
- concluded that a constant incidence of 350–400 per month could be expected until 1993, with a reduction thereafter until the disease died out (assuming that maternal and horizontal transmission did not occur); and
- stated that if maternal transmission did occur, the exact impact on the course of the disease would be impossible to assess, but it would not be enough to sustain BSE in the national cattle population.84

The Committee’s reaction

2.62 Dr Watson expressed some doubts about the conclusion that a plateau had been reached in the number of cases that could be expected each month, because the number of reported cases was still increasing. He suggested that the recycling of bovine material in the feed chain might be affecting the incidence of the disease.85

2.63 The Committee members were concerned that they had yet to see the raw data on which the current epidemiological assessment had been based. Dr Watson undertook to obtain the information required from Mr Wilesmith.86

Provision of further data

2.64 Two days after the meeting Mr Wilesmith wrote to Dr Tyrrell, offering to provide more details of the results of the epidemiological studies, and proposing that it might be more helpful to meet in person to discuss the data.87 A meeting subsequently took place on 20 April, and the epidemiology of BSE was discussed in detail again at the third meeting on 8 May (see paragraphs 2.74–2.77 below).88

Monitoring of CJD

2.65 The Southwood Working Party had thought it a reasonable assumption that if BSE was transmitted to humans, it would closely resemble CJD. It therefore recommended that monitoring of cases of CJD should take place, and identified ‘the surveillance of humans at particular “risk” and formal monitoring of CJD cases, particularly in occupational groups exposed to bovine tissues’, as an area of research that should be addressed by the Committee.89
2.66 At its first meeting, the Committee had decided that a paper on the monitoring of CJD would be needed, and that Dr Will should prepare it.\textsuperscript{90} During the Committee’s second meeting Dr Will introduced his paper entitled ‘Proposal for the Monitoring of Creutzfeldt-Jakob Disease’. The research proposal’s main features were:

- the collection and validation of diagnosis in all death certificates identifying CJD in England and Wales between 1985 and 1989, and in Scotland and Northern Ireland between 1980 and 1989;
- the notification of all newly certified cases of CJD by the Office of Population Censuses and Surveys (OPCS) or its equivalent in Scotland and Northern Ireland;
- all neurologists, neuropathologists and neurophysiologists would be asked to report all suspect CJD cases, and epidemiological information would be obtained by standard questionnaire; and
- because of the potentially long incubation time, monitoring of CJD would be necessary for at least a decade.\textsuperscript{91}

The Committee’s views on the proposals

2.67 The Committee noted that the Southwood Report’s assumption – that if BSE was passed on to humans it would be like typical CJD – might not be the case. The important questions in monitoring CJD were the accuracy of the diagnoses made and how they could be confirmed. A monitoring system would have to be maintained for longer than 10 to 20 years,\textsuperscript{92} which meant that it had to be simple to run and not require changing while in progress.\textsuperscript{93}

2.68 The Committee approved the proposals in Dr Will’s paper.\textsuperscript{94} Volume. 8: Variant CJD should be consulted for further discussion of CJD monitoring.

BSE and medicinal products

2.69 The Southwood Working Party had noted that there was a remote risk that ‘medicinal products for injection or surgical implantation which are prepared from bovine tissues, or which utilise bovine serum albumin or similar agents in their manufacture’ could transmit BSE to humans. The Working Party recommended that the attention of the Licensing Authority, the Committee on Safety of Medicines (CSM), the Committee on Dental and Surgical Materials and the Veterinary Products Committee be drawn to BSE so they could take appropriate action.\textsuperscript{95}

2.70 At its second meeting the Tyrrell Committee was presented with a paper that outlined research questions of immediate interest to the DH Medicines Division and the pharmaceutical industry:

\textsuperscript{90} YB89/3.13/3.4
\textsuperscript{91} ‘Proposal for the Monitoring of Creutzfeldt-Jakob Disease’ (YB89/05.00/5.1)
\textsuperscript{92} Dr Watson’s paper notes that the incubation period of CJD ranges from 18 months to 23 years in iatrogenic cases, and may extend to decades in kuru (a human spongiform encephalopathy occurring in New Guinea)
\textsuperscript{93} YB89/4.11/2.2
\textsuperscript{94} YB89/4.11/2.2
\textsuperscript{95} IBD1 tab 2 pp. 14 and 18
– can freedom from BSE-contamination be demonstrated in existing stocks of products at theoretical risk (many years supply of some vaccines, for example)?

– for what processes/products are the risks sufficiently high to be worth subjecting to experimental test, eg with mouse inoculation?

– how can BSE-free herds in the UK be demonstrated and material collected from these herds?

– what overseas sources of bovine material are acceptable?

– are there any products for which the risk-benefit is now unacceptable [considered for the bovine insulins and heparin, but further action not thought appropriate at present]?

– should there be similar concern about other animal species used in pharmaceutical manufacture? 96

2.71 Other papers outlining potential problems and action taken to date were appended, including:

• a list of medicinal products for human use that contained bovine ingredients or used bovine ingredients in their preparation;

• a position statement by the CSM, saying that the risk to humans of infection via medicinal products was remote, but that guidelines on good manufacturing practice had been produced as a safety measure;

• a copy of the guidelines and letter sent to all manufacturers of human and veterinary medicines; and

• a question and answer briefing prepared by DH in response to the Southwood Report, indicating the line taken up to then.

The Committee’s response

2.72 Dr Tyrrell explained that the papers were mainly for the information of the Committee, but still raised questions relevant to research needs. Further, although the CSM’s position statement correctly claimed that the risks from BSE were small, there was still a need to conduct research.97 Dr Kimberlin told the Inquiry that although the words ‘remote’ and ‘theoretical’ were used, they were not taken to mean that no work needed to be done in this area.98

2.73 Dr Will pointed out to the Committee that the papers did not cover dental products, which might be of concern given that transmission of kuru could have involved gum abrasions.99
The third meeting

2.74 The third and final meeting of the Tyrrell Committee was held on 8 May 1989. Again, all members of the Committee were present. In addition to discussing the latest summary of epidemiological findings, the Committee spent the bulk of its time considering in detail the format and the draft of the Interim Report circulated prior to the meeting.\(^{100}\)

2.75 Dr Tyrrell reported that he had met Mr Wilesmith on 20 April to discuss the epidemiological data. He had also spoken to Professor Roy Anderson, who felt that most of the conclusions on BSE had still not been rigorously proved by the epidemiology thus far. For example, it was important to obtain additional data on age distribution.\(^{101}\)

2.76 For this third meeting the CVL had provided an updated ‘Summary of Epidemiological Findings’ for the Committee’s consideration. This summary reported that while there were difficulties in ascertaining the true incidence of BSE, there was some evidence that it had reached its maximum. In particular, data on Guernsey, which had a ‘perfect reporting rate’, showed an ‘underlying, relatively constant incidence’.\(^{102}\) Dr Tyrrell noted that although data on Guernsey helped explain the CVL’s view that there should be a plateau of cases in the rest of the UK, too much reliance should not be placed on such limited information.\(^{103}\) The Committee agreed that still more data was necessary to enable a much more detailed analysis of the epidemiology.\(^{104}\)

2.77 As regards discussion of the draft Interim Report, details of amendments were not recorded in the minutes. However, a ‘clean version’ incorporating the amendments was forwarded by Dr Pickles to Dr Tyrrell the following day (see paragraph 3.15 below). It was agreed that once finalised by the end of May, the Report would be submitted to DH and MAFF, with a covering letter from the Chairman seeking guidance on the future of the Committee.\(^{105}\)

\(^{100}\) YB89/4.27/1.1–1.22 (draft report); YB89/5.8/2.1–2.3 (minutes of meeting)
\(^{101}\) YB89/5.8/2.2
\(^{102}\) YB89/5.00/8.3
\(^{103}\) YB89/5.08/2.2
\(^{104}\) YB89/5.08/2.2
\(^{105}\) YB89/5.08/2.3