7. Medicines and cosmetics

Medicines

850 We turn now to the major topic of the safety of medicines and medical devices that use bovine tissues. Unlike food products, these did not attract a great deal of public attention and debate in connection with BSE. No doubt this was because their provenance was far less apparent.

851 As indicated in Chapter 2, bovine material was used in a variety of ways in the manufacture of medicines and medical devices. Some, like insulin, hormone treatments and sutures, contained bovine material as an ingredient. Others, in particular vaccines, were rather different. Although these did not directly use bovine ingredients, bovine material was widely used to grow cells and viruses. This material did not form part of the final product, but it was not known if its use at the earlier stages of preparation could transmit infection.

852 Officials speedily realised that medicines might offer a pathway for infection either between animals, or from animals to humans. Scrapie had in the past been inadvertently transmitted between sheep through a vaccine containing contaminated brain material. Pooled pituitary glands used to derive human growth hormone had also transmitted CJD between humans. Risk from ‘biologics’ immediately occurred to the Chief Medical Officer (CMO) when he was told about BSE in March 1988.

853 We devote a large part of vol. 7: Medicines and Cosmetics to examining in detail the way matters were handled by the medicines licensing divisions in DH and MAFF.

854 There has recently been lively public interest in action on vaccines and the fate of existing stocks when their formulation was being changed so as to substitute non-UK for UK-sourced material. This interest seems to have been stimulated by the documents and statements collected and published by our Inquiry. From the documents made available to us, it was not possible to determine precise dates on which stocks of vaccines sourced from UK bovine material were used up. Although there is no evidence at this stage that medicinal products were implicated in transmitting the disease, the possibility cannot be ruled out. Accurate tracing of available products would then be helpful. We found frustrating the gaps in records and recollections about this.

855 We recognise that the relevant documents were bulky, highly technical and confidential. Witnesses spoke of files piled room high on individual products. The paper trail would have been difficult to follow at the best of times. However, matters were made worse by defects in the record-keeping systems used at the time that the implications of BSE were being considered. Questionnaires had to be sent out to all licence holders in 1989 seeking fresh information about the use of animal materials. The Medicines Control Agency (MCA) appears to have taken some years to put 101 Biological material used in the production of human and veterinary medicines, and in medical devices
matters right and to have had difficulties keeping material up to date. In 1994 it was discovered that, although the information obtained via the questionnaire had been recorded on the database, it had not been updated with information from new licence applications received after that time.

856 We were able to piece together the main bones of the story from contemporary papers and minutes, together with evidence from witnesses. What follows looks at the most significant aspects of what happened. It begins with a brief outline of the medicines licensing system, which is very different from that covering food safety. Fuller details can be found in Volume 7.

857 We have recently seen papers from DH concerning a review by the Committee on Safety of Medicines (CSM) of BSE-related issues associated with the use of seedlots\textsuperscript{102} in the manufacture of vaccines. It will be apparent that a number of assumptions made by the CSM are open to question for reasons we have set out in our Report (see vol. 8: \textit{Variant CJD}, Chapter 5). We hope that government will look at the topic again in the light of what we have said.

The medicines licensing system

858 Under the Medicines Act 1968, medicinal products could not be sold in the UK without a ‘product licence’ from the ‘licensing authority’. The Secretary of State for Health carried out this role for the UK as a whole in respect of human medicines and the Minister of Agriculture, Fisheries and Food carried out the equivalent role in respect of veterinary medicines. In order to be granted a licence, a product had to satisfy criteria of safety, quality and efficacy. The licensing authority also had power to revoke, vary and suspend product licences.

859 Licensing decisions on human products were handled on Ministers’ behalf by officials in the Medicines Division (MD) of DH, and from 1989 by the Medicines Control Agency (MCA). Those on veterinary medicines were handled in MAFF’s Animal Medicines Division (part of the Animal Health Group) advised by the Medicines Unit and the Biological Products and Standards Department of the Central Veterinary Laboratory (CVL), amalgamated in 1989 as the Veterinary Medicines Directorate (VMD). These officials were a mixture of administrators, doctors, pharmacists and toxicologists. Ministers were consulted over controversial decisions.

860 Individual licensing decisions could be appealed against and legal challenges mounted. The burden of proof lay with the licensing authority to justify its decisions. Decision-making thus had to be based on proper evidence and be demonstrably untainted by departmental and political interests. Officials and Ministers relied heavily on advice from several committees of outside experts set up under section 4 of the Medicines Act and known as ‘section 4 committees’. Many of the members were of great eminence in their field and their advice was almost invariably followed. This was certainly the case in dealing with BSE.

861 The main section 4 committees that advised on human medicinal products at risk from BSE were the Committee on Safety of Medicines (CSM), chaired by

\textsuperscript{102} Master stocks from which each batch of vaccines is derived
Professor (later Sir) William Asscher; the Committee on Dental and Surgical Materials (CDSM), chaired by Professor (later Sir) Colin Berry; and the Committee on Review of Medicines (CRM), chaired by Professor David Lawson. Two subcommittees of the CSM played a key role: the Biologials Sub-Committee (BSC) and the specially constituted BSE Working Group (BSEWG), both chaired by Professor Gerald Collee. The Veterinary Products Committee (VPC), chaired by Professor Sir James Armour, advised on all types of veterinary products.

862 One source of relevant evidence was information on adverse reactions to licensed medicinal products, reported by the medical profession and the pharmaceutical industry on yellow cards, which gave their name to the system of reporting – the yellow card system.

863 Informal methods were often preferred to formal licensing action under the Medicines Act. ‘Guidelines’ and ‘recommendations’ were issued, with which manufacturers were expected to conform. They had the merit of offering some flexibility in the light of particular circumstances and avoiding contentious litigation. We were told that in practice they were a powerful tool.

864 By 1987 the licensing arrangements in both DH and MAFF had developed a number of weaknesses. Faced with EU deadlines for reviewing ‘Product Licences of Right’ (those granted as an interim measure to products already on the market at the time that the UK licensing system was first set up), Ministers commissioned management reports from Dr N J B Evans and Mr P W Cunliffe about how arrangements might be improved. They found that the basic system was sound, but a two-year backlog in handling applications was mainly associated with understaffing, antediluvian data-holding systems and blurred management lines. The subsequent restructuring into Executive Agencies was intended to rectify some of the defects but itself caused some transitional turmoil.

**Medical devices**

865 Devices such as heart valves and pericardium patches were not covered by the Medicines Act. When BSE emerged, they were the responsibility of the Procurement Directorate (PD) of the National Health Service (NHS), which operated a voluntary registration scheme for manufacturers. The purchasing power of the NHS gave it considerable leverage over manufacturers. The need to consider this type of product in relation to BSE was not recognised until February 1989. Thereafter officials in PD lost no time in issuing guidelines that paralleled those issued to manufacturers of human and veterinary medicines (see below). Volume 7 recounts the actions they took on the products thought to carry risk. The last two such products were dealt with in early 1990 – one company had come into line with the guidelines by January 1990, while the other, after unsuccessfully attempting to find alternative material, ceased production of its device in April and recalled stocks. The response of PD was prompt and adequate.
Phase 1: the initial response on veterinary medicines

866 MAFF was quick to recognise in 1987 that veterinary medicines using bovine material might carry a risk, in particular where, as in cattle medication, there was no species barrier. Mr Wilesmith’s initial investigations of BSE cases had included medications as a potential transmission agent, but by the end of 1987 he had ruled this out as not fitting the pattern of cases.

867 However, Dr Little, the CVL Deputy Director responsible for veterinary medicines, had meanwhile been giving the implications for these medicines some thought. He went out of his way to attend a meeting on 9 September 1987 of the BSC (the section 4 subcommittee of the CSM referred to above) in order to see how it handled a licence application in which possible transmission of CJD was a concern. We have already noted in Chapter 3 that differing perceptions about what happened at that meeting were to create an unfortunate misunderstanding between MAFF and DH about how much thought the latter was giving to BSE. We return to this below when we look at initial action taken by DH.

868 Within MAFF, Dr Little carried matters forward by commissioning a paper in November 1987 from a member of his staff, Mr Peter Luff. The paper was impressive as an initial overview of what was known about BSE in relation to safety of veterinary medicines. It reviewed options for action. Unfortunately, those responsible for human medicines were not sent Mr Luff’s paper.

869 The paper was discussed twice in early 1988 by the Biologicals Committee, a working group of MAFF officials who handled routine biological product applications. They decided to leave the matter in abeyance for the time being.

870 It was resurrected in June, soon after a special discussion on BSE organised by Dr Philip Minor of the National Institute for Biological Standards and Control (NIBSC), and after Ministers’ decision to introduce a ruminant feed ban. Dr Little and his staff acted swiftly. By 6 July Mr G W Wood of the CVL had prepared a set of draft guidelines for producers of veterinary medicines using bovine material.

871 These draft guidelines were given in July to NOAH, the trade association representing veterinary medicines producers, and were discussed with them on several further occasions.

872 Meanwhile MAFF provided letters of warning both to the Veterinary Record and to individual practitioners about the dangers of pituitary hormone material prepared outside the ambit of Medicines Act licensing. The concerns about BSE coincided with a review of hormone-based products that had Product Licences of Right. A warning about BSE was issued in general guidance produced in November and approved by the VPC on completion of the review. By the end of 1988 MAFF officials were also ready to seek the endorsement of the VPC for the proposed general guidelines on BSE.

873 All these were admirable initiatives so far as veterinary medicines were concerned. The problem was that the parallel interest of those dealing with human medicines had been neglected. Apart from a copy of the MAFF draft guidelines sent to Dr Harris, the Deputy Chief Medical Officer at DH, in July 1988, at the
suggestion of Dr Minor of the NIBSC, we could find no trace of any significant contact between the two licensing authorities about BSE and medicines throughout this period.

874 In December, Dr Paul Adams of DH, who was following up recommendations by the CSM on human medicines, had some discussion with Mr Bradley at the CVL, and the penny began to drop that MAFF and DH should work together on advice about the same biological material forming the basis of both animal and human medicines.

Phase 1: the initial response on human medicines

875 We have looked at what was happening during the same 18 months within DH.

The period up to March 1988

876 As we have already seen, up to March 1988 DH had been neither informed nor consulted by MAFF about BSE. We looked at two occasions during the period when this might have happened.

877 The first was the BSC meeting on 9 September 1987, which Dr Little attended. Also present was a DH pharmacist, Mr John Sloggem, who had been researching an application for a Clinical Trial Certificate (CTC) for a product containing bovine brain extract. Fortuitously he had learned of BSE in August from Dr David Taylor at the Neuropathogenesis Unit (NPU) in Edinburgh, whom he had asked about the risk from ‘slow viruses’. Dr Little told us that he mentioned BSE at the BSC meeting, although others present could not remember this. We think it unlikely that Dr Little referred to BSE in the course of the formal proceedings in such a way as to register with any of those present. Equally, however, we believe that there must have been some informal conversation about it between Dr Little and Mr Sloggem after the formal meeting was over. From this Dr Little gained the impression that DH was aware of BSE and was giving it some thought. He reported this to Dr Watson, Director of the CVL, who in turn told the CVO, Mr Rees.

878 However, matters were not as Dr Little thought. He did not appreciate that Mr Sloggem was pursuing his interest individually, on the narrow front of the particular application in front of him, and had learned of BSE quite by chance. More generally DH was still in the dark.

879 Had Dr Little taken steps subsequently to follow up his conversation with Mr Sloggem, the true state of affairs might have emerged. Although we do not think Dr Little is to be criticised for not doing more, once he thought that DH had taken the matter on board, we do think it regrettable that the opportunity was lost for joint consideration of BSE at an early stage by those responsible for the safety of human and veterinary medicines.

880 We also considered whether Mr Sloggem might have shared the information he was collecting more widely at that stage. However, DH had not been formally notified about BSE. Mr Sloggem had learned of it only by chance in the process of
a particular investigation and thought it was a slow virus. It was not incumbent on him to inform Medicines Division or DH generally about what he had learned.

881 The second occasion on which DH might have been alerted was at a meeting of the BSC on 6 January 1988, when Mr Sloggem presented his paper about the product he had been reviewing. This was the first time that a number of those present had heard of the new disease. The CTC was turned down, partly with the ‘slow virus’ risk in mind. We do not think it unreasonable that the subcommittee and the officials of MD did not identify any wider considerations.

882 However, we think it was a pity that no system existed to capture information of the sort acquired by Mr Sloggem on a readily accessible form of working database. We see such a database about concerns and queries as being of value to both the licensing authorities.

**March–December 1988**

**Initial action by the CMO and MD**

883 We have seen already that DH was formally notified of the emergence of BSE in March 1988. When the CMO, Sir Donald Acheson, heard about the disease, he had an immediate concern about the safety of bovine insulin and of vaccines prepared using bovine serum. No doubt the unhappy story of human growth hormone was fresh in his mind. He asked his deputy, Dr Harris, who had long experience of medicines licensing, to seek advice from the NIBSC.

884 It was also agreed that the safety of biological-based medicines was a priority question for the proposed group of experts – set up shortly thereafter as the Southwood Working Party.

885 During April officials in MD saw a submission from the CMO to DH Ministers alerting them to the disease, and minuted one another about its implications. We were told they knew ‘virtually zero’ at that time about TSEs. They decided to await the outcome of the Southwood Working Party’s deliberations. Although some preliminary steps might usefully have been taken in the meantime, such as searching their database of licensed products, we thought the decision to await the views of the Working Party was a reasonable response by MD at this juncture.

**The NIBSC discussion**

886 On 16 May 1988 the NIBSC organised a discussion about BSE to consider what the disease might mean for medicines using biological material. The meeting was attended by Mr Wilesmith, the CVL epidemiologist, Dr Kimberlin from the NPU, Dr Rosalind Ridley and Dr Harry Baker from the MRC’s Clinical Research Centre, and Dr A J Beale and Dr A J M Garland from Wellcome. Surprisingly, no one from MD attended. It has not been possible now to unravel why. Dr David Jefferys, the obvious candidate as head of the new drugs and biologicals branch of MD, believes he did not receive an invitation. Among the outcomes of the discussion was a recommendation that tests of the infectivity of calf serum should be undertaken. We return to this later.
Galvanising MD

887 In May Dr Pickles, the newly appointed DH joint secretary of the Southwood Working Party, moved into action. She summoned up some information from the existing database and suggested to Dr Jefferys that a number of questions should be put to the BSC. He was not in favour of doing so, noting that the BSC had already discussed BSE informally in January. He did, however, respond with some preliminary thoughts and suggested that others in MD should also be involved in any further discussions.

888 Dr Pickles returned to the charge on 21 June immediately after the first meeting of the Working Party. In a forthright minute intended to ‘galvanise Medicines Division into action’, she listed further questions needing answers and pressed for these to go to the BSC. Dr Gerald Jones, the senior medical officer in MD, told us that by now it had become clear that they had ‘a serious problem’. They decided to refer the issue of BSE to the BSC and during July Dr Frances Rotblat, a Senior Medical Officer working for Dr Jefferys, and Dr John Purves, Pharmaceutical Assessor to the CSM and the BSC, were commissioned to write a joint paper for the BSC’s November meeting.

889 We were concerned whether the matter was put to the section 4 committees sufficiently promptly, and whose responsibility this was. One of the defects identified by the Evans/Cunliffe report was the divided responsibility in MD and lack of clear management lines on many matters. BSE was inherently an awkward topic for MD to handle. It had implications across the different administrative, medical and pharmaceutical branches and potentially affected both new, and as yet unlicensed drugs, and drugs already on the market.

890 We accept that responsibility for BSE did not naturally fall to a single branch within these arrangements, but consider that good management pointed to a lead responsibility being assigned. We consider it fell to Dr Gerald Jones, having discussed the matter with senior staff, to decide the priority to be accorded to BSE in relation to other work within MD and to set in hand appropriate action.

891 We also consider that he should have asked for the paper to be prepared for the September rather than the November meeting. It seemed from the evidence we received that, even allowing for the logistics of preparing and distributing papers in good time, this could have been achieved had Dr Jones assigned the matter a higher priority. The consequence was that two months were lost when progress might otherwise have been made.

The paper for the BSC

892 The paper prepared by Dr Rotblat and Dr Purves served its purpose. It elicited advice from the BSC in November. The subcommittee made a number of recommendations, which were to apply to all licences for new products, including:

   i. No immediate licensing action on oral products.

   ii. All bovine materials to come from appropriately certified healthy herds, not fed with animal protein. No brain or lymphoid tissue to be used in parenteral products.
iii. Manufacturing processes for parenteral products to be capable of eliminating scrapie-like agents.

iv. MAIL (Medicines Act Information Leaflet) article to request manufacturers to identify products in which bovine materials had been used. Serum to come from appropriately certified healthy herds.

893 These recommendations were subsequently endorsed by the CDSM, which among other things was responsible for sutures, the CRM, which was reviewing all the Product Licences of Right, and the subcommittee on Safety, Efficacy and Adverse Reactions (SEAR). They were then endorsed by the CSM itself on 17 November.

894 The Chairman of the CSM, Professor Sir William Asscher, told us that experience with human growth hormone and dura mater implants had made the Committee very wary of parenteral products. However, the fact that scrapie had not transmitted to man gave reassurance that BSE was unlikely to be acquired orally.

**Sir Richard Southwood’s concerns about biologicals**

895 A copy of the recommendations was sent to Sir Richard Southwood. Sir Richard had been taking a continuing close interest in the question of the safety of biologicals. He had written to the CMO in August about this and had been reassured that the topic would shortly be coming before the CSM and other committees. He had written to Professor Asscher just before the CSM’s November meeting pressing for any action to apply then to existing products and making a number of suggestions for the contents of informal advice to manufacturers. A round of further correspondence ensued, mainly consisting of Sir Richard’s continuing concern that he was not getting his point across about existing products, and Professor Asscher’s replies assuring him that he was. When he gave oral evidence Sir Richard told us that by existing products, he thought the Working Party meant products that were already licensed and stocks of those products. It is not at all clear whether Professor Asscher and the CSM appreciated that the second category was included.

896 Sir Richard Southwood also wrote in December to Dr Little about veterinary products, making similar points. It is plain from this letter that Sir Richard was unaware of the advanced preparation of MAFF guidance.

897 We have already noted that MAFF did not go out of its way to inform officials in MD, or involve them in the discussions about BSE in MAFF’s Biologicals Committee. Equally, MD officials did not seek to find out the situation on veterinary medicines when the issue of BSE and human medicines arrived on their desks in April 1988, or when the MAFF draft guidelines were despatched to them in July 1988. The consequence was that DH had to catch up with several months’ head start by MAFF before it could begin to address the problems.
Phase 2: preparing joint guidelines, January–March 1989

898 On 3 January 1989 MAFF and DH officials eventually sat down together to work out a joint policy towards medicinal products. They agreed it was essential to keep in step, especially as MAFF concerns about animal vaccines would cause DH great difficulties of supply if current stock – in some cases up to five years’ supply – had to be lost. Joint guidelines should be published in MAIL together with a request for information. These conclusions were relayed by Dr Jefferys and Dr Adams to Dr Harris.

899 Within MAFF, Mr F J H Scollen, who handled the policy side of veterinary medicines licensing in Animal Health Division, minuted Mr Cruickshank with his views. He saw the issue as one to be addressed ‘first and foremost in the human health context’ because of the risks associated with maintaining or disrupting the supply of vaccines for human health purposes. He went on: ‘Judgements about what is needed and feasible on the animal medicines front can be more readily taken afterwards.’ This was the line that was subsequently taken.

900 A text for draft joint guidelines was agreed by an ad hoc working group of officials from DH, MAFF and the NIBSC, chaired by Professor Collee, which met on 1 February. The group decided that further action, especially on current stocks of affected products, should be determined once the scale of the problem had been more precisely identified with the help of the manufacturers. Any such action ‘would need to be based on a human health risk/benefit assessment’.

The final draft of the Southwood Report

901 Licensing officials had been keen to know what the Southwood Report would say about medicines. They were looking to it to provide reasoned grounds for any action they might take. At the 1 February meeting those present were shown the currently proposed wording of this section by Dr Pickles, and reacted with dismay.

902 Mr Scollen, who had attended the meeting, gave a graphic account in a minute to Mr Cruickshank:

   There was general dismay at the drafting, which tends to highlight the (theoretical) risk via medicines and to relegate the qualification that the risk is remote.

903 After listing a number of criticisms the group had made of the draft, Mr Scollen continued:

   Even if the report is modified in the light of these reactions, its appearance seems likely to trigger a need for a major public relations job which takes full account of the medicines angle. Consistency between MAFF and DH will be essential and should be achievable. The guidelines themselves could subsequently generate similar pressures since they clearly do not address the issue of current stocks and they could prompt questions – for example – on
the standards applicable in the collection of animal material at slaughterhouses for biological medicinal purposes.

While I have no doubts about the Working Group’s staged approach and the balance to be struck between risks and benefits to human health, this will not be the easiest position to present to a potentially critical public prone to seeing the influence of commercial interests.

904 Dr Pickles, too, got the message. The next day she wrote to Sir Richard Southwood reporting:

They have now realised that virtually none of the current essential human or animal vaccines could comply with the CSM guidelines as agreed by their November meeting and there may be several years of some vaccines in stock to make matters more difficult. Public confidence in the vaccination programme must not be put in jeopardy and yet supplies of some vaccines are very limited. After a late start, it now seems that both human and veterinary sides of the medicines business are working together and putting together a package of measures that seem sensible and workable (and indeed now incorporate all the points you raised with Professor Asscher in your earlier letters, and which I had raised with them separately).

905 She went on to suggest a revised passage for the Report on the grounds that:

This treats CSM/VPC like HSE ie the problem has been referred to the body with the statutory responsibility in that area and it is then for them to take appropriate action.

906 The Southwood Working Party went along with this line of reasoning at its final meeting on 3 February and adopted the revised wording suggested. The report as finally published said on medicines:

5.3.3 The greatest risk, in theory, would be from parenteral injection of material derived from bovine brain or lymphoid tissue. 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, might also be capable of transmitting infectious agents. All medicinal products are licensed under the Medicines Act by the Licensing Authority following guidance, for example from the Committee on Safety of Medicines (CSM), the Committee on Dental and Surgical Materials (CDSM) and their subcommittees. The Licensing Authority have been alerted to potential concern about BSE in medicinal products and will ensure that scrutiny of source materials and manufacturing processes now takes account of BSE agent . . .

5.3.5 In these, as in other circumstances, the risk of transmission of BSE to humans appears remote.
The continuing concern on vaccines

907 Shortly after the final version of the *Southwood Report* was agreed, Dr Pickles sent a copy to the CMO with a draft submission to Ministers. This draft alerted Sir Donald Acheson to the continuing concerns about vaccines. He decided to take a personal hand in matters and asked Dr Harris on 9 February to look into the matter urgently with Medicines Division. He told us that this intervention was quite contrary to his normal practice; he was trying to ‘stir up more activity in the Medicines Division’.

908 Stir up activity he did. On 13 February MD officials met and agreed to carry out a telephone survey of all manufacturers of children’s vaccines. They mooted a working group of officials and experts to follow matters through, and this suggestion led eventually to the setting up of the BSE Working Group.

909 Twenty-four hours later, MD had collected a useful body of information from those manufacturers identifying what they knew about vaccines that contained bovine material or which might have used it during manufacture, and about the stocks held. This suggested that in some cases considerable stocks were held, described variously as ‘large’, five years, and 63,000 litres.

910 An *ad hoc* group of experts and officials met again on 22 February. This meeting was a key precursor to discussion and advice from the CSM the following day. For this meeting the group added to its number several outside experts – Professor Asscher, Chair of the CSM, Sir John Badenoch, Chair of the Joint Committee on Vaccination and Immunisation (JCVI), Dr Kimberlin of the NPU, Dr William Martin (Southwood Working Party member) and Professor M D Rawlins, Chair of the CSM subcommittee on Safety, Efficacy and Adverse Reactions (SEAR).

911 Those present at that meeting were told of the information on vaccines collected at Sir Donald’s instigation. They considered the *Southwood Report*, the proposed guidelines, a draft questionnaire seeking information from licence holders and a draft letter to licence holders. There clearly remained a number of concerns about the content of the guidelines and whether they ought to be going out at all. It was agreed that the guidelines should be seen as ‘gold standard’ and that this should be made clear.

CSM and VPC approval and the issue of the guidelines

912 The CSM met the next day and approved the various drafts, including a covering letter and also a position statement of its own. This said that the Committee had considered the safety of human medicines in the light of the *Southwood Report* and agreed that the risk to humans of infection via medicinal products was remote. It said the CSM and the VPC had agreed joint guidelines ‘as a precautionary measure, and for the sole aim of seeking to guard against what is no more than a theoretical risk to man’. The VPC had approved the guidelines a few days earlier.
The main points covered in the guidelines were:

- they applied to all licensed products for injection, application to the eye or to open wounds;
- no brain, neural tissue, thymus or other lymphoid tissue, placental tissue or cell cultures of bovine material should be used in manufacture;
- collection techniques to avoid contamination should include no brain-penetrative stunning, the use of sterile and disposable equipment, calves to be under 6 months, all cellular components to be removed from serum;
- sterilisation advice; and
- the guidelines applied also to material from sheep, goats, deer and other animals susceptible to TSEs.

An MCA paper for the Committee drew attention to products already produced and awaiting distribution. It noted that the questionnaire asked companies about their stocks and said: ‘The Committee’s advice on this issue will be sought at a later date.’

Ministers were told on 23 February that the CSM and VPC had concluded that the risk of transmission of BSE through vaccines was remote. To ensure the safety of medicines, however, guidelines would be going out to producers in March. The Cabinet took this into account when they discussed the Southwood Report later that day.

The guidelines and questionnaire were issued on 9/10 March by DH. The covering letter took the wording a stage further by referring to the guidance as ‘a purely precautionary measure’ and said that it represented ‘a standard that is deemed to be best practice for the future, and steps should be taken to implement it. However, it is realised that this guidance may not be fully applicable in all circumstances.’ MAFF issued parallel documents for manufacturers of veterinary products on 15 March 1989.

Was the action taken adequate?

The guidelines were the single most important step taken to secure the safety of medicines. They were the only specific protection put in place to guard against BSE infection via medicines, since the SBO Regulations of November 1989 expressly excluded from staining and sterilisation the material going for pharmaceutical use. Here we consider how matters were handled between January and March 1989, looking at:

i. the Southwood message and how it was interpreted;
ii. whether non-binding guidelines were appropriate;
iii. the scope of the guidelines; and
iv. treatment of existing stocks.
The Southwood message and how it was interpreted

When discussing the Southwood Report earlier in this volume, we noted that the wording the members of the Working Party finally adopted to describe the risks from bovine material in vaccines and other injected products failed to convey their true concerns.

The potential risks from parenteral injection had been one of the Working Party’s most serious worries. They were concerned about existing products and existing stocks. Their identification of risk as remote was predicated on action being taken to address these matters.

Those preparing the guidelines, on the other hand, believed that the risk even before taking any precautions was theoretical and remote. Dr Martin observed to the Inquiry that his impression on attending the meeting on 22 February was that those on the human medicine side regarded BSE as an animal problem, and considered that the Southwood Working Party were being excessively apprehensive.

The Working Party were anxious to avoid a vaccine scare. Nevertheless, as discussed earlier in this volume, they should not have allowed their Report to give a false impression of their assessment of the risk posed by medicinal products. The message that flowed from it was that risk was remote even if no remedial measures were taken. This interpretation became the conventional wisdom both inside Departments and among medicines manufacturers and others outside government.

Were non-binding guidelines appropriate?

It could be argued that suspect material could have been cut off promptly and decisively had formal licensing action been initiated at once on individual items of high risk. We were, however, persuaded by the arguments put to us that guidelines were a more appropriate approach. In essence these arguments were that this approach was quicker and cheaper, and as effective. We agree that had regulatory action been attempted based on an unproven risk, a shoal of legal challenges might have resulted.

Was the scope of the guidelines adequate?

The question here was whether covering parenteral products and those applied to open wounds or to the eye was enough: should orally administered and all topical products – such as creams and ointments – also have been included in the guidance?

Oral products were carefully considered by the experts who sat on the section 4 committees. Nothing in the Southwood Report pointed to the need to alter the assessments made by them in November and sent to Sir Richard at that time. No recommendations were made by the Southwood Working Party regarding subclinically infected cattle entering the food chain. We felt that it was not unreasonable for the section 4 committees to assume that if it was safe to eat meat, it must be safe for humans to eat the minimal amount of bovine material contained in oral medicines such as gelatine in capsules.
As for topical applications, the guidance covered the two most obvious risks, application to open wounds and to the eye. The decision not to include other topical material at this stage seemed reasonable.

**Were existing stocks of injected products treated appropriately?**

The issues that exercised us most were whether suspect stocks of injected products should have been immediately withdrawn and how this should have been handled and presented.

*Keeping them in use*

There were two principal arguments against immediate withdrawal of stocks. The first was the difficulty of procuring sufficient guaranteed ‘clean’ stocks to maintain the vaccination programme or provide life-preserving medication. Many of the contemporary documents and the statements we saw emphasised the difficulty of replacing stocks overnight. In particular, ‘growing’ batches of vaccines was a lengthy process. For this reason, stocks tended to be built up and kept for a number of years ahead.

The second argument was that such action risked causing a general panic that would deter parents from having their children vaccinated, as had happened on previous occasions over other ‘scares’. Discussing his later concern that the proposed ban on bovine offal should not raise alarm about pharmaceuticals, Sir Donald Acheson told us:

> I had in mind a marked and extended previous reduction in the acceptance of whooping cough vaccine which had followed incorrect public allegations by a scientist that the administration of the vaccine carried a significant risk of encephalitis. On the one hand I was aware that during the period 1980–1988, due to incomplete vaccination of our population of children, there had been 123 deaths from measles and 50 from whooping cough in England, together with a many times larger burden of illness and some long-term complications. Against this I had to balance a remote risk of a fatal disease.

Professor Asscher told us he saw the risk-benefit analysis of existing stocks as comparatively easy because the risk according to the *Southwood Report* was remote, and because vaccines were very important in protecting human health:

> The CSM’s judgement was that the risks associated with interruption of the UK vaccination programme were far greater than the potential risk of BSE being transmitted.

We weighed carefully all the evidence provided to us. It is clear that the overwhelming opinion of the medical professionals at this time was that existing stocks should not be immediately withdrawn. Officials in MD accepted this advice and in our view it was reasonable for them to do so. Experience had shown that incomplete vaccination of children led to significant numbers of deaths that would otherwise have been prevented.
Handling and presentation

931 The decision not to withdraw existing stocks immediately gave rise to a separate but related dilemma: the question of what information should be given to the public about the risks associated with BSE and the continued use of existing stocks.

932 The message in the various Q&A briefs prepared at the time of publication of the Southwood Report was that the CSM and the Southwood Working Party were agreed that the risk of transmission of BSE via medicinal products was remote, and that there was no reason to question the safety of existing stocks.

933 There was concern that publicity about the steps being taken would create the very situation that it was desired to avoid. This raised ethical as well as practical considerations, calling for judgement rather than scientific expertise. We believe that vaccine scares, like food scares, are likely to be fostered by a belief on the part of the public that the full picture is not being disclosed. A decision in an individual case not to disclose the full picture in order not to alarm the public is likely to perpetuate, in the long term, the distrust that leads to alarmist reaction. We can appreciate the short-term attraction, in the case of BSE, of not telling the public that there was a degree of concern about vaccines. Taking a long-term view, however, we believe that a policy of giving the public full information about risk is, on pragmatic grounds alone, the correct one, whether the subject matter is food, vaccines, or any other area of potential hazard. If we are correct, the ethical requirement must also be one of openness.

934 We were unable to establish in precisely what terms the decision to go on using existing stocks was brought to Ministers’ attention and what express consideration they gave to it. It seems to us that it must have been at least implicitly understood, if not expressly discussed, at a ministerial level, that there was an issue regarding existing stocks of vaccines, and that a decision had been taken that they were not to be immediately withdrawn while the guidance worked its way through. However, there is no doubt that the decision was not taken at a ministerial level.

935 When we put to various Ministers the question of whether they would have expected to be consulted or informed, we received various answers. Mr Clarke, who was Secretary of State at the time, thought that if the experts were agreed, they probably need not refer it to Ministers. Mrs Virginia Bottomley and Mrs Edwina Currie, who had also served as Ministers in DH, took a different view. Mrs Currie added that she would not dream of overruling people who were on the various senior medical committees. However, she went on to say: ‘If it was an issue that was likely to arouse public concern, for example a dodgy batch of vaccine, then Ministers would be alerted very quickly.’

936 Had the decision in February 1989 about the continued use of stocks of potentially infected vaccines and its sensitivity in relation to the vaccination programme been explicitly put to Ministers, we believe they would have accepted the overwhelming advice of the expert committees, CMO and other DH officials. However, we also believe they would have taken a lively interest in how soon the doubtful material would be phased out and the steps to encourage this. Such interest would have influenced the subsequent pace of events.
Phase 3: implementing the guidelines after March 1989

937 We look now at the third phase of action and one that has attracted great public interest. When they put the guidelines to the CSM for approval in February, officials had emphasised that they were practicable and capable of being implemented over as short a time period as possible. They now had to ensure this happened. They also had to deal with the matter of existing stocks, on which they had undertaken to come back to the CSM. Were these tasks carried out adequately for both human and veterinary medicines?

The context for handling matters

938 Before we trace the way in which DH and MAFF respectively carried out these tasks over the years that followed, we draw attention to two significant changes that took place in the context in which they were acting.

939 The first was the reorganisation of the administrative arrangements for handling licensing that we have already touched on, in order to create Executive Agencies. Preparatory changes were made in 1989 with the redesignation of MD as the MCA and the appointment of a new head from outside the public sector, Dr Keith Jones. This was paralleled by the appointment of Dr James Rutter as the head of the newly constituted VMD. After a ‘shadow’ period, during which reporting lines remained much the same, the two Executive Agencies came into formal existence in 1991 and 1990 respectively. The Medical Devices Agency followed in 1994.

940 Although these new arrangements did not alter the way the medicines licensing system worked, they affected how officials were organised, their accounting lines and the performance standards they were expected to meet.

941 The second major change was increasing EU involvement in medicines matters and the handling of BSE risk. European guidelines on BSE and human medicines came into operation in May 1992 and closely similar ones on veterinary products a year later. In addition, the World Health Organisation offered a formal view in November 1991 that the careful sourcing of material was the best way of securing safety from the remote risk in medicinal products. The international dimension to medicines dominated the later years covered by this Report.

Collecting and analysing the information

942 The first step for both Departments was to collect the information asked for in the questionnaires issued in March. The date set for questionnaire returns was 1 May 1989, with a view to discussion at the first meeting of the newly constituted BSEWG in July. Six weeks proved far too short a deadline. It was to take many months of chasing to get in all the responses. The delay in getting returns collected and analysed meant that the first meeting of the BSEWG had to be postponed until September.

943 Meanwhile work continued within the MCA on analysing the responses. The different products were ranked according to risk, and MCA officials were asked to
prepare papers on those falling in the three highest risk categories for consideration by the BSEWG when it met. We thought this was a sound approach. The ranking, which was influenced by Dr Kimberlin’s views, and was subsequently adopted by the BSEWG, was as follows:

i. Injected products with bovine brain/lymphoid tissue as ingredients.
ii. Injected products with bovine ingredients other than the above.
iii. Tissue implants, open wound dressings, surgical materials, dental and ophthalmic products with bovine ingredients.
iv. Topically administered products with bovine ingredients.
v. Orally administered products with bovine ingredients.
vi. Products with other animal/insect/bird ingredients.
vii. Products with materials produced from animal material by chemical processes, eg stearic acid, gelatine and lanolin.

The SBO ban and pharmaceuticals

Meanwhile, as we described earlier in this volume, action in MAFF was developing on another front. Mr MacGregor’s decision to introduce an SBO ban had initially made DH nervous that this would awaken public concerns about pharmaceutical safety and thus threaten the vaccination programme. However, Sir Donald Acheson told us that, apart from this anxiety, DH welcomed the proposed measure as a step to protect human health. When MAFF set about defining the scope of the ban, DH became involved in the process. This was handled mainly by Dr Metters, who was Dr Harris’s successor as Deputy Chief Medical Officer, and by Dr Pickles.

Dr Pickles quickly spotted that the list of risk tissues included some used for medicines and medical devices, such as intestines, spinal cord and thymus. However, the approach being adopted was that the SBO ban could not and should not apply to material used for pharmaceutical purposes. At a definitive MAFF meeting on 27 September 1989 about the scope of the ban, it was agreed that the Regulations ’were not the correct vehicle’ for a ban on non-food items. This was consistent with the existing exemption for unfit meat sent to a manufacturing chemist, in the 1982 Meat (Sterilisation and Staining) Regulations. In November Ministers agreed with the advice put to them that the CSM/VPC guidelines already in place were the appropriate safeguard in relation to the use of SBO in medicines. Manufacturing chemists should therefore continue to be allowed to receive the unsterilised and unstained material.

We noted that when the question of this exemption came up again in March 1991, there was a further debate and the position changed. Mr Lawrence saw the exemption as ‘rather anomalous’ and argued that it should be removed. MAFF Ministers agreed with the proposal and the new Regulations in March 1992 removed the specific exemption for ‘manufacturing chemists’. However, bovine material for pharmaceutical use may have continued to fall within the general exemption for premises used for the manufacture of products other than food.
This sequence of events highlighted the differences between the legislative frameworks for ensuring the safety of food and medicines.

We consider the legislative framework in Chapter 14, and examine there the extent of general statutory powers to ban the use of potentially hazardous bovine tissues for any purpose which might involve a risk to health, or even to destroy them. Differing legislative powers made it difficult to adopt a consistent approach to preventing the use of SBO in food, animal feed, medicines, medical devices and cosmetics.

We recognise that there are different considerations in play, and that much is dictated by relevant European legislation. However, the different frameworks make it more difficult to achieve a consistent approach. The most glaringly anomalous outcome in the case of BSE was the ban on the use of intestines for food purposes while they might still be used for sutures – thought to be a higher-risk route of infection.

How the BSEWG operated

The BSEWG was set up specifically to advise on the implications of BSE for human medicinal products. Its membership was high-powered. Chaired by Professor Collee, it included the chairmen of the section 4 committees it was advising, together with Dr Tyrrell, Dr Will and Dr Kimberlin of the Spongiform Encephalopathy Advisory Committee (SEAC) and Dr David Taylor of the NPU. Any conclusions it reached were therefore going to have great authority. However, it was purely advisory. It depended on the problematical cases and information about them being brought to its attention by officials, and on officials’ subsequent action to follow matters up. Dr A Lee, an official in the VMD, was given the role of MAFF representative on the Working Group to maintain a link with the parallel action by the VMD. Altogether the BSEWG met five times between September 1989 and July 1992. These meetings provide convenient milestones, which we follow below.

First meeting of the BSEWG on 6 September 1989

At its first meeting the Working Group considered a list of products identified by officials from questionnaire returns and other data held. It agreed the ranking of risk categories proposed by the MCA and considered that the last four gave no cause for immediate concern. In respect of the first three it made four general recommendations to the effect that:

i. no action was needed where raw materials were sourced outside the British Isles in suitable conditions;

ii. the guidelines should apply to material from the British Isles, and companies should be encouraged to comply as soon as possible. The timescale should be agreed for each individual product;

iii. no licensing action should be taken at present on non-bovine materials; and
iv. the licensing authority should follow scientific progress on BSE so as to be in a position to take future licensing action when necessary.

952 The second of these recommendations depended on officials offering the encouragement and deciding any timescales. One of the papers put to the BSEWG at this meeting gave some indication of their line of thinking about the way the exercise should be handled. It suggested that considerations to be taken into account included ‘the findings of the Southwood report in which it was stated that “the risk to man of infection via medicinal products was remote”. It is important not to undermine this considered advice by demanding unnecessary assurances and information from manufacturers.’

953 Officials in the VMD appear to have taken a similar view of the Southwood findings. Mr Alastair Kidd told us that manufacturers were advised to change sources of bovine materials as quickly as possible, where necessary, but were allowed to exhaust existing stocks, as the Southwood Report and the VPC and CVL specialists in BSE had considered that the risk of BSE transmission by medicinal products appeared remote. The VMD told us that this advice was not given generally – the use of existing stocks was considered on a case-by-case basis.

954 At the BSEWG meeting two types of product were identified as needing special consideration. On the first – some homeopathic medicines with Product Licences of Right – it was agreed that more information was needed. The CRM carried this matter forward and decided in November that no action was necessary.

955 On the second, surgical sutures, there was a difference of view within the Working Group. They had a substantial paper prepared by MCA officials before them. Discussions had been taking place for some months with the major UK manufacturer about interim measures that might be adopted while a switch was made to non-UK material. This was not a simple operation as 25 million metres of intestines were used annually. This represented 10 per cent of the annual cattle kill in Australia and nearly a quarter of the New Zealand kill. The upshot of the BSEWG discussion was that, although the company’s plans for a general switchover (in the event begun in February 1990 and completed by the summer) were acceptable, a minority thought that the sutures should be excluded forthwith from neurosurgery, on which the company itself had envisaged offering a warning. Professor Collee was one of these.

The follow-up to the first meeting

956 The CDSM opted for the majority view on sutures at its meeting on 20 September, and the CSM at its 28 September meeting endorsed the BSEWG’s general recommendations.

957 On 10 October Mr Murray Love, an administrator working in Mr David Hagger’s division in MCA, minuted Dr Jefferys and others suggesting a way forward following the BSEWG meeting. The matters he raised were highly pertinent. They included telling firms what the BSEWG had said, timescales for the three high-risk categories, dealing with stockpiled products, and the need for a coordinated licensing authority approach with clear allocation of responsibility. This minute received a lukewarm response from Dr Jefferys, who had discussed it
with Mr Hagger, Dr Adams and Dr Purves. Their view was that a meeting of the
BSEWG should be arranged for January, and that an in-house procedure for writing
to individual companies about products and setting timetables should be agreed.
Dr Jefferys told us that the follow-up with companies lay with Mr Hagger’s
division. Mr Hagger’s division, however, was already in the process of being
destructed as part of the MCA reorganisation.

Second meeting of the BSEWG on 10 January 1990

958 The key issues on this second agenda were the state of play on the 1989
questionnaire and how to deal with products not complying with the guidelines,
particularly the remaining four vaccines which by that stage did not comply.

959 Apart from these vaccines, the only products using high-risk materials were
some allergens using bovine brain in their preparation, not as an ingredient. The
Working Group wanted a tough line on these allergens. The licensing authority
should insist on a changeover to Australasian material within a reasonable
timescale. It was reported that discussions were still continuing at the time of the
next BSEWG meeting in July 1990. In October 1990 officials reported that
satisfactory progress had been made. We were unable to ascertain when a final
outcome was obtained.

960 On vaccines, Dr Rotblat now had more concrete information than that obtained
from her ring-around 11 months earlier. She identified four products, the first three
of which were produced by Evans Medical and the fourth by Wellcome:

   i.  MMR (measles, mumps and rubella) vaccine with stocks to
       December 1990 – not yet licensed
   ii. Measles vaccine with stocks to September 1990 – not used much now
   iii. Tuberculin PPD with stocks to September 1991 – no other source
        available
   iv.  DTP vaccines (diphtheria, tetanus, pertussis) with unadsorbed stocks to
        May 1991 and adsorbed to June 1990 – adsorbed used in preference to
        unadsorbed (not used much now).

961 The meeting decided that ‘the benefits accruing from continuance of the
vaccine programme outweighed the very remote risk to the population from the use
of bovine material in these products’. The minutes go on to say:

   It was considered after some discussion that negotiations should take place
to ensure that sources are changed as soon as possible and to replace existing
stocks with new material whenever feasible. Replacement of Wellcome
unadsorbed DTP vaccine, by Wellcome adsorbed vaccine should ensure that
the former, which is not much used, is replaced earlier than 1991. In the case
of the Tuberculin PPD, no other source is available at present, but the
company (Evans) should be asked to move over to the new product and
replace stocks as soon as this is feasible.
The follow-up to the second meeting

962 The CDSM, at its meeting on 17 January, praised the speed with which the company making sutures had responded to the BSEWG recommendation: it was to begin the changeover in February to Australasian sources.

963 Concerns about BSE in bovine insulin were raised that spring by the British Diabetic Association. Dr Jefferys told the Association in April 1990 that none was being sourced from the British Isles. Although 42 licensed bovine insulin products had been originally identified for the CSM in 1988, none figured among the items put to the BSEWG in the light of the questionnaire. We infer that they were by then sourced outside the UK.

Third meeting of the BSEWG on 4 July 1990

964 Professor Collee told us that at this meeting the Working Group discussed the safety of foetal calf serum at length. He had sought the advice of Dr Taylor of the NPU and others before the meeting. The Working Group reiterated its view that the risk relating to serum was low. Taken together with the fact that the risk of transmission of BSE was theoretical and the view that the benefit of availability of vaccines outweighed any potential risk from their use, the use of foetal calf serum in the process of manufacture was accepted.

965 The Working Group returned to the issue of the non-complying vaccines. Correspondence with the two companies concerned had produced updated information.

966 The Working Group decided that a licence should not be given to the first product (unlicensed MMR vaccine) unless it complied with the guidelines, and that existing trial batches should not be used.

967 There was still no alternative to the third product (Tuberculin PPD), which used glycerol beef broth during the process of manufacture. Stocks were available up to September 1991. These would be changed over ‘as appropriate’ as the new supplies, which were peptone-based, came on stream. The Working Group thought that the replacement of stocks should take place as quickly as practicable, but meanwhile, given the low risk from glycerol broth, the danger of having no stocks outweighed the risk from the product.

968 The source of the measles vaccine was being changed to New Zealand and present stocks would be depleted in three months.

969 The company preparing DTP vaccines had changed the source of its bovine media, but meanwhile was still using non-complying material. The Working Group recommended a meeting with the company to discuss bringing forward the time when there was compliance with the guidelines.

970 The safety of topical products was also reviewed at this meeting, in the light of action taken earlier that year on cosmetics. The only two products using bovine material sourced it from West Germany, and it was decided that no further action was needed on licensed topical products.
Fourth meeting of the BSEWG on 31 October 1990

971 This turned out to be the main ‘wash-up’ meeting of the Working Group. They unanimously decided that the special circumstances of the experimental transmission of BSE to a pig did not warrant a fresh look at porcine material. On allergens, they were told that progress with the company concerned was satisfactory.

972 By now the last of the replies to the questionnaire had been received, some 18 months after they had been sent out, and gave no cause for concern. On the outstanding issue of the stocks of the DTP vaccine, the Working Group was beginning to take a more hawkish line. The stock-out dates for the adsorbed vaccines were now between June and December 1991. Those for the unadsorbed vaccine ran beyond 1991. The Working Group asked its secretariat to explore with the licence holder whether the stocks of the latter could be replaced sooner.

Veterinary products

973 On the veterinary side assurances were still awaited from some companies that appropriate action had been carried through. The BSEWG had received progress reports from Dr Lee at each of its meetings, although this item appears to have been treated as purely for information. The difficulties and delays experienced by the VMD over collecting returns, clarifying obscurities and phasing out certain products had broadly mirrored those on human products. We note that when the VPC had its second and final discussion about the exercise in December 1990, there were at least two companies with considerable stocks of vaccines expected to last another four years. The VMD provided us with a table outlining the 143 products that did not initially comply with the CSM/VPC guidelines and the outcome of compliance measures taken. This indicated that apart from one fish vaccine, all manufacturers had complied with the guidelines, so far as their manufacturing processes were concerned, by 1992.

Final meeting of the BSEWG in July 1992

974 After its meeting in October 1990, the BSEWG lay fallow for almost two years. One or two proposals for a meeting came to nothing. BSE did not figure on either the CSM or BSC agenda. However, in July 1992 what proved to be the final meeting of the BSEWG was held. The Working Group considered the implications of the emergence of BSE overseas for medicines, in particular sutures from France. By now there were European guidelines in place for human medicines. These were in some respects a little looser than the UK guidelines, though based on the same principles. They did not, for example, cover sutures. The BSEWG view was that the UK should treat sutures as if they were covered by the guidelines even though other countries did not do so.

975 Once again, concerns about foetal calf serum were raised, with Professor Collee stressing that continued vigilance was necessary. Besides the unanswered question of whether it could in itself transmit infectivity, there were also concerns about collection methods. These concerns were similar to those raised by Dr Pickles
some three years earlier and referred to by Mr Scollen in his report to Mr Cruickshank in February 1989.

One item that does not appear to have been raised at the meeting was the safety of gelatine. Dr Minor had suggested shortly before that it might be discussed there. He had been disturbed to learn at a meeting in Heidelberg about the ‘shockingly mild’ German manufacturing process after ‘any old cow bone went into the production vat including spine and skull’. There was a pharmaceutical interest in gelatine because it was used for capsules as well as in some other forms. The matter was in the event followed up by a written opinion being commissioned from Professor Collee. His advice was that the BSE guidelines on sourcing should apply to gelatine. Dr Purves told us that this was taken into account in dealing with product licences subsequently. Problems over gelatine rumbled on thereafter, with British suppliers taking steps to exclude UK material in order to meet increasingly rigorous demands from their overseas customers.

Overview of the way the guidelines were implemented

We discuss at some length in Chapter 6 of Volume 7 some features of the way in which phasing out existing products was handled and the reasons for this. We note in particular three factors that directly influenced the response:

i. Uncertainty about the risk. Officials and expert committees had to operate mainly on the basis of value judgements, unable as they were to assess and cite proven adverse reactions.

ii. The management situation. The heavy task of conducting a case-by-case approach was superimposed on a creaking system that was overloaded and understaffed. Meanwhile the licensing divisions were undergoing restructuring and had new management preoccupied with other pressing tasks.

iii. Mixed messages about the urgency. The general perception after February 1989 was that although the measures were in themselves quite drastic, they did not have to be treated as an emergency given that Southwood assessed the risk as remote. The low-key presentation of risk, carefully crafted to avert public alarm about the vaccination programme while remedial action was being taken, had the unfortunate result of being taken as the message itself. This must also have influenced manufacturers’ attitudes.

Veterinary medicines

In the case of veterinary products, a decision was taken that the VMD should pace and match its action to that of the MCA. Although we thought this was a reasonable approach, it seemed, unfortunately, that playing second fiddle was one of the factors that led to a less urgent and decisive approach than was originally envisaged. We are in no doubt that a further factor was that, like the MCA, the VMD read the Southwood message as basically reassuring. Whether the decisions on veterinary medicines had an impact on the numbers of BSE cases may never be
known. It is impossible to say today whether continued use of bovine-based medication may have added to the total number of BABs.

**Human medicines**

979 In the case of human products, the problems in tackling the exercise were greater and the organisational arrangements more complex. The lack of an obvious lead branch in MD continued in the MCA. While there was a team effort, this lacked leadership to prescribe what it was expected to achieve overall and who was to do what by when. Matters were not helped along by changing responsibilities during the process of integrating the administrative and professional branches.

980 The BSEWG was a useful means of achieving speedy advice from the key experts. But the Working Group relied on the MCA to refer matters to it and to act appropriately after receiving its advice. It did not itself lay down any imperatives, such as deadlines for action to be completed, other than to urge that things be done ‘as soon as possible’ in some cases. Officials were not accountable to it. However, once the BSEWG ceased to meet, the impetus for officials to prepare progress reports appeared to disappear.

981 The three most sensitive groups of products used for humans were (i) those containing brain and other high-risk tissues as an ingredient, (ii) sutures and (iii) vaccines. We concluded on these as follows:

- **Products directly containing high-risk tissues, eg brain and glands:** the small number of products concerned were identified and dealt with reasonably promptly.

- **Sutures:** discussions were promptly and effectively conducted with the major UK producer, safeguards introduced and use of UK materials phased out as speedily as practicable. The experts’ recommendations on sutures for general use were reasonable. On the specific question of continuing use in neurosurgery, we think with hindsight that it would have been preferable if the minority view among the experts that this should not continue had prevailed. We note, however, that as yet no cases of vCJD appear to be associated with their use.

- **Vaccines:** bovine material was not an ingredient in the finished product. What was unclear was whether its use as a growth medium for cells allowed infection to transmit. Results of studies on serum carried out by the NPU in which no infectivity was detected were not available until 1993. The general view before then was that this was a very low-risk material and that there was in any event only a remote risk of the BSE agent passing to humans via medicines. Given this, and the dangers of interruption to the vaccination programme, we think it was not unreasonable to conclude that the balance of risk to benefit favoured using the existing vaccines until alternative supplies became available.

982 The corollary, it seemed to us, was that the replacement process needed to be as speedy as possible. While the individual decisions taken by DH about each of the products concerned were reasonable, it can be seen with the benefit of hindsight that they contributed overall to a protracted process of achieving compliance with the
guidelines. Parallel delays were incurred in the treatment of veterinary products. It seems highly unlikely that so long a period of grace was envisaged by those taking decisions on vaccines in February 1989. Knowing what is now known, a harder line might have been taken to reduce the length of time that both people and animals continued to be exposed to suspect products. Although this is in part attributable to the false impression on risk, there was undoubted room for improvement in the way the guidelines were followed up. In particular we think it would have been better if:

i. there had been a handling plan with well-defined leadership that ‘managed’ the whole process to specific deadlines; and

ii. there had been clear expectations about reporting to top management and Ministers. We believe Ministers should take a lively interest in what is being done in their name, and that there should be clear presentation to them of important policy decisions.

983 We have noted that, once medical devices were identified as a concern, action to ensure their safety was handled purposefully. The PD style of administrative approach (see paragraph 865 above) might with advantage have been mirrored elsewhere and have led to a brisker momentum in phasing out suspect products.

984 Taking animal and human medicines as a whole, matters that were handled well included the heroic venture of a questionnaire to all licence holders to make good the faults in the database. Despite believing that action was purely precautionary, officials worked diligently to carry the follow-up action to its conclusion. The most urgent items were identified and dealt with promptly. A voluntary total switch of sourcing was secured, despite there being no firm evidence to offer of human risk. All this was achieved while struggling with the legacy of serious past failings in the running of the licensing system that were still being addressed.

**Research into pharmaceuticals**

985 As the story of the way medicines, and in particular vaccines, were handled has shown, there was a pressing need to establish whether bovine serum was infective. The only way to do this was by research. In Chapter 7 of Volume 7 we look at what happened to proposals for research into this.

986 The need for this research had been identified at the NIBSC discussion in May 1988, though it appears that no studies into the infectivity of serum were carried out as a result of this meeting.

987 However, the subject was not forgotten. When the Tyrrell Committee prepared its Report on research in spring 1989, one of the items it identified as a top priority was research into which bovine tissues were infective. Given the limitations on the numbers of animals, staff and suitable housing to carry out this research, the Committee agonised over which items should be done first. In its Report it said: ‘Nowhere else has the decision on priorities been more difficult.’
The decision it reached included ranking work on foetal calf serum and bovine serum albumin as a three-star (ie, top) priority.

In Chapter 7 of Volume 7 we trace the events that followed after the *Tyrrell Report* was presented to MAFF and DH. The proposal had a chequered history. In August 1989 Mr Gummer proposed and Mr Freeman agreed that it should be jointly sponsored and funded by both Departments, reflecting their joint responsibilities under the Medicines Act. Money was earmarked. However, following the first BSEWG meeting in September, Dr Pickles indicated to Mr Hagger that the MCA might want to consider whether the work was still needed, given that the action agreed by the BSEWG should ensure that contaminated material would not be entering pharmaceutical processing. She pointed out the need to secure Dr Tyrrell’s support for such an approach. In January Dr Pickles informed Ministers, at the time the *Tyrrell Report* was being published, that the MCA was acting on the recommendation together with its experts.

When Mr Lawrence circulated a chart showing progress on the Tyrrell recommendations in April 1990, he noted that work on serum research was being carried out at the NPU with industry funding, adding that trade restrictions and industry sourcing from outside the UK had lowered the priority on research into serum.

It is plain now that MAFF and DH had to an extent been operating at cross-purposes. DH had been concentrating solely on the proposal allocated to it, namely to secure research on serum. The *Tyrrell Report* had identified this item as just one element in the general programme of tissue testing. That other general work was being taken forward by MAFF and the NPU.

Mr Bradley of the CVL had reached the judgement in December 1989 that foetal calf serum was one of the top priority items for the limited animal resources available. The CVO agreed with him and it was included in the quota of tissues for transmission studies in the first year of the project with the instruction that it was important to get these studies under way as soon as possible. MAFF emerges with credit for its purposeful handling of the matter.

The work was done by the NPU and the results were made available in 1993. No infectivity was shown in these tests of foetal calf serum.

Thus despite its apparent downgrading by DH, the work was actually done. However, it seemed to us that this outcome was in some respects achieved despite inconsistencies in approach and a degree of mutual misunderstanding. Four features struck us as having complicated the process:

- The notion that industry might voluntarily sponsor and share the results of the work.
- The compartmentalising of the serum and other tissue study items, first by the Tyrrell Committee and then by MAFF, in how they allocated responsibilities. This led to confusion about how the work was carried out thereafter and who was calling the shots.
- The detached attitude of the medicines licensing divisions, which had an interest in the outcome.
• The divergent perceptions of MAFF, DH and SEAC about what was actually happening on the Tyrrell proposals.

Cosmetics and toiletries

995 We have grouped our material about the risk of transmission of BSE from cosmetics and toiletries in the same volume (Volume 7) as medicines because these products had much in common. In particular, both might apply animal materials to the skin, the eye or to mucous membranes. But, as we shall see, they were covered by a very different set of safety provisions.

The main products

996 Cosmetics using bovine materials fell into three categories. Those most likely to present a risk of BSE contamination were some ‘exotica’. They included anti-ageing and anti-wrinkle creams and ‘cellular extracts’ such as premium face creams. They might contain only lightly processed brain extracts, placental material, spleen and thymus. This was the most urgent category to tackle.

997 The second category consisted of ‘High Street’ topically applied products such as creams and toiletries applied to the skin, lips and eyelids. It also included items like soaps, shaving sticks and stick deodorants. The bovine materials used were heavily processed. Although questions were asked about ensuring the safety of this group of products, they were never considered a serious risk.

998 The third category of concern was bovine collagen used in implants. Dr Pickles was concerned initially about their use in unlicensed clinics as beauty preparations. We looked into their status. DH told us that in practice this material was used under medical supervision and thus treated as ‘prescription only medicines’. We concluded that we need not explore their cosmetic use separately.

Regulation

999 The Department of Trade and Industry (DTI) had regulatory responsibility for the cosmetics industry. At the time BSE emerged, Mr Richard Roscoe, who was a Grade 7 officer, headed the branch in charge of the safety of cosmetics sold in the UK. DTI looked to DH, and in particular to Dr R J Fielder, for advice about toxicity of products that were causing concern.

1000 The legislation governing safety was the EU Cosmetics Directive and Regulations made under the Consumer Protection Act 1987. We set out details of these provisions in Volume 7. Although cosmetics had to meet various safety requirements, they did not require a licence. Enforcement lay with local authority Trading Standards Departments, which would require some evidence of harm before seeking to intervene. The Secretary of State for Trade and Industry also had certain intervention powers. In practice the regulation of the industry operated very much on an informal and voluntary basis, relying on the industry to cooperate.
1001 Although identified in the *Tyrrell Report* in June 1989 as needing consideration, the cosmetics industry received no advice or guidance until February 1990. We deal briefly first with how this happened. We then look at what happened thereafter.

The Tyrrell recommendation on cosmetics

1002 The *Tyrrell Report* submitted in June 1989 had this to say about cosmetics:

Some uncertainty remains as to whether all the possible routes of transmission from bovine (and ovine) tissues to other species have been considered and appropriate action taken. Small scale users of bovine products such as the cosmetic industry, may not be covered by the present regulations and guidelines.

1003 Coupled with a wider proposition about investigating the fate of bovine products passing through as yet unrecognised routes, this item was given a three-star recommendation for further work. We return later to what happened to this wider proposal for an audit of bovine tissues.

1004 Despite what the Report said, no steps were taken by MAFF or DH to contact DTI about cosmetics. By good fortune, Mr Roscoe at DTI learned of the possible risk from BSE and independently decided to ask DH about it in January 1990. After he had consulted medicines licensing officials and Dr Pickles, Dr Fielder provided advice to Mr Roscoe. The gist of it was that DTI should warn the cosmetics industry via its trade association, the Cosmetic, Toiletry and Perfumery Association (CTPA), that it should reformulate products so as to exclude bovine offal or source it from outside the UK.

1005 This Mr Roscoe promptly did. The CTPA in turn relayed this advice in full, first to those of its members that made ‘premium skincare products’ (the ones most likely to contain offal extracts), and second to members generally. Ms Marion Kelly of the CTPA told us she was confident from members’ replies at the time about premium face creams that no products were using UK material. Replies to a request for information from the wider membership had not been retained.

Was the initial action adequate?

1006 We considered first the failure to alert DTI in 1989 to the need to consider cosmetic products in relation to BSE. We think that Dr Pickles, who had the lead on BSE in DH, should have done so. We were not impressed with her argument that the risk had been ‘so slight that effectively it could be disregarded’. This ignored the need to inform DTI as the regulatory Department and the fact that she could not have known which products were involved.

1007 Throughout the BSE story, Dr Pickles took many prompt and commendable initiatives to alert those concerned and to carry action forward. Sadly, in this case, Dr Pickles fell short of her normal high standards. She acknowledged to us that had she informed DTI, it could have addressed the issues six months earlier than it did.
She should have done so; but this lapse is minor in comparison with the commendable action taken by her in many other respects.

Within MAFF, we considered that responsibility for informing DTI lay with Mr Lowson, the head of Animal Health Division. We were not persuaded by Mr Lowson’s argument that he had only a hazy notion of DTI involvement in the cosmetics industry and that this was a human health matter so ‘something where one would expect other Departments to take the lead, particularly the Department of Health’. In our view Mr Lowson shared responsibility with Dr Pickles for ensuring the recommendations were properly assessed and followed up. We consider that, jointly with Dr Pickles, Mr Lowson should have promptly ensured that what the Tyrell Report said on cosmetics was drawn to the attention of DTI. The failure to do so contributed to several months’ delay in initiating action to secure the safety of cosmetic products.

Was DTI action adequate?

Mr Roscoe deserves credit for registering that BSE might pose problems for the cosmetics industry, and for acting promptly in seeking advice from DH, and passing it on to the CTPA. We agree that the Department’s statutory powers to intervene were not appropriate in these circumstances and that the only realistic course open to DTI was to persuade the industry to take voluntary action. Mr Roscoe’s letter and the response by the CTPA were together the most significant single action taken to address the risk from cosmetics.

However, we think it is unfortunate that Mr Roscoe did not make efforts to contact firms which were not members of the CTPA. It was indeed, as he said, a ‘flaw in the system . . . that we could not reach all manufacturers’.

Action taken thereafter

We turn now to the way matters were handled after the CTPA had distributed the DTI warning. Initially, everything went quiet. Dr Pickles had included a question about the adequacy of the action taken on cosmetics in a draft paper for the first meeting of SEAC in May 1990, but Mr Meldrum raised some concerns about the paper, and it did not go forward.

Three members of SEAC, Dr Tyrrell, Dr Kimberlin and Dr Will, attended the meeting of the BSEWG in July 1990, at which the DTI action on cosmetics was noted, and topical medicinal products were again given the all-clear.

However, SEAC itself did not turn to cosmetics until March 1991, when it asked for a paper on the topic. This task fell to Mr Murray, who had taken over from Dr Pickles as the DH secretary to SEAC. Mr Murray asked one of his staff to make enquiries of the CTPA into the use of bovine material in cosmetics. It was unusual not to approach DTI as the Department responsible for cosmetics safety. Mr Murray’s paper identified the uncertainties about the use of bovine material in cosmetics, and about small-scale producers that were not members of the CTPA.
SEAC discussed Mr Murray’s paper in July 1991, along with a paper from Dr Pickles about non-food uses of bovine material more generally. The Committee thought that in general no problems arose, but asked that DTI be reminded of the need to update the guidance to cosmetics manufacturers in the light of the emergence of BSE in other countries. After the meeting, Mr Murray asked Dr Pickles for her view on updated guidance, and she queried whether ‘fringe’ cosmetics companies were being kept informed by DTI, and advised Mr Murray, when writing to DTI with the guidance, to ask to be told about what happened thereafter.

Although Mrs Diane Whyte in DH drafted a letter to Mr Roscoe, it appears not to have been sent. Work continued somewhat slowly on the text of a draft letter to revise the guidance, but no contact was made with DTI. Meanwhile Mr Bradley of the CVL had told Mr Lawrence with some perspicacity that ‘contacts via DH/DTI do not inspire me with confidence’. He felt that MAFF needed either to go out to the industry to assess what kind of bovine material was really used in cosmetics and for what, or to have closer contact with the trade association. He observed:

I am not satisfied yet that the industry is in the clear and it is us that may shoulder some blame if it is later found ladies are rubbing cow brain or placenta on to their faces.

DH, as it happened, shared Mr Bradley’s view that they needed hard facts about the situation, and matters now took a different turn. DH had drawn attention to the lack of knowledge in its paper for SEAC. This led the Department in early 1992 to decide to put a series of detailed questions to the industry to clarify the situation and what action was being taken. The plan now was that, depending on the outcome, a meeting with the CTPA might be arranged, and, if need be, guidance considered later. DH officials did not consult DTI about these ideas. Although the object was sound, the exercise proved abortive. It was simply impracticable for the CTPA to provide answers from its members within three weeks to a list of 20 detailed questions asked out of the blue. There was no obligation on the industry to provide such information.

However, the CPTA did put a note in the May edition of its scientific newsletter to say that an enquiry had been received from DH about the use of bovine and ovine materials, and asked any of its members using these to contact the Association urgently. There was no positive response from CTPA members.

Ms Kelly told us she read this as meaning the members were not using such materials.

The CTPA’s response led DH to press ahead instead with efforts to draft the guidance letter originally called for by SEAC a year earlier. In July, Dr Fielder who, besides being the toxicological adviser to DH, was a UK member of the EU expert committee on cosmetics, took a hand. He pointed out that there was a risk of getting into deep water with the European Commission if they sought a voluntary ban. He suggested a meeting involving DTI before the CTPA was contacted again. This was a timely proposal. Among other things, it brought DTI back into the frame.

A meeting was held in September 1992 between officials from DH, DTI and MAFF and CTPA staff and members. There was a useful exchange of information. The outcome was agreement that DH would provide advice to the CTPA on
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1020 However, there was some follow-up contact by telephone and letter. The CTPA subsequently wrote to Dr Wight at DH to say that it had contacted a company using cerebrosides and that this material would be phased out by early 1993.

1021 From this point on, action moved to the European arena, with DTI in the lead. Before long the EU Working Party on Cosmetics became involved, with a view to preparing guidance at the European level. The DH reaction was that this was welcome as it helped to avoid the impression that the problem was solely one for the UK cosmetics industry. However, Dr Fielder flagged up the danger that the exercise might drag on, when in fact guidance needed to go out as soon as possible.

1022 Dr Fielder’s fears were realised – the exercise did indeed drag on. Preparation of European guidance became embroiled in slow procedures, infrequent meetings and national differences of view. COLIPA, the European trade association, played an active role providing reassurance that voluntary action had been taken.

1023 In March 1994, at the EU Health Council, all Member States except Germany supported the view that existing measures to contain BSE and protect public health were sufficient. It was eventually decided that the Cosmetics Directive need not be amended to ban the use of bovine material. It was later amended, after the period covered by this Inquiry and the emergence of vCJD.

1024 Meanwhile the CTPA had told DTI that it would prepare UK guidelines jointly with the French industry. The CTPA guidance to UK manufacturers was eventually issued in March 1994. It followed closely guidance from the World Health Organisation that had been issued in 1991 on inactivating TSEs and categorising tissues into four categories of infectivity. It is difficult to see how much, if any, value was added by the long delay.

The adequacy of the response

1025 A problem in assessing the adequacy of the response is the lack of knowledge that persists today about what cosmetics that contained bovine ingredients were on offer at the time and what precisely they were used for. With hindsight, we agree with Mr Bradley’s view that first-hand knowledge needed to be sought. We revert to this matter in Chapter 9.

1026 We recognise the handling problem created by the limited powers available to deal with an unproven threat like BSE which affected raw materials. We have commented elsewhere on the desirability of statutory powers to destroy dangerous material at source.
Given these considerations it can be seen with hindsight that two things were needed.

The first was purposeful leadership. There was continuing vagueness about who was in the lead. This confusion operated both between Departments and within DH. We are in no doubt that the lead should have lain with DTI, with professional advice from DH. Dr Pickles’s instinct that DTI should be asked to carry forward the guidance and required to report progress was sound.

The second was a sense of urgency. This was patently lacking. DH thought the risk was remote. Dr Wight told us that when she arrived in DH in 1991 to take over from Dr Pickles, she understood that all the significant action on BSE had by now been taken and her role was principally a watching brief. The perception that revised guidance for cosmetics was urgently needed and that certain matters needed to be vigorously followed up had faded away. Manufacturers were left to use up stocks, and checks were not made to ensure that they had reformulated their products.

Taken together, the effect was to leave large gaps in knowledge and to delay inordinately the issue of further advice. As with medicines, this has left unanswered questions about the products affected, how long production continued and on what scale. It seems to us undesirable that so little is known about products which offer a potential pathway to infection. This is a matter we believe DTI should review.