7. Conclusions drawn from the scientific response to BSE

Summary of main conclusions

7.1 We have given short summaries at the end of Chapter 2 and 3 respectively of our conclusions on the knowledge of TSEs available in 1986 and the scientific investigation thereafter into the nature and cause of BSE. Summaries of our views on the link between BSE and CJD, and on questions of diagnosis and therapy, are at the end of Chapter 4 and 5.

7.2 In this chapter we identify what we believe to be the main conclusions emerging from scientific study to date, and we examine whether there were shortcomings in the research that was put in place in response to BSE. We then turn to look at the lessons for scientific study and research that may be learnt from the BSE story, in relation to research management and coordination, animal disease surveillance, and the investigation and management of actual or potential zoonoses.

7.3 The following main conclusions can be drawn from scientific study of the BSE epidemic and the emergence of vCJD:

i. **The vector responsible for the epidemic of BSE in cattle was MBM (Chapter 3, paragraphs 3.11–3.26).**
   The spread of BSE in cattle to the point where it became an epidemic came about from the use of meat and bone meal in cattle feed. The MBM in question was infective because it had been made by rendering infective offal from cattle suffering from or merely incubating the disease. As little as a gram of this material could cause death if ingested by other cattle. It was so infective that accidental contamination of cattle feed with pig or poultry feed containing MBM was a significant factor which continued to spread BSE after the ban on the use of MBM in cattle feed. Apart from MBM in feed, transmission from mother to calf is likely to have played a part. We cannot yet say whether contamination of pastures played a part. The suggestion has been made that the BSE agent may have been spread in the early stages in hormones or other bovine material used in veterinary preparations. This possibility cannot be discounted. But the overwhelming vector of the epidemic was MBM in cattle feed.

ii. **The unmodified scrapie agents were not the agents responsible for BSE (paragraphs 3.48–3.61).**
   While it was reasonable in February 1989 to accept the hypothesis that the cases of BSE being reported had come about through the rendering of carcasses of sheep infected with extant strains of scrapie established in the national flock, this is no longer plausible. We think it likely that the passive surveillance system failed to detect several cycles of BSE in the South West of England in the 1970s and early 1980s. Each cycle was
followed by more extensive contamination of MBM. Much of the recycling could not be detected because tissues from animals incubating the disease but not showing signs were involved; but it is likely that there were isolated animals which did develop signs and were slaughtered or died of the disease. BSE was unknown at the time and it seems possible that the disease in such cattle, sometimes called ‘downer’ cattle, might have been ascribed to known disorders such as hypomagnesaemia. These early cycles began because a novel TSE agent originated in the early 1970s. The cause of this novel agent is likely to have been a new prion mutation in cattle, or possibly sheep. Moreover, other mammalian species whose carcass waste was included in MBM cannot be excluded. It is conceivable that the conversion of normal prion protein into its infective form was initiated not by a gene mutation, but by an environmental agent, such as a toxic chemical, although this has not yet been achieved experimentally. It is now not possible to be sure which of the hypotheses as to the origin of the novel agent is correct. Current knowledge suggests that the original agent was not the unmodified scrapie agent or agents. We have also noted a number of pointers which could have led to the conclusion by mid-1990, and certainly well before 20 March 1996, that the agent fuelling the BSE epidemic was not then (if it ever had been) the unmodified scrapie agent or agents.


It is a common misconception that reduction in temperature or a failure to prescribe minimum holding times in the rendering of carcass waste led to failure of inactivation of the scrapie agent and transmission across the species barrier to cattle. Changes in the rendering process in the late 1970s and early 1980s, namely the switch from batch to continuous processing and the abandonment of solvent extraction of tallow, might have led to reduction in inactivation of the agent in MBM, but it is now known that the processes used previously were also incapable of completely inactivating TSE agents. No commercial rendering procedure has been designed capable of completely inactivating BSE in MBM before or since.

iv. Confirmation of the central role of prion protein (paragraphs 2.172, 3.9, 5.47).

All evidence points to the specific association of an abnormal form of the prion protein and TSEs. In its normal shape, the prion protein (PrPC) does not cause harm. In its abnormal shape (signified by PrPSC – a generic term for the agents causing TSEs) it is resistant to the normal cellular processes of degradation. Contact between normally shaped and abnormally shaped proteins induces the normal to convert to the abnormal. This leads to a build up of the abnormal form of the protein, which accumulates in and eventually causes the death of nerve cells. Nerve cells are particularly susceptible to PrPSC because they cannot regenerate. The presence of PrPSC can be demonstrated in the brain and spinal cord of all humans and animals affected with TSEs. Incubation in experimental animals it has been shown recently that high levels of prion replication can occur unrecognised and without causing a TSE within the lifetime of the animal. Nonetheless, when brain material from such subclinical cases is inoculated into another species, it may cause disease after a comparatively short incubation period. Thus, definitions of the species barrier based on clinical end-points require reassessment. Hill, A.F., Jorrier, S., Lineham, J., Debruslais, M., Lantos, P. and Collinge, J. (2000) Species-barrier-independent prion replication in apparently resistant species, Proceedings of the National Academy of Sciences, 97, 10248–53
times in experimental animals correlate with the infective dose of the agent, and these times are increased by treatment with agents (β-sheet breaker peptides) which reverse the conformational change leading to PrPSc (paragraph 5.47). These observations virtually eliminate other hypotheses as to the direct cause of TSEs, such as autoimmune disease of the CNS, because those hypotheses do not incriminate the prion protein. In both scrapie and vCJD, susceptibility and resistance to disease is associated with polymorphisms within the prion protein gene (though no such susceptibility factors have yet been identified for BSE). It remains possible that environmental factors, including toxic chemicals, may additionally be implicated in susceptibility to prion disease (paragraph 3.83).

v. **BSE is caused by a single strain of agent (paragraphs 3.56, 3.240–2).** Strain-typing in mice has shown that all sources of the BSE agent so far examined produce the same lesion profile and incubation times in experimental mice. The same strain has been identified in cats, which have developed FSE since 1990, and in exotic ungulates and carnivores from zoological parks.

vi. **Variant CJD is caused by the BSE agent (paragraphs 4.6–4.15).** Strain-typing studies in mice reveal that the disease patterns produced by the agents causing BSE and vCJD are identical. The glycosylation patterns of the prion protein associated with each condition are also identical and different from other TSE strains. In transgenic mice in which the mouse prion gene has been replaced by the bovine prion gene, inoculation with the BSE agent from cattle brain produces the same disease pattern and incubation period as agent derived from patients with vCJD. Following inoculation with the scrapie agent, the incubation period and disease patterns in the transgenic mice are markedly different from those produced by BSE and vCJD. In the absence of any other plausible factor, the evidence that BSE caused vCJD is so strong that all other hypotheses are now excluded.

7.4 Some of the research on which the above summary is based did not produce results until late in the BSE epidemic, and some, such as the strain-typing results (1997) and the studies using mice transgenic for the bovine prion protein gene (1999), did not become apparent until well after the emergence of vCJD in March 1996.

**Assessment of research in response to BSE**

7.5 A substantial body of research was undertaken in response to the emergence and identification of BSE. We discuss in vol. 3: *The Early Years, 1986–88* our concerns about the delay in involving the NPU. We were also concerned that there were other specific areas in which research should have made a more valuable contribution than it did – whether because relevant research was not carried out at all before March 1996, or because it was delayed, or because there were problems with the design of individual experiments. However, when we examined those specific areas, we were satisfied that it was not appropriate to criticise individuals. We discuss the reasons why we reached this view in relation to a number of projects in
this section. We discuss a number of other specific items of research in other relevant volumes of the Report, and we identify them below.

7.6 We emphasise that we have not undertaken a critical examination of the whole programme of research carried out by MAFF and the Research Councils. Some aspects of the research programme might have been approached or prioritised differently and, with hindsight, other approaches might have produced better or quicker answers – which in turn might have assisted in risk assessment and policy-making. However, once again, we do not suggest that this was a matter for individual criticism.

7.7 Much of the research commissioned during the period covered by our terms of reference was timely and of a high quality, and in this regard the work of the NPU, of the CJD Surveillance Unit, and of the Prion Diseases Group at St Mary’s Hospital in London deserves specific commendation.

7.8 We also think it important to note that we do not suggest that a different approach to the research programme would have led to the earlier recognition of vCJD.

The origin of BSE – transmission of scrapie to cattle

7.9 The early epidemiology gave rise to the belief that the cause of BSE was the transmission of conventional scrapie agent(s) from sheep to cattle. It was thought that each new case of BSE was an index case, and that changes in the rendering process had enabled this to occur. The belief that BSE was caused by conventional scrapie agent(s) meant that it was thought likely to present the same risk to humans as scrapie. Reassurance was derived from the fact that scrapie-infected sheep had long been eaten without apparently causing CJD. In recommending in June 1988 that MBM should be tested on cattle and laboratory animals, the Southwood Working Party recognised the importance of validating the hypothesis upon which the assessment that BSE posed only a remote risk to humans was based.

7.10 Research, and development of knowledge (eg, the wide host range of BSE, the occurrence of a TSE in domestic cats and transmission of BSE to a pig), progressively cast doubt on the theory that BSE was caused by conventional scrapie agent(s), or that it would behave in the same way as conventional scrapie, but the uncertainty was not immediately appreciated.

7.11 One experiment that would have offered some insight into the origin of BSE was attempted transmission of conventional scrapie agent(s) to cattle. This was recognised by Mr Bradley in his ‘logical approach to research’ paper, written at the end of 1987, which included as item 6: ‘Demonstrate transmissibility of sheep scrapie to cattle.’ Yet such research was not initiated until 1997 and 1998 (projects SE1942 and SE1941), outside our terms of reference. Why was it not done earlier?

7.12 Consideration was given to such an experiment at various stages during the development of the R&D programme – Dr MacOwan and Mr Wells both described this consideration in detail in written statements to us.\(^\text{982}\) We note that the Tyrrell Committee did not recommend such an experiment in June 1989; that the minutes

\(^{982}\) S100B MacOwan paras 1–10; S65A Wells paras 63–65
of the March 1991 SEAC meeting stated that the transmission of natural scrapie to cattle by the oral route would not be pursued;\textsuperscript{983} and that at a meeting between MAFF’s Animal Health Policy Division and the Chief Scientist’s Group on 9 February 1993, the policy viewpoint was that the study was of academic interest only, had not been recommended by the \textit{Southwood Report} or the Tyrrell Committee, and would not lead to new policy initiatives.\textsuperscript{984} The proposal was rejected and it was stated that it would not be considered further.

7.13 We describe in Chapter 3 some of the reasons why the experiment was not pursued. Dr Tyrrell provided information explaining why the Tyrrell Committee did not recommend such an experiment,\textsuperscript{985} and Mr Bradley also outlined some of the reasons in a written statement to us:

\begin{quote}
24. The control measures which were put in place operated to cut off the source of infection. In practical terms it did not matter that policy advisers did not know where the disease had come from because the control measures would still be effective in eradicating the disease in cattle. Further, the results of such an experiment would not be available for a number of years. By the time they would have been available, the results would not have altered policy in a significant way because the control measures put in place by 1990 took account of the need to protect all species from the BSE agent in cattle, and all ruminants from any TSE agent (including scrapie agent) \textit{via} feed.

25. Notwithstanding the points made above, there remains the question of whether the experiment should have been carried out and if so when. This is a complicated question to answer. I have had the benefit of reading Dr MacOwan’s letter dated 22nd July, 1998\textsuperscript{986} to the Inquiry on this matter and am broadly in agreement with the points which he makes. In particular, it should be borne in mind that similar research had been and was being carried out in the United States and there was therefore a question of whether the resources could be better directed into other experiments. Other questions surrounded the objective and design of any experiment.

26. The hypothesis that BSE was derived from scrapie would only be supported by an experiment which demonstrated that when scrapie was transmitted to cattle the disease which developed in cattle was the same as BSE. Any other result would be inconclusive. However, there are a large number of different strains of scrapie and it was possible that BSE was caused by one particular strain. It is therefore arguable that it would have been necessary to attempt to transmit every strain of scrapie to cattle to properly test the hypothesis. This would have been extremely difficult as well as expensive, especially as the agents would have to be cloned in sufficient quantity for a cattle challenge. Alternatively, pooled sheep brains could have been used but this caused a difficulty because it was not known if BSE existed in sheep. If pooled sheep brains were used (thus aiming to include all the strains that occurred in the UK including possibly the BSE precursor strain or BSE strain itself), it would not be known whether BSE was present or not unless additional strain typing studies were also carried out. Further, it would not establish whether the BSE precursor strain had
\end{quote}
been naturally present in sheep historically (ie, before BSE) or whether it had been introduced into sheep via MBM and feed during the BSE era. 987

7.14 It seemed to us that the principal reasons were:

- a scrapie to cattle experiment had been done in the US;
- the exercise was regarded as academic – although the origin of disease in cattle was of great scientific interest, it was not of fundamental importance to the animal and public health consequences of BSE;
- other information about the disease, such as the possible influence of genetic makeup on the susceptibility of cattle, was not known and needed to be ascertained before such an experiment was attempted;
- a large and expensive experiment was needed because there were 20 different known strains of scrapie that would have required inoculation;
- other experiments were being conducted on cattle at the CVL and would either have to be abandoned or new accommodation would be required; and
- the results would be hard to interpret and might well be inconclusive.

7.15 Some of these reasons were less persuasive than others. The US research showed that it was possible to produce a scrapie-like disease in cattle inoculated with scrapie, but the resulting TSE differed in many respects from BSE. This was not a satisfactory substitute for the scrapie-into-cattle experiment proposed in the UK.

7.16 On the other hand, there were clearly difficulties with the design of the experiment: inoculation of each of the 20 known different scrapie strains would have been difficult and expensive, and, for the reasons Mr Bradley explained, using pooled scrapie would not have provided a conclusive answer.

7.17 It is clear that other matters were regarded as being of more direct relevance and thus of immediate value. This study, by contrast, was regarded as being of academic interest – policy had to be determined before the results would be available in any event – and we can understand why it was not immediately initiated. The general public, however, did not consider the question to be academic. Nor, indeed, did scientists such as Sir Donald Acheson.

7.18 Discussion of whether attempts should be made to transmit scrapie to cattle began again in 1993. Dr MacOwan described in a written statement the progress of those discussions, leading ultimately to the initiation of the work. 988 We note that in 1995, in his report of the Review of MAFF-funded research into TSEs, Dr Kimberlin identified this as an ‘underemphasised’ area of research. 989 He said that the origin of BSE was the one major question about the disease that had not been addressed scientifically, and that the scientific community was becoming increasingly critical of the gap in knowledge, particularly in the light of two recent findings: (a) the BSE agent was different from scrapie; and (b) the experimental transmissions of scrapie to cattle in the USA produced a disease that did not
resemble BSE. Dr Kimberlin argued that the fact that a bovine origin of BSE was quite plausible undermined considerably the risk assessment for other species of food animals. In his view it was essential to attempt an oral transmission of UK scrapie to cattle.

7.19 We share Dr Kimberlin’s view, but accept that in doing so we are applying hindsight.

**Maternal transmission**

7.20 We describe in Chapter 3 research carried out to ascertain whether maternal and lateral transmission played a part in the spread of BSE. It was believed that scrapie was maintained in the UK sheep flock by a combination of vertical (maternal) and lateral transmission (although the emergence of BSE raised the question of whether MBM might play a role in transmitting scrapie). We discuss below the difficulties in obtaining funding for the maternal transmission study in cattle. There were also problems with the design of the experiment. In particular, it was recognised that both case and control animals might have been exposed to infected feed. MAFF officials and the Tyrrell Committee gave consideration to this problem. However, it was thought preferable to proceed with the experiment, which was designed to show whether calves then available from affected cows had a significantly greater incidence of disease than contemporary controls, rather than to delay it by a further two years in order to use only animals that had definitely not been exposed to infected feed. Dr Tyrrell explained this balancing process in his letter to Mr Andrews on 21 March 1989. We discussed it with Mr Bradley when he gave oral evidence:

**Mr Bradley:** We were under the clear scientific knowledge that results about maternal transmission were highly important in the control of BSE. The stimulation from the Southwood Committee and subsequently by the Tyrrell Committee reinforced that, so there was a time – the quicker we could get the study underway, the quicker we would know the result. But the earlier we started it, the greater the risk we ran with the feed ban problem. . . .

And so, obviously, an ideal situation as I suggested previously would be to start with offspring from cattle which were removed essentially at birth and reared independently, if that was what we meant by maternal transmission. Actually John Wilesmith defined it as in utero or in the immediate post natal period. How long is this? Let us say until the calf is taken from the cow which, in the case of the dairy cow, would have been 24 or 48 hours. In that case it would almost eliminate a source from feed, because they would not be eating a concentrate at that age. That would be ideal. Then it would mean every calf you purchased at that particular point was only a few days old. Then you had to get 600 of them that satisfied the conditions. This would have taken longer, so you would have delayed the end result.

**Lord Phillips:** It would have been very difficult, would it not, to get your 300 calves of BSE infected mothers? Unless you could find a cow which was infected with BSE about to [calve], you would not know?
Mr Bradley: Exactly, so all the practical difficulties are all weighed in the balance. You asked the question, was it ideal; scientifically it was not, and I explained why, practically it was as ideal as we could get it.990

7.21 This pragmatic decision seemed to us reasonable, given that all were agreed on the urgency of starting the study. It was better to obtain some, albeit imperfect, information than to wait a further two years.

7.22 As discussed in Chapter 3, the results of the experiment were finally obtained in 1996, and showed that BSE occurred in 14 per cent of the offspring of affected dams and in 4.3 per cent of the controls. With hindsight, as we note earlier, it appears that the increased risk for offspring of BSE-affected dams would have been apparent several years before the completion of the study, had emerging results been monitored and analysed by a Data Monitoring Committee. We consider in Chapter 3 the results of the 1993 case control study, which investigated maternal and lateral transmission.

7.23 When the results were obtained, there was a difficulty in analysing them. Although the experiment had been designed to be large enough to give an answer despite the possible exposure of the animals to infected feed, it was not possible to establish with certainty whether the increased incidence in offspring of affected dams was the result of maternal transmission of BSE, or maternal transmission of genetic susceptibility to BSE.

7.24 We explain in Chapter 3 that a complex genetic association study using multiple polymorphic genetic markers would have been needed to determine if there were significant differences in genotype between subjects and controls. Such a study would not have been possible in 1989. However, the consequence is that uncertainty remains about the interpretation of the results of the study.

Risk of BSE becoming endemic in sheep

7.25 We discuss in vol. 11: Scientists after Southwood the consideration of research into the risk of BSE transmitting to, and becoming endemic in, sheep. The need for such research was discussed on a number of occasions. We identify in volume 11 some of the experimental and practical difficulties in carrying it out, and indicate the reasons why it was not pursued until relatively late in the day. The question whether BSE is endemic in sheep is perhaps now the most important unanswered question about the epidemic. With hindsight it is plain that it would have been desirable to set about answering this question when it was first asked.

Minimum oral infective dose – attack rate study

7.26 We discuss in detail in Chapter 3 the widespread misconception about the amount of infective material necessary to transmit infection by the oral route. The implications of this misconception feature in volumes 5 and 6, on Animal and Human Health (1989–96) respectively.
7.27 The question of the minimum oral infective dose of the BSE agent was not addressed experimentally until January 1992, and then only indirectly as part of the attack rate study. As we indicate, the implications of experiments carried out at the NPU, in which BSE had by November 1990 been successfully transmitted to a sheep by oral administration of 0.5 g of brain material, had apparently not been appreciated by that stage. Nor had the epidemiological pointers been appreciated: cattle feed contained generally no more than 5 per cent MBM, not all of which would have been made from infective material; and compound feed, with the exception of that for young calves from dairy herds, comprised only part of cattle rations.

7.28 Once more, Mr Bradley had identified the need to demonstrate ‘minimal infective doses’ for cattle, primates and laboratory animals in his ‘logical approach’ paper in December 1987. Why were experiments not set in hand to do so? The Tyrrell Committee did not recommend either epidemiological investigations into the minimum oral infective dose, or an attack rate experiment to establish this. They explained to us why they had not done so:

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. For example, calculations of the exposure of cattle to sheep scrapie required estimates of the prevalence of infection in sheep (which was unknown), the effects of different rendering processes on infectivity (which was unknown) and the extent of the species barrier between sheep and cattle (which was unknown). Furthermore, the extent of the species barrier would depend on the individual strains of agent and variations in the PrP genotypes in sheep and cattle. Similarly, calculations of the exposure of cattle to recycled BSE, that is BSE through meat and bone meal in a cow’s rations would require estimates of the prevalence of BSE infection in cattle, the infectivity titres of BSE in different tissues at different times after infection and the effects of rendering processes. These are the difficulties, which led the members of the Committee not to recommend specifically the first of the two suggested possible approaches. However, some of these matters were the subject of recommendations for research made by the Report, albeit primarily for other purposes which were judged to be of greater potential value. For example, paragraph C1(e) of the Report dealt with bio-assays of BSE agent in tissues of infected cattle and paragraph C3 of the Report recommended, and gave two stars to, research into different rendering processes so that knowledge could be acquired about inactivating infectious agents.
The Committee could also have recommended that an attack rate experiment be undertaken. The members of the Committee believed that such an experiment belonged to a later generation of studies in cattle which would only become possible when information had been obtained on the variation of bovine genetic factors and their effect on susceptibility to BSE infection. To do otherwise might lead to an experiment being performed using animals which were found to be genetically not susceptible to the agent. 991

7.29 As regards the last point, Dr Watson told us that he learnt on 26 July 1989 that BSE had recently been successfully transmitted from cattle to cattle by experimental means at the CVL for the first time. 992 He continued:

This meant that the species in which the disease was occurring could be infected experimentally and these findings opened the way to major experiments on dose rate and pathogenesis studies in this species.

7.30 We agree that this study did not belong in the first generation of experiments but had to await the outcome of other work. Perhaps with prompting from policymakers to whom this knowledge would have been useful, work might have begun earlier. With hindsight it is regrettable that other indications about the small quantity of physical material capable of transmitting infection were not appreciated.

7.31 The attack rate study provided experimental evidence in 1994 that as little as 1 gram of infective BSE brain material given orally could cause disease. It is now known that this quantity is sufficient to cause disease in 70 per cent of animals. This fact has implications that are serious and wide-ranging. They feature in many different aspects of the story, for example, in relation to the role of cross-contamination of cattle feed in infecting cattle born after the ruminant feed ban (BABs) (see vol. 5: Animal Health, 1989–96); the related question of the importance of developing an ELISA test to detect contamination of feed; and the need for strict enforcement of the SBO Regulations (see volumes 5 and 6, on Animal and Human Health respectively).

**Sensitivity of the mouse bioassay**

7.32 The need to establish the infectivity of different organs, tissues and body fluids was identified at an early stage. It, too, featured in Mr Bradley’s ‘logical approach to research’ paper. We describe in Chapter 3 the results of the NPU tissue infectivity study and of the CVL pathogenesis study. Following the successful transmission of BSE to mice, it was decided that a mouse bioassay should be used. The use of calves was regarded, in our view fairly, as prohibitively expensive. Corresponding studies into scrapie infectivity carried out by Hadlow had successfully used mice.

7.33 However, as we describe in Chapter 3, the preliminary results of the NPU studies, published in 1992, showed that tissues which were known to be infective in scrapie-infected sheep, particularly spleen, failed to produce disease in the mouse strain most susceptible to BSE infection. By the time of the eighth BSE R&D meeting between the CVL and NPU in October 1991, spleen had failed to produce disease after 810 days. This and other hitherto negative results raised the question of whether the mouse assay was sufficiently sensitive to detect BSE infectivity, and

991 S488A Tyrrell paras 98–100
992 S70A Watson para. 91
it was suggested that spleen should be inoculated into calves. Others, for example Dr Dealler and Professor Lacey, raised concerns about the sensitivity of the mouse assay as early as April 1991. 993

7.34 The spleen proposal was considered at the beginning of 1992. At a meeting on 10 January between staff of the CSG, MAFF’s Animal Health Division (AHD) and the CVL to decide on the allocation of some available research funds (£280,000), it was agreed that inoculation of spleen from a clinical case into calves was a priority. An experiment was to be designed and costed, and Mr Bradley was to produce a paper for MAFF colleagues on whether or not it was scientifically desirable to validate the mouse assay for BSE by comparing the sensitivity of calves and mice. 994 Mr Robert Lowson of AHD and Mr Bradley later spoke to the CVO and it was agreed that BSE should be inoculated into calves as a priority. 995

Mr Wells told us:

At the seventh CVL/NPU R&D meeting on 23rd April, 1991 (YB91/4.23/1.1) it was noted that the absence of detected infectivity in spleens to date from field cases of BSE was an unexpected result. One of the issues this raised was whether the mouse assay system was sufficiently sensitive. A study was therefore initiated in April 1992, to determine the extent of the under-estimation of infectivity titre in BSE tissues when titrated across a species barrier in mice. The study is incomplete, but has demonstrated so far that there is at least a thousand fold difference in the sensitivity of the bioassay in mice and cattle. That is, a thousand fold greater sensitivity of detection of the BSE agent by bioassay in cattle. 996

7.35 A progress report on the experiment produced by Mr Wells in April 1993 stated that the mice had actually been inoculated in January 1993. 997

7.36 With hindsight it is unfortunate that the use of mice to assay BSE infectivity in different tissues did not prove as successful as their use to assay scrapie infectivity. This has necessitated further work in calves in order to provide more definitive answers – these are needed for a full range of tissues, including milk (to test for maternal transmission), faeces and urine (to test for lateral transmission).

**Post-mortem test for BSE in cattle**

7.37 We note in vol. 11: *Scientists after Southwood* that there was a practical need for a simple post-mortem test for BSE, but that this did not feature in the report of the Tyrrell Committee. Such a test would have been invaluable in screening to establish the extent of subclinical cases of BSE, and even for screening meat. We discuss below the possibility that a research supremo or coordinating body might have assisted in this area. The work of Dr Narang and the appraisal of his touch test to detect BSE infectivity in cattle is considered in volume 11.
Test for ruminant protein in feed – ELISA test

7.38 We also note in volume 11 that the need for a test in order to identify the presence of ruminant protein in feed was not drawn to the attention of the Tyrrell Committee and did not feature in their report. Accordingly it did not receive priority treatment. One approach to this – the development of an ELISA test for detection of ruminant protein in feed – is discussed fully in vol. 5: Animal Health, 1989–96.

Uses of bovine material

7.39 The only three-star recommendation of the Tyrrell Committee that was not set in hand immediately was A1d, namely that consideration should be given to commissioning a study into the fate of bovine (and ovine) tissues and products that could lead to infection being spread by as-yet-unrecognised routes. It seemed to us that one reason why it fell through the cracks was that it was not scientific research in the way that the other projects were. We consider the need for such an audit, and the fate of the Tyrrell recommendation, in vol. 7: Medicines and Cosmetics.

Policies on research management and evaluation

7.40 We have not undertaken a critical examination of the programme of scientific research carried out by MAFF and the Research Councils. Nevertheless, our consideration of the use of research in response to BSE has been sufficient to identify a number of lessons to be learnt about the management and evaluation of research. We discuss them in this section. We are conscious that there have been many changes in the period since 20 March 1996. It is the task of others to evaluate the extent to which those changes address the matters we have identified. In doing so, and in dealing with similar situations in the future, they should not lose sight of these lessons from the BSE story.

Funding

7.41 We deal first with a common misconception, namely that necessary research into BSE was not carried out because the Government would not provide money to fund it. For most of the necessary research, we did not find any evidence to support this: when additional funding was not forthcoming from the Treasury, resources were diverted from other non-BSE projects. We identify below the small number of areas where lack of, or delay in providing, funds played a real part in delaying necessary research. For the most part delay occurred because of the protracted procedures for obtaining funds, not because they were refused.

Before the bid for supplementary funds was rejected

7.42 A striking feature was the lengthy process of actually bidding for funding. We describe in Chapter 6 the PES system for planning government expenditure. This system required Departments to work to a strict annual cycle for seeking funds for research as for other expenditure. Bids covering three years were submitted in the spring, and, following a series of negotiations, the Department’s share of the overall...
public expenditure was fixed in the autumn by the Cabinet. The detailed Estimates of spending for the next financial year were then presented to Parliament in the spring. If a need for further spending arose during the financial year, the Treasury expected Departments to meet the need by switching resources from other budgets, where possible. If this search proved impracticable, Departments might approach the Treasury for extra resources from the Reserve, but this was regarded as a last resort. The Reserve was rightly kept back by the Treasury for real emergencies. Bids made earlier in the year were less likely to be successful, given that Departments would more readily be able to switch funds from other budgets.

7.43 It was via these procedures that MAFF had to obtain additional funds for its BSE R&D programme. Chapter 6 describes the protracted sequence of events leading eventually to a bid for funds from the Reserve in August 1989, and for strategic funds for R&D in the PES round. This process had taken some two years, involving consultation and drafting and redrafting of submissions and project proposals. An added complication was the involvement of the Southwood Working Party and Tyrrell Committee, and the need for their recommendations to be taken into account in the process. Mr Bradley was clearly frustrated in December 1988 by the ‘prelude of time-consuming administrative procedures’ which he said was causing progress to stagnate. There had been little progress six months later, when Mr Bradley again expressed his frustration, this time in a minute to the CVO:

... If we are to succeed in cracking this disease and provide information for Ministers to make decisions or defend actions, we must short cut the ‘red tape’ and obtain what we can from the Treasury so the new R&D can begin ... 

... Dr Watson and I commenced preparing information for submission to the Minister on BSE R&D as early as January 1988. It is regrettable that we are still doing the same nearly 18 months later and are unable to progress the offspring experiment, the infectivity studies (via NPU) and new work due to lack of funds and staff.998

7.44 It is to the credit of those involved that the research programme was not simply halted by this process. As is clear from Chapter 6, research was funded by diverting resources from other projects during this period, despite the cuts that were prevalent at the time. Mr Bradley’s updated programme paper at the end of 1988 also demonstrated that in many cases projects had been held up not through lack of funds, but for other reasons. For instance, some awaited the establishment of a suitable animal model – the first stage of which was achieved only in September 1988 with the transmission of BSE to mice.

7.45 However, it was clear that one project in particular did suffer during this period from lack of funds: the maternal transmission study. As we describe in detail in Chapter 6, the importance of ascertaining whether BSE was transmitted vertically from dam to calf was recognised at an early stage. It was identified in the CVO’s submission to Mr Thompson in June 1988, and its importance was confirmed repeatedly by, among others, the Southwood Working Party, the Tyrrell Committee, Dr Kimberlin, Dr Ridley and senior officials. Yet there was a considerable delay before the study was finally initiated in August 1989. Although the offspring of affected cattle had been identified and monitored before then, for

998 YB89/5.22/4.1
CONCLUSIONS DRAWN FROM THE SCIENTIFIC RESPONSE TO BSE

the reasons Mr Meldrum gave Professor Bell on 31 May 1989, this was not a satisfactory alternative to MAFF acquiring and monitoring the animals. It seemed to us that the principal reason for this delay was lack of funds, coupled with the protracted process of actually bidding for funding. When the go-ahead was finally given for the project in June 1989, it was not as a result of a successful bid for additional funds from the Treasury, but because Professor Bell had found a way of deferring some of the costs, and because the remainder were to be underwritten as an interim measure from within the SVS budget.

7.46 The consequence, it seemed to us, was a delay of some months in acquiring the animals and initiating the study proper.

7.47 Our understanding is that the Chief Scientist’s ‘special fund’ could not be used to fund in-house research, and thus could not have been used in this case. However, this episode illustrated to us the tremendous value in having available a small strategic fund that could have been used in such circumstances.

Effect of rejection of bid for funds

7.48 As described in Chapter 6, the bid for funds from the Reserve made in August 1989 was rejected: it was thought that the necessary funds could be found within MAFF’s overall research budget. As a result of PES negotiations in the autumn, the bid for strategic funds for BSE R&D was withdrawn, although there was some uprating of funding for externally commissioned research.

7.49 We asked a number of those involved what the effect of this failure to obtain additional funds was. Dr Shannon told us:

I think we were severely disappointed that this bid was rejected, but I suppose we picked up the pieces and tried to get on and put as much work in place as possible.

7.50 We also explored the question with Dr Watson and Mr Bradley. When we asked Mr Bradley whether there were other experiments, besides the maternal transmission study, that they were unable to progress because of the funding difficulties, he said:

I do not think in a specific nature like this one because this one was a very expensive study and it was a big decision to go ahead or not. The other experiments, for reasons we have explained previously, due to lack of resource, lack of funding, there were potentially degrees of delay but I do not think significantly so compared with the position at this particular time. As it turned out, in the shortness of time, we did get the experiment under way and very little was actually lost.

7.51 Mr Bradley thought that lack of funding was one of the constraints on tissue infectivity studies using mice:

999 T39 p. 62
1000 T39 p. 103
1001 T42 pp. 36–7
... when the studies into mice to which Dr Watson refers were initiated, we had a whole range of tissues which we wished to inoculate into mice and which were scientifically sensible, we thought. And obviously multiple sources for each of these tissues as well. And yet we were subsequently rationed to inoculating 30 tissues in one year, 30 in the next and 20 in the final year. Had we had more funding and there had been more resource available, admittedly that work was done without the CVL, done at NPU, it would have progressed quicker.1002

7.52 Dr Watson was asked whether studies using hamsters, cattle and pigs carried out at the CVL could have been started earlier if the funding had been available:

There were other constraints in all of this, and accommodation was one in particular, particularly with cattle experiments. We did, I think, utilise funds from other sources and staff and so on to carry out the transmission work that we had planned. It is very, very difficult to say what part funding or lack of funding played in some of this, to be frank ...

... If one is looking you know into the crystal ball and how funding might have helped the situation in the longer term, I am sure that, you know, one could have been thinking of more high security cattle accommodation. This was a major lack in the research institute. Pirbright had it for foot and mouth, it was tied up; Compton had it, it was tied up with work there on BVD. And ours was limited, it was not fully satisfactory.1003

7.53 However, he said that a bid for cattle accommodation was not made at that time:

... I do not think so, because we had already committed and were completing a major capital expenditure programme for small animal accommodation... We used a major tranche of capital allowance for this accommodation, but to be honest I do not think we had put forward plans for additional cattle accommodation at that time because we were relying for transmission work heavily on the NPU and mouse inoculation, which had been agreed at a meeting chaired by the CVO in November 1988, I think the allocation of work between the two institutes, collaborating institutes.1004

7.54 With more funding doubtless more could have been done more quickly. The position was of course different after a link between BSE and vCJD had been announced. Dr MacOwan pointed out:

Post 1996, however, there was a need to expand the BSE programme rapidly after the link to nvCJD was announced. This diverted much of the funding to the necessary investment in the research infrastructure to accommodate the additional projects before the projects themselves could begin. This related to many aspects of the overall programme but notably substantial funds were allocated to pay for the building of large animal accommodation. I understand that the spend on this and other capital items was a total of over £40 million. Prior to the announcement of the link between BSE and nvCJD

1002 T42 p. 44
1003 T42 pp. 50–1, incorporating revisions proposed in S70E, Watson
1004 T42 pp. 51–2
it would have been impossible to obtain funds of this magnitude for research on BSE.\footnote{S100B MacOwan para. 35}

7.55 However, notwithstanding that funds were more limited, with the exception of the delays in the maternal transmission studies, it did not seem to us that the carrying out of research into BSE that had been identified as necessary was prevented by lack of funding. As Dr MacOwan said:

> While [the refusal of extra funding in 1989] did not deter MAFF from funding BSE research, it did mean it was necessary to free up funds from other commitments and to recruit and train new staff in a field where expertise was scarce worldwide. The gradual build up of the BSE research spend was initially concentrated on the high priority projects recommended by the Tyrrell Research Consultative Committee. As a result projects given lower priority by the Tyrrell Consultative Committee and possibly research subsequently identified as necessary did not receive immediate funding. It was recognised by all concerned that there were limited resources available and that the projects had to be dealt with in order of priority.\footnote{S100B MacOwan para. 34}

The background of cuts in research funding

7.56 The background of cuts in research budgets prior to the emergence of BSE, described in Chapter 6, played a part in determining the resources and infrastructure in place to enable research into BSE to be carried out when the disease emerged. ‘Resources’ went beyond funding \textit{per se} – as alluded to by Mr Bradley when he spoke about constraints on the tissue infectivity studies – and included skilled staff, for example. Professor Bell explained:

> . . . you had to make use of existing people. You cannot suddenly produce people who are experts in this kind of thing.\footnote{T53 p. 57}

7.57 His successor, Dr Bunyan, made the same point:

> . . . you cannot manufacture expertise, it has to grow.\footnote{T53 p. 57}

7.58 Animal accommodation was another resource affected by limited funds. We note Dr MacOwan’s description of the expenditure on new animal accommodation and capital items when more funds became available after March 1996.

7.59 We also note in this context the relatively precarious position of the NPU prior to and during the BSE period, as a result of pressure to reduce overheads. We consider it to have been extremely fortunate that this centre of expertise was available throughout the period.

Planning and coordination

7.60 Chapter 6 illustrates that the majority of BSE research was carried out in-house by the CVL, and was not subjected to open competition or peer review.
Moreover, not only did the CVL perform the role of the contractor, but also its views in large measure determined the research that was undertaken.

7.61 Had the necessary research fallen principally within the province of DH, a very different approach would have been adopted. The research needed would have been identified by DH in conjunction with the MRC, and would then have been put out to contract to whichever contractor appeared best able to provide it, through projects subjected to external peer review. An open call for proposals has the advantage that scientists working in diverse areas may identify a wider range of potential avenues of investigation.

7.62 With hindsight, such an arrangement might have proved preferable in the case of research into BSE.

7.63 An alternative approach would have been to subject the research programme to the overview of an independent research ‘supremo’ or committee whose remit was, in discussion with MAFF and DH, to coordinate the research and to ensure that contracts were awarded, following open competition, to whoever appeared best able to carry it out appropriately. Professor Almond said of such an approach, following the Review of MAFF-funded TSE research in February 1995: ‘This would have the advantage that overlap could be avoided and funds could be directed to the best experts in the field. Moreover a longer term strategic view of the need for certain types of research (e.g., the development of transgenic animals) could be developed.’

7.64 There had previously been proposals for a research ‘supremo’ to coordinate BSE research – we discuss their fate in vol. 11: Scientists after Southwood.

7.65 Had such a system been adopted in the case of the BSE research programme, alternative strategies to address some of the questions and policy needs might have been identified and explored. It is of course a matter of speculation to seek to identify the differences that such an approach might have made, but we draw attention below to some areas which, with hindsight, it strikes us might have benefited from a research supremo or directed research programme:

- **Epidemiology**
  We discuss in vol. 3: The Early Years, 1986–88 the early work of the Epidemiology Department of the CVL. Valuable additional work, including sophisticated modelling based on detailed analysis of a wide variety of data on affected cattle, feed and other factors, has been carried out by other groups, notably under Professor Anderson at Oxford University, and Professor Morris at Massey University, New Zealand. Many of the techniques deployed have been developed only during the period since the emergence of BSE. A research supremo or appropriate body might have helped to bring about the involvement of epidemiologists outside the CVL, and facilitate data sharing with them.

  An important question was whether the epidemic was fuelled by animals slaughtered for human food at a stage when they were incubating the disease. Another question for epidemiologists was to identify the cause of BABs. Related to both these questions was the need to establish the minimum
amount of infective material capable of transmitting the disease orally. We
discuss the wide-ranging relevance of this issue above, and note here that its
importance might have been apparent at an earlier stage to someone charged
with directing and overseeing the whole BSE research programme.

- **Diagnosis**
  As indicated in Chapter 3, diagnosis of BSE and other TSEs has depended
largely on post-mortem histopathological examination of brain and
examination for SAFs by electron microscopy. More recently western
blotting and ELISA techniques have been developed. Experimental results
of a promising ante-mortem test from the USA using capillary
electrophoresis immunoassay, to assay the level of PrPSc in white cell
concentrates from blood samples, were published in 1999. Similar research
has not been carried out in the UK, although investigations into potential
biochemical markers in blood and urine have been undertaken at the CVL.

There are many uses for simple, cheap and reliable ante- and post-mortem
tests for BSE. A reliable blood test for the diagnosis of subclinical BSE
would have been extremely valuable in the management of the BSE
epidemic, and might have avoided the cull of a very large number of healthy
animals after March 1996 under the Over Thirty Months Scheme. A test
suitable for screening either ante- or post-mortem could be used (and could
have been used) to assess the number of subclinically infected animals, and
in particular to ensure that such animals were excluded from the human food
chain.

In his report on the Review of MAFF-funded TSE research in February
1995, Professor Almond noted the difficulty in this area and the unique
problems encountered.\(^{1010}\) He thought it ‘somewhat disappointing, but
perhaps not surprising’ that in spite of the significant amount of money being
spent (£1.3 million in 1995/96), there had been little progress towards the
development of a diagnostic test that could be used in live animals. We note
the detailed evaluation of the different approaches to this problem, and the
conclusion that some of them were definitely worth pursuing, while the
value of others was doubtful. In his comments on the Review, Professor
Hueston noted the importance of identifying clearly the policy objectives
behind the search for an ante-mortem test.\(^{1011}\)

An open call for proposals, and strategic overview and coordination of the
research, might have been of benefit in this difficult area. A resource centre,
charged with the distribution of BSE-affected brain samples, antibodies and
other biological reagents might also have been very helpful.

- **BSE in sheep and scrapie into cattle**
  We discuss above the importance both of seeking to confirm experimentally
the hypothesis that BSE was caused by transmission of conventional scrapie
agent(s) to cattle, and of the unanswered question about whether BSE is
endemic in sheep. A strategic overview of the research programme, and of
the emerging results, might have prompted earlier consideration of these
questions and initiation of appropriate experiments.
• **Sensitivity of mouse bioassay**
  We have noted the doubts about the sensitivity of the mouse bioassay expressed as early as 1991. A research supremo might have assisted in initiating a comparative bioassay at the earliest possible opportunity, and in encouraging alternative approaches to infectivity studies, such as the development and use of bovine PrP transgenic mice.

• **Lateral transmission**
  It seems to us that more attention might have been given to the investigation of lateral transmission of BSE in cattle following the tentative results of the 1993 case cohort study to which we have referred above. A coordinated study, based on the experiments which successfully demonstrated lateral transmission in sheep in the past, might have been very informative on this issue.

7.66 Finally, a ‘supremo’ arrangement of this kind would have given more scope for independent scientists to make imaginative proposals.

### Animal disease surveillance

7.67 We now turn to consider lessons that may be learnt about animal disease surveillance. The BSE story demonstrates the importance of the speedy identification of the emergence of any new animal disease – particularly any disease that may have implications for human health.

7.68 We discuss in vol. 3: *The Early Years, 1986–88* the system of passive animal disease surveillance in the UK at the time that BSE was first identified. Early warning of outbreaks of novel diseases still relies largely on passive surveillance, i.e., it depends on the reporting of affected animals from the farm or slaughterhouse, by individual farmers or veterinary surgeons, to the Veterinary Laboratories Agency (VLA) regional laboratories (formerly the Veterinary Investigation Centres). This situation was recognised in a consultation document on the effectiveness of the active and passive surveillance systems published by MAFF earlier this year, which lists among the objects of veterinary surveillance:

> To provide an early warning system for new animal diseases, infections or intoxications.\(^{1012}\)

7.69 The document observes of the task:

This is provided mainly through submissions from private veterinary surgeons to the VLA regional laboratories and follow-up investigations and ‘intelligence’ gathered through interaction with private veterinarians. It has been put to us that the animal health surveillance system picked up BSE at a very early stage in the epidemic and, furthermore, this would have not been the case were it not for the regional laboratories noticing a new syndrome in cattle and comparing notes.\(^{1013}\)

\(^{1012}\) Ministry of Agriculture Fisheries and Food, *Veterinary Surveillance in England and Wales – A Review*, 10 April 2000, para. 1.10. This is a consultation document issued to interested parties (and available on MAFF’s website) as part of the Ministry’s work to develop a comprehensive strategy for veterinary surveillance in England and Wales. MAFF is aiming to publish a draft strategy by April 2001

\(^{1013}\) Ibid. para. 4.9
The observations in relation to BSE are not entirely accurate. As we have explained in volume 3, we do not believe that the surveillance system picked up BSE at a very early stage of the epidemic. Recycling was already advanced before BSE was identified, and there is anecdotal evidence of cows in the early 1980s and possibly earlier suffering from symptoms similar to those of BSE. Nor was there encouragement for the regional laboratories to compare notes. Nonetheless the passive surveillance system did result in the identification of the emergence of BSE at a relatively early stage of the epidemic.

We discuss in volume 3 evidence about the ability of the passive surveillance system to detect cases of BSE. In our view one reason why BSE was not picked up at a very early stage by the system was the lack of incentive for farmers to refer an isolated case of an unrecognised disease in their herd for laboratory investigation. Indeed, there was a positive disincentive, namely the cost of a post-mortem examination.

Since the emergence of BSE, it appears that the efficacy of the passive surveillance system as a means of detecting new diseases has worsened. MAFF’s consultation document records in an annex a significant decline in the number of samples submitted for analysis to the Veterinary Investigation Centres/regional laboratories between 1990 and 1998:

<table>
<thead>
<tr>
<th></th>
<th>1990</th>
<th>1998</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>2,838</td>
<td>1,415</td>
</tr>
<tr>
<td>Sheep</td>
<td>3,838</td>
<td>2,267</td>
</tr>
<tr>
<td>Pigs</td>
<td>2,108</td>
<td>795</td>
</tr>
<tr>
<td>Birds</td>
<td>8,093</td>
<td>2,673</td>
</tr>
</tbody>
</table>

It also reports a reduction in number of regional laboratories from 19 to 14 in 1990, and an indication that these are effectively operating as ‘sentinel centres’ rather than representatively sampling the herds. The document includes a lengthy section on the strengths and weaknesses of passive surveillance. This begins:

The system of passive surveillance has been described in terms of a ‘pyramid of scrutiny’. Under this description, for a passive system of scrutiny to be successful, animals must be under vigilance sufficient to permit the identification of changes from the ‘norm’. The first level of scrutiny is provided by the livestock producer, who may decide not to seek assistance. The second level is provided by the alert private practitioner or veterinary inspector, who may decide that laboratory diagnostic testing is unnecessary. These two levels apply a screening process, through their discretionary choices, that stops many disease occurrences from benefiting from a definitive diagnosis offered by the laboratory, which represents the third level of scrutiny. On a continuous basis, the resulting laboratory volume reflects, in major part, the industry’s and veterinary practitioners’ assessment of the cost:benefit ratio associated with specimen submission.
7.74 The consultation document questions ‘whether the current arrangement is an adequate basis for meeting MAFF’s risk management needs’. 1017

7.75 We urge those whose task it is to answer this question not to lose sight of the importance of an effective early warning system for an outbreak of a disease such as BSE, and of the corresponding need to encourage referral of cases by individual farmers and veterinarians.

7.76 We recognise the cost implications of maintaining the current network of laboratories, let alone providing more diagnostic tests more cheaply or freely in order to encourage submissions. It is unlikely that even a free service would ensure the submission of 100 per cent of cases that with hindsight turned out to be informative or significant. What is important is that some systematic assessment is made of the costs and benefits of the different approaches, such as targets for representative submissions, facilitated by vouchers or discounts, or agreements with sentinel veterinary practices, or other options. Economic realities mean that some form of subsidy needs to be considered if the cost:benefit ratio is to be swung in favour of specimen submission.

7.77 The emergence of BSE might now act as a case study against which such options could be assessed, to see when, where and how each might have been able to identify the new disease and at what additional cost. This is not to suggest that new diseases will be like BSE; rather that BSE with its long incubation period, lack of ante-mortem test and low in-herd incidence presents a severe challenge to any surveillance system and thus might act as a benchmark for any extreme case likely to be faced, and the costs and benefits of different ways of dealing with it.

The investigation and management of potential zoonoses

7.78 The magnitude of the BSE epidemic and its tragic consequences, particularly for those affected by vCJD, raise concerns about whether the UK has an adequate structure for the investigation and management of potential zoonoses. There are very many diseases of animals that are known to cause illness in humans, and for which a reservoir of infection in animals may exist. Novel ones will doubtless continue to emerge or be identified.1018 Diseases of humans carried by animals in one way or another are a significant public health problem facing the UK. The ‘Overview of Communicable Diseases’ produced by the Public Health Laboratory Service (PHLS)1019 listed a number of zoonotic diseases with reservoirs of infection in animals that pose serious threats to public health. These include, by way of example, salmonellosis, *E. coli* 0157, listeriosis and vCJD.

7.79 There already exist specialist agencies with duties and expertise in animal health (the SVS and VLA) and public health – for instance the PHLS. The same types of laboratory expertise are required in the investigation of pathogens that cause disease in both humans and animals. Similarly, the epidemiological methodology required for the study of outbreaks of infectious disease in both
animals and humans is essentially the same. The BSE story illustrates the importance of the agencies dealing with human health and those dealing with animal health working together if threats to human health posed by zoonoses or potential zoonoses are to be managed in the most effective way.

7.80 By way of example, there are a number of respects in which the PHLS might have been able to offer MAFF assistance in relation to BSE. The PHLS is described in more detail in vol. 8: *Variant CJD*, but briefly it has two centres for communicable disease surveillance and a regional network of laboratories closely associated with NHS hospitals, university medical schools and institutes of public health throughout the country. In addition, each region now has a specialist epidemiologist associated with a group of PHLS laboratories. The service has an efficient communication system to primary care doctors and nurses and to NHS consultants in communicable disease control in every district authority. Its central public health laboratories at Colindale in London provide a referral centre to regional laboratories for strain-typing of pathogens and other specialist services. The facilities and expertise of the PHLS might have been of assistance to MAFF in, for example, the development of ELISA tests.

7.81 We understand that since 1996 a number of joint committees have been established to encourage cooperation and collaboration between those responsible for human and animal health when dealing with zoonoses or potential zoonoses. They include:

- the National Zoonoses Group for England (1999);
- the Epidemiology of Foodborne Infections Group (1996);
- the Surveillance Group on Disease and Infections of Animals (1999);
- the Joint Food Safety and Standards Group (1997), now absorbed into the Food Standards Agency (2000); and
- the High Level Committee on Research into TSEs (1997).

7.82 We reiterate the importance of continuing to develop closer collaboration in the investigation and management of human and animal disease.

7.83 What matters equally is that administrators, vets, physicians and others recognise the importance of alerting each other to new potential zoonoses, or to new outbreaks of such diseases, and of working together on appropriate investigations and control measures where necessary. They should do so whatever the formal structures within which people are working and whether there are many agencies and institutes involved or only a few. This did not happen in the early days of BSE. The BSE story suggests to us that such collaboration may be facilitated by clear allocation of a lead responsibility for a new disease, or a new outbreak of disease, to an organisation and, within that, to an individual who will need to consider which other organisations need to be involved.

7.84 We think that the BSE story also suggests that consideration should be given to joint working at a more detailed level, especially where there is very limited specialist expertise. For example, there could be practical advantages in combining what are currently separate VLA and PHLS laboratories which may work on subtyping the same organism. A centralised laboratory could serve both animal and
human infections. Similarly consideration should be given to whether two separate organisations are needed to study the epidemiology of a disease which affects both animals and humans. A number of those giving evidence to the Inquiry commented on the lack of veterinary epidemiologists in the UK. Yet, as we said above, the methodologies used by epidemiologists in human and animal disease are essentially the same. Joint training programmes and joint working in laboratories or institutes seems likely to make the best and most flexible use of existing and future experience. Enhancing the role of epidemiologists in this way may also help to attract talented individuals into this specialism.