

**DFA 17 – MEDICINES
UPDATE 21 JANUARY 2000**

Para	Amendment
45	<p>[Insert new para 45A:]</p> <p>During his oral evidence Dr Jefferys was asked about the review of products that had been granted licences of right: [New footnote 56A: T112 p 14 line 18 – p 15 line 15]</p> <p>MR WALKER: ... The responsibilities for review that you have mentioned in relation to Branch MB3B, you are referring there to the review of safety, quality and efficacy of things that were on the market before the 1968 Medicines Act came into force?</p> <p>DR JEFFERYS: That is correct, and those products which were licensed up to 1975 also.</p> <p>MR WALKER: So licences of right were granted to products which were on the market as at 1968?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: Did products up to 1975 also have licences of right or was there some other reason for reviewing them?</p> <p>DR JEFFERYS: There were certain products which were granted licences around the period perhaps through to 1971 and 1972, which were also caught in the review, because although the Medicines Act was introduced in 1968, I think the first appointed day was in 1971 and there would be some products which would have been in-house at that period.</p> <p>MR WALKER: Thank you. I think there was a Section 4 Committee established to advise on those matters, that was the Committee on the Review of Medicines?</p> <p>DR JEFFERYS: That is correct.</p>
100 #	<p>[Insert new para 100A:]</p> <p>During his oral evidence Dr Jefferys was asked about the structure in Medicines Division: [New footnote 131A: T112 p 10 line 19 – p 12 line 9.]</p> <p>MR WALKER: ... If we then go on to paragraph 97, which I think we will find on page 28, we see that of course the Ministers cannot perform all these tasks personally. The executive arm of Government responsible for this areas was the Medicines Division. Paragraph 100 tells us that in medical structure in the Medicines Division, the Senior Principal Medical Officer, Dr Gerald Jones, was responsible for all professional work concerning drug regulation, new drug applications, adverse reactions, review of existing products, advertising the legislation and the servicing of all the advisory committees. In his statement, Dr Gerald Jones has told us that he had responsibility for policy formulation and advice to Ministers. Do you agree with that?</p> <p>DR JEFFERYS: Yes, I do. The only matter that is not covered here, of course, is that there were three parallel structures -- it does not mention the Pharmaceutical Secretariat -- very importantly both in MB5, which was concerned with the assessment, and in the Inspectorate. They reported through the Deputy Chief Pharmaceutical Officer and through to the Chief Pharmacist. There was a dotted-line relationship between them and Dr Gerald Jones, the Senior Principal Medical Officer, but there were in fact three parallel hierarchies, and that is actually detailed in the Evans-C[unliffe] Report, which the Committee also has before it.</p> <p>MR WALKER: That is correct. Paragraph 100 is simply dealing with the medical structure. I think that is how it begins. The three structures were the medical side, the physicians, the pharmaceutical side, the pharmacists, and the administrative side, the administrators?</p> <p>DR JEFFERYS: Yes. That also includes in certain information scientists, in other words who were included with the administrative branch.</p> <p>MR WALKER: The last point made in paragraph 100 is that Dr Gerald Jones reported to the Deputy Chief Medical Officer. I think that was Dr Harris at this time?</p> <p>DR JEFFERYS: Yes, I believe it was.</p>
101	<p>[Insert new para 101A:]</p> <p>During his oral evidence Dr Jefferys was asked about responsibility for making scientific judgments: [New footnote 132A: T112 p 12 line 10 – p 13 line 1]</p>

	<p>MR WALKER: ... In paragraph 101, we find a further point noted from Dr Gerald Jones' statement. That paragraph quotes his statement that his task was of an overall supervisory role, rather than to intervene in the scientific judgments of the individual expert committees. Do you agree with that?</p> <p>DR JEFFERYS: Yes, I do, although when there were particular matters of concern, he would be involved in the overall science as well. I think that does not quite come out there.</p> <p>MR WALKER: Thank you. You would be involved yourself if there were particular matters of concern in the overall science, would you?</p> <p>DR JEFFERYS: Yes, I would within my own branch, yes.</p> <p>MR WALKER: If there was a point which warranted discussing with Dr Jones, then you would discuss it with him?</p> <p>DR JEFFERYS: I certainly would, yes.</p>
102	<p>[Amend sub-paragraphs (ii) and (iii) to read as follows:]</p> <p>(ii.) MB3B: Review of medicines and the CDSM – Dr S Wood to September 1988 and Dr Adams from September 1988 to May 1990.</p> <p>(iii.) MB4: Adverse reactions and post-marketing surveillance – Dr WJ Jenkins to September 1988 and Dr S Wood from September 1988 until 1990.</p> <p>[Add to footnote 133: T112, pp 15–16]</p>
102	<p>[Insert new para 102A:]</p> <p>During his oral evidence Dr Jefferys was asked about the branches in Medicines Division: [New footnote 133A: T112 p 13 line 2 – p 14 line 17]</p> <p>MR WALKER: ... You mentioned the three hierarchies. We have a chart, I am afraid a fairly rudimentary one, which we have in our bundle DH01, tab 16, if that can be provided? I think it would be helpful at this point just to leave the DFA open, if that is possible, and glance at bundle DH01. I think the first document at tab 16 is a letter dated 30th November 1998, from the Medicines Control Agency, dealing with MCA material. If you leaf on about half a dozen pages, you will come to a page which confusingly has the number “1” in the bottom right-hand corner. When you reach it, you need to put the bundle on its side and then to squint because I am afraid the print is not very good. The heading is “Senior Staff in the Medicines Division and Medicines Control Agency”. We find the first row setting out the situation as at February 1988, and the second row setting out the situation as at December 1988. For the most part, situations are almost identical. The branch that you were Head of is MB3A, which is the third one across. As I understand it, the other medical branches are MB3B and MB4; is that right?</p> <p>DR JEFFERYS: That is correct, yes.</p> <p>MR WALKER: You tell us in your statement that Dr Wood, in May 1988, was Head of MB3B. We, I think, mistakenly on the basis of this document, had down Dr Adams, but as I understand it MB3B was responsible for review and for the Committee on Dental and Surgical Materials?</p> <p>DR JEFFERYS: That is correct, yes. Dr Wood moved across to take over from Dr Jenkins in, I think, September 1988, when Dr Adams was promoted to take over in charge of MB3B.</p> <p>MR WALKER: Yes.</p> <p>DR JEFFERYS: I also note it may be helpful on this organogram that the Senior Principal Medical Officer was not listed as the Joint Head here, it only mentions the Under-Secretary.</p>
102	<p>[Insert new para 102B:]</p> <p>During his oral evidence Dr Jefferys was asked about Branch MB4: [New footnote 133B: T112 p 15 line 16 – p 16 line 17]</p> <p>MR WALKER: It also told us about Dr Jenkins and he was Head, I think you told us, of Branch MB4, responsible for adverse reactions and new problems in respect of marketed drugs?</p> <p>DR JEFFERYS: Yes, that is correct. That is what today we would call “pharmacovigilance”, a term which was coming into use around that time, that was concerned with the safety of</p>

	<p>products already on the market.</p> <p>MR WALKER: Thank you. That first row looks as though it is incorrect there when it has Dr Mann as in charge of MB4?</p> <p>DR JEFFERYS: I think that might have been -- Dr Mann had been in charge of, I think, MB4, but some time previously Dr William Jenkins had taken over from him, I think in the period early 1985, mid 1985, but it was many years ago.</p> <p>MR WALKER: As I understand it, Dr Jenkins left Medicines Division in September 1988 and so Dr Wood took over responsibility for MB4?</p> <p>DR JEFFERYS: Yes she transferred into MB4 and Dr Adams was promoted to look after the review and the Committee on Dental and Surgical Materials, CDSM.</p> <p>MR WALKER: Thank you. It might be useful if I just note, for the purposes of our transcript, that these points would involve some slight revisions to paragraph 102 of DFA 17, where we have been working, I think, off this organogram, and we are now in a better state of knowledge as a result of your fourth statement.</p>
102	<p>[Insert new para 102C]</p> <p>In a supplementary statement to the Inquiry Dr Jefferys gave evidence about the role of MB4 in relation to BSE: [New footnote 133C: S Jefferys 5 (WS 419D) para 10.]</p> <p>10. In 1988, MB4 was responsible for monitoring the safety of licensed medicinal products; today this would be called Pharmacovigilance. This meant that the problems posed by BSE for existing products most naturally fell within its remit. This point was picked up by Professor Ferguson-Smith during my oral evidence to the Inquiry:</p> <p><i>“PROFESSOR FERGUSON-SMITH: Where there is a question of a risk of a particular ingredient, and that is notified to Medicines, then is that not equivalent to the notification of an adverse reaction?”</i></p> <p><i>DR JEFFERYS: Yes it is ...” (T 112 [Vol T12 Tab 2] page 39)</i></p> <p>Hence paragraph 8 of my minute to Dr Pickles dated 24 May 1988 (YB 88/5.24/3.1-3.2 at 3.2), where I wrote: “It also occurs to me that this is more of a long term issue and that it may well involve William Jenkins <u>since this is rather more an ADR problem than a New Drugs Group issue</u>. I am therefore copying your minute to him” (emphasis added).</p>
102	<p>[Insert new para 102D:]</p> <p>During his oral evidence Dr Jefferys was asked about his Branch, MB3A: [New footnote 133D: T112 p 20 line 4 – p 20 line 18]</p> <p>MR WALKER: If we turn then to your Branch MB3A ... it was responsible for the assessment of product licence applications with the exception of dental and surgical products?</p> <p>DR JEFFERYS: That is correct. It was responsible for the assessment of both new and abridged applications, but not those for dental and surgical materials, which were handled by the review group.</p> <p>MR WALKER: Thank you. That was sometimes referred to as “new drugs”?</p> <p>DR JEFFERYS: Yes.</p> <p>MR WALKER: They were new in the sense that they had not got a licence before?</p> <p>DR JEFFERYS: That is correct.</p>
102	<p>[Insert new para 102E:]</p> <p>During his oral evidence Dr Jefferys was asked about responsibility for new biological products: [New footnote 133E: T112 p 20 line 19 – p 23 line 13]</p> <p>MR WALKER: When one is talking about new drugs, that would include new biological materials?</p> <p>DR JEFFERYS: It would include the medical assessment of new biological applications, but not the pharmaceutical group, where I understand from looking through some of the papers in preparing for this, Dr Purves refers to what he called the “Biological Team” within MB5.</p>

	<p>MR WALKER: Thank you. Biologicals, as I understand it, are products which are derived from living organisms or products of living organisms; is that roughly right?</p> <p>DR JEFFERYS: Yes. They would comprise, at that time, two groups. They would comprise those of biotechnology-derived products, which were defined in the Directive, and what we might call the older biologicals, which as you rightly say were from animal or human origin.</p> <p>MR WALKER: Thank you. In your branch, Dr Rotblat in particular had expertise on biologicals?</p> <p>DR JEFFERYS: Yes, we had at that time five Senior Medical Officers, one of whom was working fulltime on the Opren litigation. Dr Rotblat had the expertise of vaccines and biotechnology products, although I should say that she was also very heavily involved in the assessment of new chemical entities.</p> <p>MR WALKER: Was there anybody else in your branch who had expertise on biologicals?</p> <p>DR JEFFERYS: No, there was not at that time. Could I perhaps add though that if one is talking about the assessment of the efficacy of medicinal product, that is a special skill of a reviewer who does not need to be an expert in biologicals to assess the medical data, because in the clinical trials of a new thrombolytic agent or in a new product, it is the same approach to analysing the data whether it would be a biological clinical trial -- a trial, rather, of a biological product -- or of a chemical product in terms of the efficacy part for the data. It may be important to state that.</p> <p>MR WALKER: Is the same true of safety?</p> <p>DR JEFFERYS: The same would be true of adverse reactions. Dr Rotblat had a particular expertise beyond that, which she had acquired in the field of biologicals and vaccines, but if we are talking about the assessment of a product, that would be a different matter.</p> <p>MR WALKER: If did you not have clinical trials to go on, or you did not have adverse reactions to examine, you would need Dr Rotblat's skills as opposed to the skills of others in your branch; is that right?</p> <p>DR JEFFERYS: She certainly had additional skills which were available to the Division, but the point I am making is that other biologicals may well have been assessed at that time by other members of staff, because there is no difference in a clinical trial in terms of its analysis, whether it is a biological or a chemical entity.</p> <p>...</p> <p>MR WALKER: Thank you. If medical policy issues arose in relation to applications for licences for biologicals, then that would be for your branch to advise on, is that right?</p> <p>DR JEFFERYS: In conjunction with the pharmacists, it is very rare that you would have a purely medical issue. If it were to be purely medical, then yes.</p> <p>MR WALKER: If it were joint, it would be your branch in conjunction with the pharmacists?</p> <p>DR JEFFERYS: Indeed.</p>
102	<p>[Insert new para 102F]</p> <p>In his supplementary statement to the Inquiry, Dr Jones gave evidence about the responsibilities of branch MB3A: [New footnote 133F: S Jones G 3 (WS 190B) paras 2-5.]</p> <p><i>Responsibilities of MB3A</i></p> <ol style="list-style-type: none"> 2. It seems that some misunderstanding may have arisen as to the sphere of responsibilities of MB3A, which was the branch headed by Dr Jefferys. It was not the case that Dr Jefferys' branch had any lead on BSE, nor was this the natural or logical branch to which such responsibility would fall. There was in fact no such branch (see paragraphs 9 to 11 below). 3. As the Inquiry is aware, at the relevant time, Medicines Division was organised into three parallel structures: doctors, administrators and pharmacists. The Division was jointly headed by Mr Clive Wilson and myself, with the administrators reporting to Mr Wilson and the "professionals" (doctors and pharmacists) reporting to me. 4. Dr Jefferys' branch was responsible for processing new drug applications only, together with variations and abridged applications, unless those applications related to dental and surgical materials, in which case they were

	<p>handled by MB3B. The fact that Dr Jefferys' branch was termed "New Drugs and Biologicals" is misleading, since that term implies that Dr Jefferys' branch had a general responsibility for biological matters. That is not the case. My understanding is that the group was described as "New Drugs and Biologicals" simply because it was responsible for assessing the safety of new drugs manufactured from both synthetic and biological materials. The methods of evaluating those two types of drug applications were different.</p> <p>5. There was in fact no particular branch with a general responsibility for biological matters, or which would be the automatic point of reference if a problem were to arise with regard to a drug with a biological component. Generally speaking, if the problem arose in relation to starting material, that would be the province of the pharmacist inspectorate; if there was a safety issue which had arisen as a result of adverse reaction reporting, the problem would be dealt with by the doctors in the adverse reaction branch.</p>
102	<p>[Insert new para 102G]</p> <p>In a supplementary statement to the Inquiry, Dr Jefferys gave further evidence about the role of Branch MB3A: [New footnote 133G: S Jefferys 5 (WS419D) paras 2-9.]</p> <p>3. The Inquiry has expressed an interest in the issue of whether, in April 1988, I could have considered whether there was anything which could usefully be done before BSE went before the Biologicals subcommittee and before the Southwood Working Party provided any advice. In particular, the Inquiry has asked whether I could have ordered that a database search to see whether and to what extent the database provided information on the use of bovine based biologicals.</p> <p>4. In considering these issues, I am concerned that the Inquiry may believe that my Branch, MB3A, was responsible for <u>all</u> biological products including existing biological products. Such a view is incorrect. MB3A was not responsible for any existing products (the only exception being the medical assessment of variations). It was responsible for the medical assessment of new (drugs and biological products) as distinguished from the medical assessment of new (surgical and dental materials) which were the responsibility of MB3B. MB3A was only responsible for medical and toxicological assessments; the pharmaceutical and quality assessment of all products was the responsibility of MB5.</p> <p>5. Further, as head of MB3A I had no responsibility for the Medicines Division database which fell within the remit of, and was the responsibility of, MB1. On this point I should remind the Inquiry that the staff of MB1 included information pharmacists, such as Mrs Alderman, who were trained in and responsible for operating the database.</p> <p>6. The Inquiry has expressed an interest in which Branch of Medicines Division was responsible for those existing biological products which did not fall within the remit of the Committee on the Review of Medicines and MB3B. Such products would have fallen into two distinct categories. First, older existing products which had previously held product licences of right but had been granted full product licences following consideration by MB3B as advised by the CRM. Secondly, more recent existing products which had been granted full product licences following consideration by MB3A (and MB5 in relation to pharmaceutical and quality issues) as advised by the Committee on the Safety of Medicines.</p> <p>7. The first point to make is that MB3A was in general terms responsible for neither category of products. I am concerned that the Inquiry has not fully</p>

	<p>appreciated the implications of the fact that the work of MB3A was application driven. By this I mean that it involved considering the medical aspects of applications submitted by pharmaceutical companies for new, varied and abridged product licences. It was no part of the role of MB3A to assess the safety of existing products unless an application was submitted by <u>a pharmaceutical company to the Licensing Authority</u> for a varied product licence. Compulsory safety variations (variations initiated by the Licensing Authority for safety reasons) were the responsibility of MB4 not MB3A.</p> <p>8. Once a product has been licensed its manufacturer is entitled to sell that product for a period of 5 years without further reference to Medicines Division provided that the manufacturer does not alter the ingredients used or the manner in which the product is made. If the manufacturer does wish to make any such alterations he must apply for a varied or abridged product licence and that application will be considered by MB5. If the manufacturer wishes to change only the indications or the dosage of the product that application will be considered by MB3A. If the manufacturer makes no such application, it is free to sell the product for 5 years after which it must apply for the product licence to be renewed. The application for renewal of the product licence would not, in 1988, have been the responsibility of MB3A because “renewals of product licences were handled purely administratively without input from physicians because of the staff shortages” [S Jefferys WS 419B paragraph 10]. My recollection is that this decision was taken at a meeting chaired by Norman Hale and Gerald Jones and attended by all branch heads. I believe that the meeting probably took place in late 1986 or early 1987. This policy remained in place for several years. The Inquiry may be interested to know that renewals are currently handled by the Post-Licensing division (the successor to MB4) rather than by the Licensing Division.</p> <p>9. The only exception to the procedure described above relates to circumstances in which doubts are raised about the safety of an existing product. This is an important issue and there is, and was in 1988, a separate Branch of Medicines Division specifically dedicated to dealing with such issues. In 1988, the relevant Branch was MB4 headed by Dr William Jenkins. In the present day MCA the equivalent function is performed by the Post-Licensing Division.</p>
103	<p>[Insert new para 103A]</p> <p>Dr Gerald Jones said in oral evidence to the Inquiry:</p> <p>‘...The medical staff here, you have mentioned Dr Jeffreys, Wood and Jenkins, they reported to me directly. The administrative staff, on the left Hagger, Robertson and Franks -- sorry, he is right over the other side -- those three reported to Wilson directly. One of the easiest ways to understand in the Civil Service who is in charge of what is to ask who writes your annual report. I wrote Dr Jeffrey’s annual report and it was countersigned by my senior officer. The senior pharmacists had a triple arrangement. They reported to Brian Wills and to me and to Clive Wilson. So there were three people signing the annual reports. But it was always understood that for professional things in the Division I would assume responsibility.’ [Insert new footnote 134A: T136, p 6, line 3]</p>
103	<p>[Insert new para 103B:]</p> <p>During his oral evidence Dr Jefferys was asked about Branches MB1 and 2: [New footnote 134B: T112 p 19 line 17 – p 20 line 3]</p> <p>MR WALKER: We will come back to the database. The other branches in Medicines Division were MB1 and MB2. They comprised administrative staff who reported to the Under-Secretary?</p> <p>DR JEFFERYS: Correct. Also, as I did mention, there would be information scientists</p>

	<p>working there and on the database in MB1, as I recall.</p> <p>MR WALKER: You have told the Committee that you worked closely with Mr David Hagger, who was the Grade 5 in charge of MB1, and he reported to the Under-Secretary, who by 1988 was Mr Wilson?</p> <p>DR JEFFERYS: Correct.</p>
104	<p>[Insert new para 104A:]</p> <p>During his oral evidence Dr Jefferys was asked about the responsibility of Branch MB3A in relation to BSE: [New footnote 135A: T112 p 23 line 14 – p 25 line 15]</p> <p>MR WALKER: ... You have said that no branch had sole responsibility for BSE. In the event we know that your branch did have a role in relation to BSE. Would you say that your branch had a responsibility to lead on policy advice concerning the potential impact of BSE on biological products?</p> <p>DR JEFFERYS: Certainly not in the first phase, no. Our initial approach was to be involved in the assessment of those new products coming through. Indeed, I noted in May of 1988 there was a clinical trial for a product where this issue was raised by the Biological Subcommittee. If you look at the minutes there, it is recorded that concerns over viral inactivation were raised, and in the minutes of that meeting, it refers to the need for the applicant to demonstrate the ability to inactivate hardy viruses, and indeed for spiking studies, and that is in the minutes of the Biological Subcommittee and the CSO of May 1988. So we were taking the action on new products as this information became available to us in the late April.</p> <p>MR WALKER: That is very helpful. I have seen from the papers that there had been a requirement for spiking studies, and you have just been discussing the position in relation to an application for a product licence and the requirement that will be made there was could you please do the spiking studies? That involved your branch?</p> <p>DR JEFFERYS: This would have been an issue which would have been raised by the pharmacists because clearly it is a matter of quality in there, but I was noting that this was an issue which was being applied to a new drug application, in fact a Clinical Trial Certificate which was before us in the May of 1988.</p> <p>MR WALKER: Yes. I think what you were saying earlier, you were saying that your branch had a role in that?</p> <p>DR JEFFERYS: We were responsible for the medical input to that, but clearly this would ultimately be one set of questions put to an applicant, but it would be largely the pharmaceutical branch who would be making these points because it was their area of concern over the safety of the starting material.</p> <p>LORD PHILLIPS: Spiking studies involve what precisely?</p> <p>DR JEFFERYS: These would be taking a hardy virus which would be introduced into the product to see whether this was inactivated by the manufacturing processes.</p> <p>MR WALKER: Could you help me a little bit more about why your branch in the early stages would not have had a responsibility for anything other than the new application side?</p> <p>DR JEFFERYS: I think solely, that that our responsibility at that time was for assessing the new drug applications. That was our remit.</p>
104	<p>[Insert new para 104B:]</p> <p>During his oral evidence Dr Jefferys was asked about responsibility within Medicines Division for older products in relation to BSE: [New footnote 135B: T112 page p 25 line 15 – p 29 line 25]</p> <p>DR JEFFERYS: ... There were others in the Division who would have had responsibility for the older products, and indeed for other types of products, the dental and surgical materials.</p> <p>MR WALKER: The older products, that is dealt with under the review process?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: I think you mentioned just now that might have gone for licences up to 1975. In that review process, if a question arose as to a biological product, would the people conducting the review turn to those with expertise in biologicals?</p> <p>DR JEFFERYS: They would have been, interestingly, as I explained, MB5 had a horizontal structure, so the pharmacists assessing on the review side would have been the same as assessing for new drug applications. So the pharmacists would have been dealing with this</p>

	<p>and then working with the physicians on the review team, MB3B.</p> <p>MR WALKER: If a question arose as to a biological product in relation to that review, the relevant Section 4 Committee would be the Committee on Safety of Medicines?</p> <p>DR JEFFERYS: No, the Committee on the Review of Medicines. My staff would not have been involved in that, just as if there was a dental and surgical material, the pharmacists would have been from MB5, the physicians for that would also have been from MB3B, their team. There was this lack of different structures for the pharmacists as for the physicians. That is why I made the point earlier. I think it may have been missed. It was a complex structure to operate.</p> <p>MR WALKER: It had not been missed. What I am trying to do is just to explore what it actually means. If then we have a product which is licenced after 1975, a biological product, licensed after 1975, and a question arises on some aspect of that biological product, what part of the medical team in the Medicines Division had responsibility for it?</p> <p>DR JEFFERYS: This is a difficult issue, because a decision, as I recall, had been made some little while before, about 18 months, two years before, that for resource reasons the renewals would be purely handled administratively. It was a situation which persisted for a little time. The normal way of dealing with those type of products would be through the renewal. A product licence would last for five years and was then called in for renewal. Today we have a team -- this is a post-licensing function, and it would be handled by the renewals team. It is fair to say there was a small number of products which we might say were a lacunae gap, which were not the provision of any professional branches at that time. If there were to have been, they would have fallen within the Safety Group because they were products already marketed.</p> <p>MR WALKER: Which is the Safety Group?</p> <p>DR JEFFERYS: This would be MB4, which today is what we would call "pharmacovigilance", but that term was only coming into use about that era.</p> <p>PROFESSOR FERGUSON-SMITH: I am not clear about these old products that would be handled administratively. What does that mean?</p> <p>DR JEFFERYS: It means that the renewal would be issued purely as an administrative act. There would not have been a professional assessment of the renewal as there is a target assessment today. Today every licence has to reapply at a five-year point and is reconsidered.</p> <p>PROFESSOR FERGUSON-SMITH: What was the purpose of the review of the old medicines, then, if it was not to look at their efficacy and safety?</p> <p>DR JEFFERYS: Well, I thought the review was to look at those which had been given product licences of right and were already on the market from 1971 and 1972, so those products were all being reviewed over that period under the requirement of the EC Directive. What I am saying, in answer to the question, is that there were a number of products, probably very small in terms of biologicals, which did not fit with the particular structure which we had in Medicines Division at that time, not something that pertains today.</p> <p>MR WALKER: As I understand it, we have three groups of medicinal products, one is those which have been given a licence any time up to 1975 which, might well be licences of right. The Committee on Review of Medicines was responsible for advising on those, and the Reviews Section, the review branch, MB3B, handled the medical issues which arose in relation to those?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: At the other end, we have applications for a licence, and they are part of your routine day-to-day work in MB3A?</p> <p>DR JEFFERYS: They would be the responsibility of my branch, yes.</p> <p>MR WALKER: On those, you would turn for advice to the Committee on Safety of Medicines?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: The difficult area that we are trying to explore, and where it seems from what you say that there was something of a lacuna, is products which have got a licence some time after 1975 and where a question arose, in particular biological products. As I understand it, on the medical side, there was no part of the Medicines Division which had responsibility for that, is that what you are saying?</p> <p>DR JEFFERYS: That is correct in terms of at that moment. Clearly, when guidance was issued, it was made very clear that the guidance applied to all products. If you are asking me about the period, which I think you are, of April, May, June, then there were a small number of products which fell into that gap, where there was not an obvious home for them in the</p>
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	structure which existed. It is not something which happens today, but yes, there was at that time.
104	<p>[Insert new para 104C:]</p> <p>During his oral evidence Dr Jefferys was asked about the responsibilities of the section 4 committees in relation to these older products: [New footnote 135C: T112 p 30 line 1 – p 32 line 21]</p> <p>MR WALKER: On the advisory side, looking at the advisory committees, if we are looking at these products which had received a licence after 1975, the Section 4 Committee to advise on them would be the Committee on the Safety of Medicines?</p> <p>DR JEFFERYS: Yes, they would fall within the Committee on the Safety of Medicines or the Committee on Dental and Surgical Materials. I should just perhaps correct that the majority of products which fall into the review, the cut-off date would have been 1971.</p> <p>MR WALKER: Thank you. If we were concerned with biologicals, so far as the Committee on Safety of Medicines were concerned, they would then turn to their subcommittee, the Biological Subcommittee?</p> <p>DR JEFFERYS: Yes, that committee would have given advice to the CSM.</p> <p>MR WALKER: Would I be right in thinking that the Biological Subcommittee would have a particular responsibility for considering advice with respect to safety in relation to human use of biological products?</p> <p>DR JEFFERYS: Safety in relation to quality. The Biological Subcommittee was primarily concerned with the quality issues, but if you are referring to BSE, which was a matter of the quality of the starting material, yes, that would have been the group.</p> <p>MR WALKER: I would just like to ascertain why it is you are restricting this to quality rather to safety and efficacy. The Biological Subcommittee would not just be looking at pharmaceutical questions with pharmacists; it would be looking at medical questions as well with physicians, would it not?</p> <p>DR JEFFERYS: No, it would not. The Biological Subcommittee was concerned with looking at the quality of biologicals and therefore was analogous to the other subcommittee, the Committee on Chemistry, Pharmacy and Standards, CPS. They were two parallel groups. The efficacy and the safety of biologicals would have been considered by the Subcommittee, SEAR, subcommittee on Safety, Efficacy and Adverse Reactions, which looked at both biologicals and chemicals, making no distinction, the point I made earlier, and that is witnessed by if you look at the consideration of the paper produced by Dr Purves and Dr Rotblat, that was seen by both subcommittees. So the Biological Subcommittee only had the expertise to look at the quality issues for biological products. Safety and efficacy would have been looked at, and still are, by the SEAR Subcommittee.</p> <p>MR WALKER: We know that in the event BSE was looked at by both?</p> <p>DR JEFFERYS: Indeed it was.</p> <p>MR WALKER: The responsibility for looking after the medical side of those two subcommittees, both the Biological Subcommittee and SEAR, fell to your branch, did it not?</p> <p>DR JEFFERYS: We were the majority users of the Biological Subcommittee and the SEAR Subcommittee, but again I would point out that actually with SEAR, approximately half the work, as its name implied, would also come through from the adverse reactions side; that was its remit, the safety side on that. For the biologicals, yes, we would provide medical commentary on that, but the principal input to the Biological Subcommittee would come from the pharmacists. Indeed, it was noteworthy that it would be the pharmacists' papers on an application which would go to the Biological Subcommittee, and in the majority of instances the medical paper would only been joined with that at the time it went to the Committee on the Safety of Medicines. I am saying the medical paper would have gone to the Subcommittee on Efficacy and Adverse Reactions, and the two were then put together to remain for the Committee on the Safety of Medicines.</p>
105	<p>[Insert new paragraph 105A]</p> <p>Dr Gerald Jones said in a supplementary statement to the Inquiry:</p> <p>'BSE had implications across the Division. The guidelines applied to all medicinal products, including dental and surgical materials. They applied equally to drugs which were already on the market and new drugs, which had not yet been granted a licence. The former category</p>

	<p>included drugs which had been given a product licence of right, prior to the enactment of the Medicines Act (these were waiting to be reviewed); those drugs which had once held a licence of right but which had been reviewed and those drugs which had been granted a licence after 1975.</p> <p>It was therefore perceived that BSE should be dealt with not by any particular individual or branch but on a team basis across the Division, within its existing structure. Clearly, however, this was new work, which was additional to and different from work ordinarily carried out by those involved in it. Administrators, doctors and pharmacists worked together.'</p> <p>[Insert new footnote 136A: S Jones G 2 (WS190B), paras 9–10]</p>
109	<p>[Insert new para 109A]</p> <p>Dr Gerald Jones commented further on the structure of Medicines Division during oral evidence to the Inquiry. In discussions about the pharmaceutical branches, MB5A, MB5B, and MB5C the following exchange occurred:</p> <p>'MR WALKER: The three sub-branches were there in 1988, were they? DR JONES: Of pharmacists? MR WALKER: Yes, pharmacists. DR JONES: Yes, these three pharmacists were in place throughout 1988 and early 1989. MR WALKER: They reported to you. They also reported to Dr Wills, is that correct? DR JONES: Yes, Mr Wills. As I recall, yes. MR WALKER: And on what things did they report to you and on what things did they report to others? DR JONES: It was not on separate things. I cannot remember the exact format of these wretched annual reports, but there is room for different people to write comments and to put a signature in; and people just filled in. I suppose I would be restricting myself to professional things. MR WALKER: Thank you. Unless there is anything else you would like to say about this organogram and the branches, I was going to turn to another little chart. DR JONES: Very briefly, to make it a bit easier, you are probably not going to be interested very much in Dr Rogers. He was the senior pharmacist in charge of the BP, British Pharmacopoeia, which I do not think enters into any of the discussions that you have had about medicines at all. Everybody else will have been involved at some point in Medicines Division on the issues you are talking about. MR WALKER: In relation to BSE? DR JONES: In relation to BSE Mr Hagger, Mr Robertson, Dr Jefferys, Dr Wood, Dr Jenkins, Mr Stewart, not Mr Hartley, Mr Franks indirectly, Mr Grimshaw almost not at this time, and of course Wilson and Jones. MR WALKER: Mr Hartley you said not involved? DR JONES: Not over this particular -- Mr Hartley was in charge of the inspectorate; the pharmacists we had in London and throughout the country inspecting pharmaceutical manufacturing sites. That is a job that was going on all the time. The reason I say that I have to mention him is because one of the most pressing and urgent issues you might ever face in the division would come from Mr Hartley's section, that intravenous fluids are contaminated with bacteria; and you have to be ready to move within 24 hours. That was not an issue with BSE, so he was not a part of that at all. MR WALKER: Mr Grimshaw you mention, MB8 we have down here as being in existence from 1989. What was his role? DR JONES: He was in the Division before he was promoted, after I left in 1989, to Assistant Secretary. Before then he was the Principal. He was in charge of most of the computer liaison going on in the Division. I am not sure why he appeared in the chart, except after I left he had his well deserved promotion to Grade 5, then of course he looks as if he was one of the senior staff. He was not a branch head during the period we are talking about in 1988 and early 1989. He would have no direct role, except he was responsible for the massive computer change going on at that time. MR WALKER: Dr Jefferys mentioned there were information specialists. Do you recall that from his transcript? DR JONES: Yes, I do.</p>

	<p>MR WALKER: Which branch were they in?</p> <p>DR JONES: I think they reported to Mr Stewart.</p> <p>MR WALKER: In the pharmaceutical branch?</p> <p>DR JONES: Correct. They are information pharmacists, if you like. They have a background in pharmacy which was required before you could put any data about drugs into a computer.'</p> <p>[Insert new footnote 140A: T136, p 7, line 19]</p>
109	<p>[Insert new para 109B]</p> <p>Dr Gerald Jones was asked about the section 4 committees and sub-committees during his oral evidence:</p> <p>'MR WALKER: Could we take you to the little chart of committees? I hope we have accurately set out there the Section 4 committees. That is the first row: the Committee on Safety of Medicines, the Committee on Dental and Surgical Materials, the Committee on Review of Medicines, the Veterinary Products Committee and the British Pharmacopoeia Commission. As I understand it the first three of those committees had available to them three sub-committees. So that each of the three sub-committees would do work for each of the first three of the main committees; is that right?</p> <p>DR JONES: Correct.</p> <p>MR WALKER: By contrast, the Veterinary Products Committee had its own Biologicals Sub-committee, is that your understanding?</p> <p>DR JONES: I cannot confirm the VPC arrangements because it was the responsibility of MAFF. I did not know anything about it and never attended it. So I cannot confirm that directly, I am afraid.</p> <p>MR WALKER: This chart does not mention the Medicines Commission. Were you involved with the Medicines Commission?</p> <p>DR JONES: Yes, that was the only of these committees from which I would read all the papers religiously every meeting. I was a medical assessor to the Section 2 Medicines Commission.'</p> <p>[Insert new footnote 140B: T136, p 10, line 19]</p>
109	<p>[Insert new para 109C:]</p> <p>During his oral evidence Dr Jefferys was asked about Branch MB5: [New footnote 140C: T112 p 16 line 18 – p 19 line 6]</p> <p>MR WALKER: Still looking at the organogram, we have a Branch MB5. As I understand it, that comprised the pharmacists?</p> <p>DR JEFFERYS: That comprised the pharmaceutical assessors. It might help the Committee to know that that was organised in a rather different structure in that the pharmacists would cover all aspects, so they were not organised in terms of the review or in terms of new drugs, and just to rather complicate matters, they were organised on a geographical regional basis. That is the country was divided into certain regions which happened to coincide with those which were under the Inspectorate, also a group which interestingly is not on -- it is on the lower third chart here, under "Mr Hartley", but they were grouped in regions. Therefore the pharmaceutical assessor might be working on a product for the review for the Committee on Dental and Surgical Materials, as well as a new drug application. So the two structures, the pharmaceutical and medical, were not superimposable structures at that time.</p> <p>MR WALKER: Is it possible to say in general terms what the distinction was between the nature of the work that the pharmacists were doing and the nature of the work that the physicians in the medical branches were doing?</p> <p>DR JEFFERYS: Yes, the physicians were responsible for assessing what we call "part 4" of the dossier, that is the efficacy and the safety resulting from clinical trials. Also within my branch at that time were the toxicologists, who would be looking at preclinical-- that is animal toxicology and animal pharmacology. The pharmacists would be looking at the quality issues, the starting materials, the manufacture, the composition of the product and its processing, and the specification of the final product itself. That would be the same process whether it was a biological agent or whether it was a chemical agent.</p> <p>MR WALKER: If a question of medical policy arose, would that fall to the physicians to deal</p>

	<p>with?</p> <p>DR JEFFERYS: If it was a medical issue, yes, that would be for the physicians. If it was a matter of quality, that would fall to the pharmacists.</p> <p>MR WALKER: Thank you. Is there some overlap?</p> <p>DR JEFFERYS: There can always be matters of quality which may have some implication on efficacy and/or safety. I think it was recognised, and was recognised contemporaneously with this in the Evans-Cunliffe Report that perhaps this was not the optimal structure, and indeed it is very different from the structure which we now have as a control agency, which is that of integrated functions and teams focused on the dossier, whereby physicians, toxicologists, statisticians and physicians work together in one team. That was not the structure which we had in 1988.</p> <p>MR WALKER: If one were to use as a rule of thumb questions of efficacy and safety, questions for physicians, questions of quality for pharmacists, one would have to recognise there is scope for overlap?</p> <p>DR JEFFERYS: Indeed, and of course safety in manufacturing would be an issue which would be raised by the pharmacists. Indeed, the current directive does not actually refer to quality, it refers to quality in relation to safety, an interesting nuance which is in the European legislation, EC Dir. 65/65.</p>
118	<p>[Insert new para 118A:]</p> <p>During his oral evidence Dr Jefferys was asked about the workload and resources of Medicines Division: [New footnote 151A: T112 p 75 line 7 – p 79 line 9]</p> <p>MR WALKER: I was then going to move on to touch briefly on workload and resources. You have mentioned a number of aspects of your workload, deadlines, and you have also mentioned difficulties with the computer. In relation to the gold files that you mentioned earlier, there was a problem about tracking them within the building, as I understand it?</p> <p>DR JEFFERYS: Yes, there was. We had difficulties with the file tracking system which was suboptimal at that stage and I think again the Evans-Cunliffe Report highlights this and a new tracking system was being put in. Just to put this into context, we are talking of 18,000 gold files. Perhaps members of the Committee might imagine they are a couple of inches thick. Many have daughter files and can be one to two metres thick of files. There are 18,000 of these and you can imagine the amount that is stored off site. So to give you an idea of the files, that excludes the data, and the data involving a new drug at that time would be probably one to 200 volumes of data. Today, for a new drug, 700 volumes of data, each one of which would be the size of one of these bundles. To put it into context.</p> <p>PROFESSOR FERGUSON-SMITH: It would be quicker to go back to the manufacturers than to thumb through all these miles of files?</p> <p>DR JEFFERYS: It might have been on occasions, but equally a product evolves over time, so it might for some of them, yes, it might not for others.</p> <p>MR WALKER: The routine work, if I can call it that, for your branch, medical assessments of applications for licences, to what extent was that fixed by reference to the dates of meetings of the relevant committees?</p> <p>DR JEFFERYS: My branch at the time had a complement of five senior medical officers, one of whom had been taken away from my command to work on the Open, the litigation where Ministers were in the courts on this at that particular time. We had three toxicologists, two on extended maternity leave. That was the scope of my branch, with associated sections.</p> <p>I think in the routine work was the processing of new drug applications and the abridged applications. It is worth putting into context that many of those were not routine and I think I was given notice of this as it were, and looking back through the Committee on the Safety of Medicine minutes, I think in September 1988 I reported to the committee, and it is in the bundles, that we had assessed 51 -- or rather they had seen, we had assessed, 51 new drug licence applications that year and processed some 34 hearings, as I recall from memory. Much of that work of course was under two sorts of deadlines. The first is they were now one year into the new European consultation procedure set up under Directive 87/21 which defined time limits in which the United Kingdom, if selected, had to put a report to the relevant European Committee. Some of these were lifesaving medicines in the field of cancer. We were handling the first of the clock busters for infarctions for thrombolytics with very great advances for the treatment of heart attack.</p> <p>We were also handling, I note at that time, erythropoietin, a very important hormone</p>

	<p>which has revolutionised the lives of patients on dialysis. The division -- my branch was involved in some of the litigation over haemophilia and the consequences of the litigation on exclusivity, a matter that still continues in the courts, and this is a battle between the innovative and generic industry about whether the data could be used for generic SmithKline & French judgment at the time.</p> <p>In addition, we were handling -- and the minutes shows this -- the important issues in my own division of the consequences of HIV. We were looking at the new products which had been introduced, new techniques for inactivating HIV for the treatment of haemophilia and other clotting disorders which were urgently needed. Those are the issues my branch was facing. The division as a whole, as Gerald Jones highlighted, was facing a number of serious public health issues. I suppose at the time --</p> <p>MR WALKER: I was interested to know how much your work load tied in with the dates of meetings of the relevant committees. That is my question.</p> <p>DR JEFFERYS: If we were meeting European deadlines, and all these things do, if they are to involve the Committee for Safety of Medicines, they had to be before them otherwise within a short period of time under which the UK was under treaty obligations to provide the answers. Equally, as Evans-Cunliffe shows at the time, the consequence is we had a backlog of abridged applications. That is why they changed the whole structure and funding arrangements which came in and that is what led to the creation of the Medicines Control Agency. We were facing threats of litigation because there was a European deadline. If that is not met, the company can bring litigation and seek damages against Ministers for this, but equally beyond that, if you are not licencing, then there are important public health medicines out there which were not getting to patients. I think it needs to be set -- all this is detailed in the public domain because there was a review at the time.</p>
136	<p>[Insert new para 136A:]</p> <p>During his oral evidence Dr Jefferys was asked about the role of the Principal Medical Assessor to the biologicals subcommittee: [New footnote 169A: T112 p 32 line 22– p 34 line 14]</p> <p>MR WALKER: You were the Principal Medical Assessor to the Biological Subcommittee?</p> <p>DR JEFFERYS: That is correct.</p> <p>MR WALKER: What did that involve you in, if the Biological Subcommittee was simply looking at quality?</p> <p>DR JEFFERYS: My role there would be to give advice, if needed, on particular issues of the medical context of a product, because obviously if one is looking at quality, there may be a need to have a comment made on certain medical aspects there, but it was why I would not routinely attend all the meetings. Dr Purves, as the pharmaceutical assessor, would sit through the whole of the meetings. I would attend parts of them, if there was a particular matter, but I would not routinely attend the Biological Subcommittee meeting, or the whole of it, whereas I would sit through and attend the whole of the SEAR Subcommittee meeting.</p> <p>MR WALKER: If there was a question about safety which cropped up in something that the Biological Subcommittee was looking at, would it be your role to raise that?</p> <p>DR JEFFERYS: That would normally be handled by the individual medical assessor looking for the products there. The role of the principal assessor is to be there as a more senior figure who the Chairman can turn to if there are particular matters that he wants taking forward or issues. It was that sort of a role.</p> <p>MR WALKER: The medical assessor would be somebody in your branch?</p> <p>DR JEFFERYS: Yes, usually, or if it was dental and surgical material in the other branch, or if it was a review product. To answer you correctly, no, it would be from whichever branch the question had been put before the Subcommittee. I don't think that is witnessed in the various minutes which you see, dental, surgical and review products flowing through the Subcommittee. I should perhaps stress, the Subcommittee was also a Subcommittee of the CDSM and the CRM. It was not wholly a subcommittee of the Committee on Safety of Medicines.</p> <p>MR WALKER: So for the earlier products, the Committee on Review of Medicines might refer that to the Biological Subcommittee for advice?</p> <p>DR JEFFERYS: Indeed it did, yes.</p>
136	<p>[Insert new para 136B:]</p>

	<p>During his oral evidence Dr Jefferys was asked about the role of the principal medical assessor for SEAR: [New footnote 169B: T112 p 34 line 15 – p 37 line 1]</p> <p>MR WALKER: Similarly, you were the principal medical assessor for SEAR and the medical assessments for matters that were being dealt with by SEAR would come from people in your branch, if it related to things other than the dental and surgical materials or the review?</p> <p>DR JEFFERYS: Yes, or safety issues, yes. If they related to new drug applications, they would come from staff at my branch, correct.</p> <p>MR WALKER: If SEAR had occasion to consider a drug which had received a licence after the licence which was subject to review, who would they turn to for medical advice?</p> <p>DR JEFFERYS: Well, the assessor -- I think there is a slight misunderstanding. SEAR would also have there the assessor for safety, who was also of course one of the two principal medical assessors to the Committee on Safety of Medicines, so in that instance they would refer to that individual, either Dr Wood or Dr Jenkins.</p> <p>MR WALKER: Thank you. I had understood that you were the Principal Medical Assessor to SEAR?</p> <p>DR JEFFERYS: SEAR had two principal medical assessors, although it actually had a subgroup known as ARGOS, which used to meet before that Committee, which did quite a bit of the work for SEAR, but nevertheless there were two attendees there, as there were until very recently, when the Committee became assessed, but there were two main branches which had obtained there, just as there were for the main Committee on the Safety of Medicines; there were two principal safety medical assessors.</p> <p>MR WALKER: In relation to safety, how would SEAR deal with a question where an issue as to biologicals arose, as to the safety of biologicals?</p> <p>DR JEFFERYS: I think the Subcommittee would be looking at signals, and the signal would be the same whether this came from a biological product or from a chemical product, so it would handle it in exactly the same manner. Indeed, that is how things operate today.</p> <p>LORD PHILLIPS: When you say “signal”, are we now looking again at the results rather than --</p> <p>DR JEFFERYS: Yes, at results. For example, if we had an issue today with a biological product, an issue has arisen for monitoring in the marketplace, then that would again come through our safety branch, and we would take the lead on this.</p> <p>PROFESSOR FERGUSON-SMITH: So this would only be through notification of an adverse reaction, for example, on a yellow form or something of this sort?</p> <p>DR JEFFERYS: That was the principle at this stage, but it could arise through a case controlled study, which would show that there was increased mortality shall we say in the group. It could arise through an animal study, a carcinogenicity study, a variety of -- I use the term “signals” can be brought for a safety issue on a product which is on the market.</p> <p>PROFESSOR FERGUSON-SMITH: At that time the Principal Medical Assessor for Safety would act, would be informed?</p> <p>DR JEFFERYS: Yes.</p> <p>PROFESSOR FERGUSON-SMITH: It would not be you?</p> <p>DR JEFFERYS: It would not be my group, no. ...</p>
142	<p>[Insert new para 142A]</p> <p>Dr Rotblat said in a statement to the Inquiry:</p> <p>‘The CSM reported to the Medicines Division (later the MCA); in receiving the CSM’s reports, Medicines Division stood “in the shoes of the Licensing Authority”. It was for officials in Medicines Division to decide whether and how to report the advice of the CSM to Ministers.’</p> <p>[Insert new footnote 178A: S Rotblat (WS422), para 26]</p>
182	<p>[Replace paragraph 182 with:]</p> <p>On 31 August 1987 Dr Taylor wrote a further letter to Mr Sloggem. [Insert new footnote 218A: YB 87/08.31/1.1] Mr Sloggem had asked for his opinion because the product in question was for oral administration. [Footnote 219: S Sloggem para 31] The letter stated:</p> <p>‘Regarding oral transmission of the scrapie-like diseases, yes, this occurs. In the case of Kuru</p>

	<p>in New Guinea, the most commonly held opinion is that this disease was perpetuated in the affected tribe by cannibalistic ritual which included eating the lightly-cooked brains of their deceased.</p> <p>We also know from our own experience, and that of others, that mice can become infected with scrapie when they consume the brain of a dead, scrapie-affected cage-mate – quite a normal social practice in mice.</p> <p>With transmissible mink encephalopathy there is a widespread belief that this disease was introduced into mink by inadvertently feeding them scrapie-infected mutton.</p> <p>In natural scrapie it is considered that the normal instinct if ewes to consume placentae is a significant factor in transmission.</p> <p>Under experimental conditions we have transmitted mouse scrapie by feeding infected brain homogenate, and in the United States, Gibbs and Gajdusek successfully transmitted Kuru, Creutzfeldt-Jakob disease and scrapie to squirrel monkeys by feeding them brain material. I'm sure there are other examples in the literature, but the case is already convincing enough.</p> <p>Oral transmission has not been studied experimentally to anything like the extent that the intraneural route has, and so we know little of the efficiency of the route for infection or how the agent gets from the gut to the brain. One would think instinctively of it being a less efficient route but it is impossible to quantify this on the basis of existing data.'</p>
210	<p>[Insert new para 210A:]</p> <p>During his oral evidence Dr Jefferys was asked about the CMO's submission of 21 March 1988: [New footnote 256A: T112 p42 line 16 – p43 line 16]</p> <p>MR WALKER: ... They have looked at various ways in which there might be a risk to human health, and one of them is: "Through the use of bovine tissue-based biologicals in the pharmaceutical industry. Their view was that this risk was likely to be low, but in view of the lethal nature of the virus and the uncertainties, further expert advice was needed as soon as possible." We will return to the phrase, "the use of bovine tissue-based biologicals in the pharmaceutical industry". We are looking here at a question of medical policy. On that question of medical policy, would your branch not be the logical one to advise on the use of bovine tissue-based biologicals?</p> <p>DR JEFFERYS: I think certainly we would have had and did take part in the discussions across the division on here. I would say on the medical side there would be all the other branches, as we have seen, would need to be involved. The major input would probably come from the pharmacists, the pharmaceutical side, in so far as we are looking at the safety of starting material. I would stress this was collective view which was -- what I am saying is that across the division a number of people would be involved within branches and would be looking at this in the division to come to the correct way to take this important issue further.</p>
212	<p>[Insert new para 212A]</p> <p>In oral evidence Dr Gerald Jones was asked about the documents about BSE that were available to Medicines Division in April 1988:</p> <p>MR WALKER: You said just now that in early April 1988 there were only two documents in Medical Division about BSE?</p> <p>DR JONES: Hmm, hmm.</p> <p>MR WALKER: What documents did you have in mind?</p> <p>DR JONES: I clearly recollect myself, I do not know if they are documented here: one was the letter from MAFF to the Department of Health informing us of the epidemic in outline and telling us -- not telling us, asking us: you might like to consider its implications for human health. I think it is dated in March and I saw it in early April. The other, followed inevitably, by Sir Donald Acheson's submission to Ministers requesting permission to set up an expert group. Those were the two documents.'</p>

	[Insert new footnote 258A: T136, p 19, line 2]
219	<p>[Insert new para 219A]</p> <p>At his oral hearing, Dr Gerald Jones discussed the approach of Medicines Division to the issue of BSE:</p> <p>MR WALKER: Would it be right in April that the obvious person to do work on this was Dr Rotblat?</p> <p>DR JONES: Not in April. You must look at this in context. These two documents come into Medicines Division in April 1998. There is nobody in the Department actually who was familiar with spongiform encephalopathies. Donald Acheson had done the obvious thing, he set up the Expert Group. That is what we would have done in Medicines Division if the problem had been ours. Over the next few weeks, indeed over the next two months, in fact before a minute you referred to later at the end of June, following the first meeting of the Southwood Working Group, long before then our knowledge was advancing.</p> <p>Obviously from start, the virtually zero knowledge about a subject there is a vast increase in your knowledge as the weeks go by -- and maybe we will come back to this later. My recollection is that before the end of June it was quite clear that this was going to be a serious problem, in the sense that the Department had a great deal of work to do. Medicines Division would be involved. Its involvement would take the form of a paper, as obviously it always did, which would be discussed in due course by committees. I think by the end of June, for obvious reasons, the paper would be prepared by Drs Rotblat and Purves. I cannot specify when they started. I think they would have started thinking about it by then. I cannot say that any specific plan was in place by the end of June, when would it go to committees or sub-committees later in the year; but there was a very steep learning curve from the beginning of April, from the position of near total ignorance, to the end of June, even before, although again this is not documented, that minute of Dr Pickles arriving in late June.</p> <p>That could be interpreted as the first time Medicines Division realises it is going to be expected to do something. In a sense Dr Pickles' minute with that last paragraph does suggest that this is a form of written request. It was clear before then that Medicines Division would be making a contribution.'</p> <p>[Insert new footnote 267A: T136, p 23, line 1]</p>
219	<p>[Insert new para 219B]</p> <p>Dr Gerald Jones also added in oral evidence:</p> <p>'DR JONES: Could I say from the outset, in 1998 or at any other time, Medicines Division was responsible on behalf of the British Government for the quality, safety and efficacy of all medicinal products either under development, under clinical trial or on the British market at all times; that goes without saying.</p> <p>I think the confusion has arisen because of the analysis of these wretched charts. You are particularly looking at the medical staff, I think, and Dr Jeffreys' role. The medical staff in Medicines Division at that time were organised essentially into these three groups, which, for the sake of brevity were labelled: New Drugs, Adverse Reactions and Review with CDSM. There is nothing particularly novel or original about that arrangement; in fact, it is an arrangement that would be used by most agencies throughout the world, and was. The exception might be that not every country had to do a review.</p> <p>The virtue of that arrangement is that it puts in separate branches people doing related work and clearly the vast bulk of the work flowing into the Division would fit automatically into one of those branches without question. There was nothing unique in the case of BSE. There had been examples before, when an issue comes into the Division, for example we can say BSE, if there is a concern about BSE in medicinal products it is, in a sense, to do with safety or quality in relation to safety. There is a branch of doctors dealing with safety called Adverse Reactions. There is a group of doctors dealing with new drug applications.</p> <p>Presumably in April, May, June there would be one or two applications for biological products. Many biological products, even at that time, would have product licences of right so they could be in the review. This work is not -- the term "lacuna" is a bit strange; it is not that there is a gap. It actually could be the responsibility of all of them. It is in fact the</p>

	<p>responsibility of the Division. Now your conversation with Dr Jeffreys I think was going round and round this, because I think you are trying to identify a lead person in the Division who would automatically take it on as soon as the problem arose. That is not so. Before 1984 I had done each of these branch head positions myself, New Drugs, Adverse Reactions and Review. I would sometimes find my section was dealing with an issue which technically was across the Division. How was that chosen? Normally there would not be a great argument in the Division with demarcation disputes going on with the staff. We are dealing with reasonable people working in a management structure, that -- it is not that it is rigid, it has to be fixed in some way. The outside world has no obligation to fit into your management structure. Your management structure must deal flexibly with the outside world. This particular case was not unique. It must have been, obvious, as I say, some time between April and June that Medicines Division would have to make a substantive contribution in the form of a paper to be discussed by committees, and it was obvious it was going to be Dr Rotblat and Dr Purves, because of their expertise and experience; and Dr Rotblat happened to be reporting to Dr Jeffreys, and Dr Purves reported to Mr Stewart. But that does not make Dr Jeffreys the sort of lead person in Medicines Division, nor Mr Stewart. And I do not think -- we could go round this subject for hours. The crucial thing is that the organisation does identify the most appropriate people to do the work at a time that I thought was appropriate. I hope that clears up some of this confusion.'</p> <p>[Insert new footnote 267B: T136, p 30, line 1]</p>
219	<p>[Insert new para 219C:]</p> <p>During his oral evidence Dr Jefferys was asked about his minute of 13 April 1988: [New footnote 267C: T112 p 43 line 17 – p 53 line 21]</p> <p>MR WALKER: I would like to turn to look at what actual role you took. The first document where you discuss BSE, that we have, is a little further on in this bundle, YB 88/4.13/5.1. This is a minute from you to Mr Wilson, the Under Secretary, dated 30th April 1988; is that right?</p> <p>DR JEFFERYS: Yes, that is correct.</p> <p>MR WALKER: I will just read paragraph 1: "Your minute of 11th April 1988 and CMO's minute of 21st March 1988 refer." I think you have told us that you have not been able to trace a copy of Mr Wilson's minute?</p> <p>DR JEFFERYS: No, I have not.</p> <p>MR WALKER: You recall Mr Wilson had asked you for some immediate comments on the possible implications of the appearance of BSE in cattle for the use of bovine tissue-based biologicals in the pharmaceutical industry. That is right, is it not it. It is your first statement, paragraph 59. Look at paragraph 59 of your first statement. You say in the first place you have not been able to trace the minute. You go on: "However, I recall that Mr Wilson had asked me for some immediate comments on the possible implications of the appearance of BSE in cattle for the use of bovine tissue-based biologicals in the pharmaceutical industry."</p> <p>DR JEFFERYS: Yes, I think I said subsequently that I rather believed that I was asked for this because I may have been deputising for Dr Gerald Jones at the time. I had not been able to -- I had not been able to locate the minute which this refers to, but I think my reply makes it clear that this was asking for views which I gave, some very preliminary thoughts on this, just some two days later.</p> <p>MR WALKER: The first point I would like to seek agreement on is that there was good reason to ask for immediate comments. The CMO had highlighted that this was a disease of a lethal nature and that there were uncertainties and that he needed urgent advice. You agree that this was a matter that called for immediate comments?</p> <p>DR JEFFERYS: I think I would see the context slightly, maybe, differently. I think this was Mr Wilson who was turning to me, deputising for Dr Jones, to ask what the implications might be for Medicines Division. Indeed, if I look on, I think that he then refers my comments to others in policy areas in the Department of Health, saying "Can you keep Medicines Division informed -- I am paraphrasing -- as events unfold". I think that is a minute which is in the bundle, which I have seen. So I think this was Mr Wilson, the Under Secretary, asking for some comments for him at this time. Unfortunately, the minute to which he refers is not available, as so many others do not seem to be.</p> <p>MR WALKER: I wonder whether it would be logical for him to seek comments from you,</p>

	<p>because your branch was the branch particularly concerned with biologicals?</p> <p>DR JEFFERYS: I think at the time this was from the Chief Medical Officer, and it would perhaps seem logical to have a medical response to this, but I think at that stage we knew so little about this, I think to say that it was logical to be my branch rather than the pharmacists I think may be a little difficult. What was needed was a view of what this might mean, and I think this is what I was seeking to set out in my minute of 13th April, again, from a low entry point.</p> <p>PROFESSOR FERGUSON-SMITH: As it happened, you had knowledge about CJDs and transmission of spongiform encephalopathies, but it would be unlikely for a pharmacist to have such knowledge; is that right?</p> <p>DR JEFFERYS: I think in terms of the virus, perhaps the other way on, remembering that some of those staff had been working on dura mater, which was the dental and surgical material. My knowledge was simply having looked at a patient with this tragic condition when I was a locum consultant in 1984, and having done reading round this for, as I remember, a case conference in the hospital in Tunbridge Wells at the time, but that was my rather limited knowledge here.</p> <p>PROFESSOR FERGUSON-SMITH: Just as a point of clarification, just in that paragraph, I have not come across the word "hardy virus". What would the hardy virus be that was used to spike --</p> <p>DR JEFFERYS: I think this was a phraseology which was quite widely used at the time for resistant viruses. It was the Hanta virus, as I recall, which was used as a marker, that if that was eradicated or was inactivated, then this was a useful marker for other resistant viruses, if this was a viral determination.</p> <p>PROFESSOR FERGUSON-SMITH: The Hanta virus was used routinely for this purpose?</p> <p>DR JEFFERYS: Yes, it was.</p> <p>MR WALKER: In this minute you use the word "we". You say in paragraph 2: "For recent products we have taken a very stringent view. We have demanded spiking studies". In paragraph 5 you say: "A further final thought is recently we have required certificates that the animals in question come from -- that the animals from which the biological products are derived are healthy". In your second statement you discuss the word "we", in particular of the context of paragraph 5. If we just turn on to that, do you have your second statement? It is electronic number statement number 491A. You say you think the "we" was the Biological Subcommittee?</p> <p>DR JEFFERYS: Yes. This again is very difficult, almost 11 and a half years on, but I am basing that on the minutes of that time of the Biological Subcommittee, which shows that they had been requiring the certificates. It was probably introduced on the suggestion of the Pharmaceutical Secretariat, who would have proposed this issue, but again endorsed by the Biological Subcommittee. This was certainly a point that had been made for some new drug applications which had been turned down on this point, and that point had been put to the pharmaceutical applicant.</p> <p>MR WALKER: This had arisen, both the point about spiking in paragraph 2 of your minute and the requirement that animals from which the biological products were derived were healthy, it had arisen in relation to applications for licences?</p> <p>DR JEFFERYS: Yes, that is correct. I think it might help the Committee to understand that there were two issues very much in the mind at this time. We had been -- and by "we" here I mean the decision, my own branch, had been handling the dental and surgical materials and the dura mater issue was fresh in people's minds. Secondly, as I referred earlier, inactivation of viral contamination was very much in issue because of HIV and other matters before the Committee. This is something that certainly the Committee was very much focusing on at that time, and obviously hence the Secretariat would be highlighting this during their assessment.</p> <p>MR WALKER: Both the points that you are making in paragraph 2 and paragraph 5 were points which involved your branch's responsibility in relation to applications for product licences?</p> <p>DR JEFFERYS: I think that may be going a little far. I think I was being asked, deputising for Dr Jones, the "we" here would be referring to what the division was doing rather than the branch. What I am saying is that this was the standard which was being set by the Biological Subcommittee and hence the CSM for new products that we, the Committees, were requiring, hence the division were requiring, spiking studies, and they had recently introduced the requirement of certificates that the animals were healthy. I think that probably did come from</p>
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	<p>the Biological Subcommittee members. It is very difficult to say 11 and a half years on.</p> <p>MR WALKER: I would just finish this off by raising two further points on the minute with you. The first concerns paragraph 3. There you are referring to the review procedure and you are saying it might be worth raising that with Dr Wood. So that is suggesting to Mr Wilson that he raises it with Dr Wood; is that right?</p> <p>DR JEFFERYS: Yes.</p> <p>MR WALKER: That seems rather inconsistent with the idea that you are responding on behalf of Dr Jones and that the “we” that you are using in this minute is a “we” which refers to the whole of Medicines Division, the whole of the medical side of the Medicines Division rather than just your branch?</p> <p>DR JEFFERYS: I would not quite see it that way, because one is referring to what the division was doing in terms of particular requirement for healthy certification, and I think under point 3 I was raising the issue, the wider issue of the older products, which would have been for the review. As I say, it is unfortunate one does not have the context of this, but I note from my first paragraph that I am referring to his minute of the 11th, that, knowing the internal post then and now, almost certainly means I would have responded to this within the day, so this was a first look. Again, the amount of information, although the CMO’s minute is 21st April, I think that was only circulated on 4th April, and I happened to have noticed very recently that I was in Washington immediately around that time on a mission meeting with the FDA and the American Biotechnology Association. I noticed that from something I saw in my room the other day, so I had literally only just seen this matter before receiving the note from Clive Wilson and then the response. So this was very much an immediate matter.</p> <p>MR WALKER: The other point on the minute is paragraph 6: “I would be happy to look into this matter further.” That is a response that you are making. If it was being sent to you because Dr Jones was not available, would it not be appropriate to respond by saying that you would ask him to look into the matter?</p> <p>DR JEFFERYS: I do not think in those days I would have actually written a minute quite like that in the civil service to suggest that I would to ask a senior officer to look into this. I think there are a number of issues here and I think even bringing this minute together I would probably have discussed the issue with perhaps Dr Purves, maybe with Dr Rotblat -- we used to take lunch together every day around that time. This might well have been raised just to take some soundings on this. But I think what I was saying here was perhaps rather a way of ending a note, saying if there were other issues I would be happy to look into this further. This is a receipt of a note and this is very much an initial response to an issue. Again, I would stress, at a very low entry point in terms of expertise here.</p> <p>MR WALKER: Perhaps we can agree on this: when you were writing this reply to Mr Wilson, saying what you have said in paragraph 6, you had a responsibility to consider whether there were things that could usefully be done in advance of the deliberations of the proposed expert group?</p> <p>DR JEFFERYS: I think the disadvantage I have is that I do not have the terms of his original minute, and I think that perhaps it is being read into this that I was being asked to set out the division’s reply to the CMO minute. I rather suspect it might not have been like that. It may have been that this was an issue which he had become aware of, what might be the general issues around this, as he would have been head of the division perhaps in the absence of Dr Jones at that time, but I really cannot recall and go into any greater depth than that. It is difficult to put my rely into context without having the minutes unfortunately to which it refers.</p> <p>MR WALKER: I was just suggesting that before you said “My view is we should await the deliberations of the proposed expert group”, you had a responsibility to consider whether there were things that could usefully be done before you got to the deliberations of that group?</p> <p>DR JEFFERYS: What I was setting out here was very much an initial view and reading this an expert group had been set up to consider all the aspects related to human health. We certainly did not have the expertise within the division at the time, nor indeed necessarily would the Committees have done so, in what was an issue which we knew so little about. This is predicated on the basis this was a viral infection. Events then moved on. It needs to be looked at in that initial period of April 1988.</p> <p>MR WALKER: The other thing we should just not is that there is a manuscript notation on this minute at the top. This is from Mr Wilson to Dr Jones, is it not? Is that right?</p> <p>DR JEFFERYS: I assume so, yes.</p> <p>MR WALKER: It just says: “You will wish to see and perhaps show to Dr Wood, and subject</p>
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	<p>to that I will go along with 6 below’.</p> <p>DR JEFFERYS: It was not unusual at that time for senior administrative staff to simply ask in brief notes “What does this mean? What might be the issue around this.” I put this into the context in which that minute might have been written to me at the time.</p>
219	<p>[Insert new para 219D:]</p> <p>During his oral evidence Dr Jefferys was asked further about his minute of 13 April 1988 to Mr Wilson: [New footnote 267D: T112 p 85 line 25 – p 86 line 24; p 90 line 9– p 91 line 10]</p> <p>MR WALKER: ... I just return to your paragraph 6. Might it be right to say that given you were dealing with a potentially lethal infection and there might be a need for prompt action, you should have given thought to the adequacy of the database in 1988?</p> <p>DR JEFFERYS: I think, as I have tried to put this, and I am at some disadvantage as I do not have the original in front of me, but I think it was me replying some 24 hours later to what I reasonably believe, having seen other minutes at the time, was a what is this all about type question in here, responding to that point. I think I had highlighted what was occurring for new drugs in here. I had already identified within that period there was probably a wider problem. My understanding is that this was discussed across the division and decisions were made. It would not have been my staff who would have cross-questioned this database and have been able to get the information. It is not like today, where I would have run an inquiry on there. The database was not located inside the division, and so on and so forth; the information scientists who would have done that. I am not sure it is true to say that an inquiry was not run. I just do not know what was done at that time particularly by the pharmacists here.</p> <p>...</p> <p>MR WALKER: My concern is whether it might be right to say that if your branch had got more involved at this stage then the problems with the database would have been identified earlier and that would have saved you time later on?</p> <p>DR JEFFERYS: I am not sure it is fair to say that professional parts of the division were not involved. Indeed, we go back to this being an issue of safe starting materials. It may well have been that Dr Purves and his team were asking questions on this. There were several information pharmacists on there. If you are asking me did I personally order such a search, to the best of my knowledge I did not. My responsibility was head of the new drugs branch, but I think my understanding at the time -- and we are trying to look at the period of May/June -- is that the database would have revealed activities and excipients in here. I can also say, rolling the video forward, one of my responsibilities today is for a database. That data was brought across into the new database from the NORISK system there. There are fields added, but a lot of the information is very much there, so I think it is an example of how easy it was to extract this, but these were not just junior clerks doing this. It was a rather more senior person answering this one and they had a team of information pharmacists doing all this.</p>
225	<p>[Insert new para 225A:]</p> <p>Dr Minor of the NIBSC gave evidence regarding this meeting in his statement to the Inquiry: [New footnote 273A: S Minor (WS 576) paras 14-18]</p> <p>14. I organised a meeting to discuss BSE which took place at the NIBSC on 16 May 1988 [YB88/05.16/2.1-2.12]. I believe that it came out of a suggestion by Dr Schild that the NIBSC should act on BSE in the course of a discussion about BSE. The result was that I convened the Viral Products Advisory Panel. This was an ad hoc group which as head of the Virology Division, I would bring together if an issue arose on which outside expertise would be useful. The meeting on BSE was only ever intended to be a “one-off” session in which knowledge would be pooled and a paper produced which would offer a synopsis of the state of knowledge on the issue for the benefit of those working on biological medicines.</p> <p>15. I selected the participants; they are listed on the last page of the paper produced [YB88/05.16/2.1-2.12 at 2.12]. Dr Wilesmith was an epidemiologist from the Central Veterinary Laboratory. Drs Ridley and Baker had worked on CJD. Dr Kimberlin had been involved in the issue of transmission of CJD through growth hormones. Dr Beale and Dr Garland worked on the manufacture of vaccines in the pharmaceutical industry. Dr Schild and Dr Ferguson were colleagues from the NIBSC. I sent out the invitations to attend the meeting</p>

	<p>and a discussion paper which I had prepared.</p> <p>16. Part of the purpose of the meeting [YB88/05.16/2.1-2.12] was to provide information to MD; it was part of MD's function to consider whether to license a particular manufacturing process, which might involve bovine materials. The issue of whether the use of bovine materials was safe was therefore clearly part of the MCA's remit. The safety of such medicines is of course also part of the NIBSC's concern, as is their effectiveness. I invited Dr David Jefferys of MD to attend by telephone but he did not do so.</p> <p>17. In the end I was satisfied with the resultant paper [YB88/05.16/2.1-2.12] and it was sent to Dr Ed Harris the Deputy Chief Medical Officer and Dr Jefferys at MD; it was circulated to the Committee on Safety of Medicines, Sub-Committee on Biological Products("CSM-B"), as well as published in the journal <i>Biologicals</i> 1990, vol 18, pp 78-80 [J/BIOL/18/77] where it could be read by people such as those running vaccination programmes, and others in the field of public health.</p> <p>18. The paper [YB88/05.16/2.1-2.12] proposed (amongst other things) that studies should be set up with Wellcome Biotechnology. They were in fact conducted by Wellcome Biotechnology independently. I recall however being told of the results of that research at some stage, although I do not think I saw the research itself.</p>
225	<p>[Insert new para 225B:]</p> <p>Dr Schild of the NIBSC gave evidence regarding this meeting in his statement to the Inquiry: [New footnote 273B: S Schild (WS 575) paras 37-39]</p> <p>37. In early 1988, I discussed the question of BSE with Dr Philip Minor. We agreed that the NIBSC's Viral Products Advisory Panel ("the Panel") should meet to discuss BSE. The Panel was an ad hoc committee, called by the Head of the Virology Division from time to time to discuss a particular issue. Although BSE was not thought to be caused by a virus, scientifically the Panel appeared to be the most relevant group to consider it. It could draw on members with wide experience of vaccine safety issues and principles of vaccine safety which were relevant. The purpose of this particular meeting was to obtain the advice and comments of scientists outside the NIBSC on the nature of the epidemic and its implications for biological medicines. Although questions of licensing are for the MCA (which sets the conditions under which manufacture of biological substances is permitted) we have an obvious professional interest in the safety and efficacy of biological medicines, and an advisory role in that respect.</p> <p>38. I attended the meeting of the Panel on 16 May 1988 at which BSE was discussed [YB88/05.16/2.1-2.12]. The report produced of that meeting by Dr Minor was forwarded on 12 July 1988 to Dr David Jefferys of the MCA, and to Dr Ed Harris, the Deputy Chief Medical Officer, amongst others. It was also eventually published in the journal <i>Biologicals</i> [J/BIOL/18/77]. That is the only BSE related document I would make any claim to have commissioned.</p> <p>39. Looking at the report now, I am impressed by how well it has stood up to the passage of time. In particular I would draw attention to the statement: "If BSE is held to be a problem, the only option is to ensure that bovine materials for manufacture of biological medicinal products are derived from cattle free of the disease." That has been the cornerstone of the regulatory approach adopted in this field ever since. I would like to draw attention to recommendation 2 that "Consideration should be given to a survey of licensed products in respect to the use of bovine or ovine materials in their manufacture and the origin of the bovine or ovine materials." Looking at the conclusions:</p> <ol style="list-style-type: none"> (1) In the event, the proposed studies to be set up with Wellcome Biotechnology were conducted independently by Wellcome Biotechnology. I am told by Dr Minor that he recalls seeing the results, although I do not. (2) The suggested survey of licensed products took place, as can be seen from the minutes of the CSM-B and the CSM BSE Working Party, which I shall discuss below.

	<p>(3) No further informal scientific meetings took place at the NIBSC dealing with BSE. On reflection, this was most probably because the other CSM committees I shall discuss below began to address the issue, in particular, the CSM BSE Working Party.</p> <p>...</p>
229	<p>[Insert new para 229A:]</p> <p>During his oral evidence Dr Jefferys was asked about Dr Pickles' minute of 20 May 1988: [New footnote 276A: T112 p 54 line 4 – p 54 line 18]</p> <p>MR WALKER: Dr Pickles told you that the joint MAFF/DHSS group on BSE would like to be sure that problem transmissions through medicinal products could be ruled out. We see that in paragraph 2. She asked you whether this was an issue you should put before the Biological Subcommittee. Was it your role to consider whether problems of this kind should be put before the Biological Subcommittee?</p> <p>DR JEFFERYS: It would certainly -- I would be one of the people involved in that, yes. An issue like this would almost certainly be involved in a decision made across the division, and certainly would not have been made by myself without referring this to the senior principal medical officer and, because of the structure, the Under Secretary.</p>
233	<p>[Insert new para 233A:]</p> <p>During his oral evidence Dr Jefferys was asked about his minute of 24 May 1988 to Dr Pickles: [New footnote 279A: T112 p 54 line 19 –p 58 line 5]</p> <p>MR WALKER: If we look at your response a few pages on YB88/5.24/3.1, this is a minute from you dated 24th May 1988 to Dr Pickles, which you copied to Dr Wood and Dr Jenkins?</p> <p>DR JEFFERYS: And Dr Purves I think also.</p> <p>MR WALKER: Yes. You point out that you were aware of the joint working group on BSE and it was in the light of that that you prepared your preliminary comments in the minute of 13th April. That is your paragraph 2. You do not suggest that this was something outside your normal responsibility in that regard, do you.</p> <p>DR JEFFERYS: I think I made a neutral statement that the minutes had been copied to me and I was replying that I was aware of this. That is the minute, I think which you referred to, that Mr Hagger had copied to me, that made that point.</p> <p>MR WALKER: You do mention that there are two others who might be involved in this reply. One was Sue Wood, and that was the point in relation to the review procedure that you had mentioned in your minute of 13th April; is that right?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: The other is Dr William Jenkins in charge of MB4. We see that in paragraph 8 of the minute. You say there that it occurred to you this is more of a long-term issue rather more "an ADR problem than a new drugs group issue". ADR is the adverse reactions, is it?</p> <p>DR JEFFERYS: Correct, yes.</p> <p>MR WALKER: Did anything come of your suggestion that this might be rather more of a problem for Dr Jenkins than for you?</p> <p>DR JEFFERYS: As far as this was concerned, the minutes have not survived, but I am virtually certain that this would have been discussed between the professional staff of the division and would have been raised at what is known as the Divisional Management Group meetings, so-called DMG meetings, which were held every month, when a significant part of those meetings were for any new issues to be discussed and implications considered. So, although I do not have the documentary evidence, I would be fairly confident that something like this would have been discussed at those meetings and would also have been discussed by the senior people in the division. Certainly very much the pharmacists would have been heavily involved in this, as would administrative colleagues also. I note that Dr Pickles had copied her original letter to the Secretary to the Committee on the Safety of Medicines for example, in branch MB1, Aileen Simkins.</p> <p>MR WALKER: I think that you said earlier that you had a responsibility to consider whether the matter could come before the Biological Subcommittee, and there were others who also had a similar responsibility, as I understand your evidence. Would it be right to say that when</p>

	<p>considering whether the matter might have to come before the Biological Committee, you had a responsibility to consider whether there was anything that could usefully be done before it went to that Subcommittee?</p> <p>DR JEFFERYS: I think I look at it in a slightly different way, that the Biological Subcommittee is the Committee on the CSM, the Committee on the Safety of Medicines, and therefore the issue would just go before the Committee on the Safety of Medicines. The Biological Subcommittee was brought in, and I think Professor As[sc]her, Chairman of the CSM made that point rather clearly. So I think that is the first issue on that. I think the decision that was made across the division was to await more information on this from the Southwood Committee, in so far as it was seen at that stage that this was a group charged by Ministers to assess the aspects of this emerging situation for human health, including pharmaceuticals, that some preliminary work was being undertaken within the division, across the division, but that we should await at this stage of the May for more information before we would put something to the Committee on the Safety of Medicines, and hence the Biological Subcommittee. The reason for doing that is to know what issue we would put to the CSM. The CSM was accustomed to having fairly detailed papers put before it with recommendations and with analysis, and at that stage I think the feeling was that we should work in tandem with the Southwood Committee because we did not have information to put before the CSM at that time. I think we are referring here to the end of May.</p>
233	<p>[Insert new para 233B]</p> <p>At Dr Gerald Jones' oral hearing the following exchange occurred regarding this minute:</p> <p>'MR WALKER: I asked Dr Jeffreys about paragraph 2 and paragraph 5 in this minute, where he uses the word "we". He said in paragraph 2, in the last two sentences: "For recent products we have taken a very stringent view on the quality control to avoid the risk of transmitting infection. We have demanded 'spiking' studies with hardy viruses (these are rather similar to the scrapie virus)." In paragraph 5 he said: "A further final thought is that recently we have required certificates that the animals from which biological products are derived are healthy." Dr Jeffreys said at one stage that "we" referred to the Biologicals Sub-committee. A bit later on, for our note the reference is page 49 of the transcript for Day 112, he referred to "we" as being Medicines Division. Can you help us at all, Dr Jones, on who you understand "we" to refer to in paragraphs 2 and 5?</p> <p>DR JONES: Obviously I cannot specify exactly what Dr Jeffreys had in his mind. From my experience in the Division at the time, it is absolutely straightforward. I think you are trying to distinguish between the advisory committees, like the Biologicals Sub-committee and the medical pharmaceutical staff in the Division. I assume "we" means the professional staff and the advisory body. And I cannot see any other interpretation to place upon it.</p> <p>MR WALKER: I had wondered whether "we" meant Dr Jeffrey's own branch?</p> <p>DR JONES: Well, yes, but again, as I thought I made clear afterwards, maybe I should do it now rather than before. The applications for product licences involving biological products would be dealt with by the New Drugs Section on the medical side, some people from Mr Stewart's section on the pharmaceutical side. So there would be medical and pharmaceutical staff looking at the applications, attending the Biologicals Sub-committee and the CSM. The "we" there would refer to the professional staff in the Division and the Biologicals Sub-committee, and obviously, as the Sub-committee has no legal status, that would be the CSM. The "we" would be a collective noun for those people. I do not see why you are saying to me you are concerned about it.</p> <p>MR WALKER: Within the Division?</p> <p>DR JONES: Within the Division it would be the professional staff working with -- as he says, recent products would be biological products, licence applications and "we" alone would have to include the advisory bodies. The Biologicals Sub-committee, like all the sub-committees, has no legal status at all; it does not exist under the Medicines Act. You will not follow any of its recommendations so they would have to be confirmed by one of the Section 4 committees. For the new products and biologicals that would obviously be the CSM. I do not see how any other interpretation could be put upon it, other than the one Dr Jeffreys have. It may be that he has emphasised the professional staff in one statement, and the collective group in the other. But it must mean that group of individuals.</p> <p>MR WALKER: The requirement for spiking studies was a requirement that Dr Jeffreys' branch was insisting on in relation to new products?</p>

	<p>DR JONES: I think it would be the medical staff in Dr Jefferys' branch, obviously Dr Rotblat and the pharmaceutical staff in Mr Stewart's branch that would work together. We are talking about an issue of quality, and quality in relation to safety. So it would involve pharmaceutical and medical staff.</p> <p>[Insert new footnote 279B: T136, p 14, line 4]</p>
248	<p>[Insert new para 248A:]</p> <p>During his oral evidence Dr Jefferys was asked about the period following receipt of Dr Pickles' minute of 21 June 1988: [New footnote 295A: T112 p 91 line 14 – p 105 line 8]</p> <p>MR WALKER: ... I would like to discuss whether it might be right to say you should have ensured a paper on BSE was prepared for the September meeting of the Biologicals Subcommittee. I think we should for this purpose have a copy of Dr Pickles' minute of 21st June in front of us. It is in the FAD bundle 6.21/4.1. This is a minute from Dr Pickles to Dr Jones and copied to you among others?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: Dr Pickles records that the Working Party had had its first meeting, and continues in paragraph 2: "We are clearly concerned that BSE agent may be transmitted in medicines." Then she goes on to discuss that.</p> <p>DR JEFFERYS: Yes.</p> <p>MR WALKER: I would like to ask you first about what Dr Gerald Jones has said in relation to this minute. We need to look at his first statement. That is Dr Gerald Jones 1, paragraph 11. What he says is that he has: "... no direct memory. No doubt upon receiving this letter I would have picked up the phone to you and ascertained that the review process was by then well in hand." Can you help on that? It is the suggestion that there was a review process well in hand by 21st June 1988.</p> <p>DR JEFFERYS: Yes. From the best of my memory it was -- I have outlined earlier to the Committee, I think there were preliminary considerations taking place up to the receipt of this minute. I do not recall having been asked or that there was a review that had been started at that period. Rather it is my understanding that following the receipt of that minute, it was decided that yes, this was obviously the day after, if I recall, the first meeting of the Southwood Working Party that this should be put before the relevant Section 4 committees, and that subsequent to this that two individuals were identified; one from my area, Dr Rotblat who would have been a natural person with her background to develop this paper, and one allocated from the pharmaceutical team. In the event it was a rather senior individual, Dr Purves, to generate this paper. That was my understanding of the events, so I do not quite see that a review was in hand at this stage. If it means that the paper had already started to be worked on, no, it had not at that time.</p> <p>MR WALKER: We can look on to Dr Jones's second statement. That is in the same bundle, the next tab. I think it is paragraph 16 where says there is an element of reconstruction, but he says what he thinks is likely to have happened and in subparagraph 1 he says: "It is likely I would have discussed Dr Pickles' minute with Dr Jefferys and that Dr Jefferys would then have met with his staff and the pharmaceutical clients to decide the way in which the assistance of the subcommittees could best be utilised and to allocate a particular doctor and pharmacist to carry out the necessary work. This would have involved ensuring the availability of that doctor and pharmacist over the summer period and inevitably had regard to the rest of their work load." That seemed to me to suggest that Dr Jones's recollection was that he effectively left it up to you to decide whether the paper should go to the Biologicals Subcommittee in September or in November. Do you think that is right?</p> <p>DR JEFFERYS: I think again this is very difficult more than 11 and a half years on as I said earlier. I am pretty confident that following the receipt of the minute from Dr Pickles to Dr Jones, that this would have been discussed by a team and those involved, certainly the three principal medical officers reporting to him and the pharmacists, and I imagine also the administrative colleagues would be brought in. I am pretty confident this would have been discussed at the Divisional Management Group among other discussions and, arising from that, a decision would have been made for a paper to be put as soon as possible and I would stress that my understanding was that this was given as significant a priority as it could be in the division at that time, and would be put to the Biologicals Subcommittee. It is a slightly different way but that is my recollection of what would have happened and, in discussing that</p>

	<p>with other colleagues around at the time, that would be their understanding of what would have taken place.</p> <p>MR WALKER: I have nothing further on Dr Jones's statement for the time being, so I think we can put those away. We need to go to your statements again. In your first statement you have dealt with this at paragraph 65 to 66. In 65 you deal with the receipt of a copy of Dr Pickles' minute. In the last sentence you say you recall that: "... the Medicines Committee had begun to prepare its review of the usage of bovine material in medicinal products by the date of the first meeting of the Southwood Working Party." That is subject to what you said in oral evidence just now, is it?</p> <p>DR JEFFERYS: Yes. I think what I was saying there is if you are referring to the commencement of the preparation of the paper, no. If we are gathering information, and I referred to the rabies vaccine and others, I think preparatory work was underway, but I understood you to ask me in terms of the commencement of the paper and if that is what is meant by "review" then, no, the paper had not been commenced at that time.</p> <p>MR WALKER: Paragraph 66 you describe your impression of Dr Pickles. You say in your first sentence: "Dr Pickles clearly felt that BSE should be considered by the Biologicals Subcommittee at the first available opportunity." I think in your next two sentences you make the point that it would not be possible to get it before them in July, and you conclude there by saying: "The first available opportunity would have been the September meeting."</p> <p>DR JEFFERYS: Yes, I think I dealt with this earlier in one of my statements, but with the exception of one occasion, the Committee on the Safety of Medicines has only ever met once in August in its history. The subcommittees have never met. The first available opportunity would have been September.</p> <p>MR WALKER: It was important to deal with this at the first available opportunity given the lethal nature of the disease as pointed out by the CMO and the uncertainties?</p> <p>DR JEFFERYS: I think it was important to put a well constructed paper with clear evaluation and recommendations to the relevant Section 4 Committee. I think it might have been possible to put a one page or two page document before the subcommittees in September, but I think that that would not have been sufficient and it simply would have looked nice and then the substantive discussion would have taken place at the later meeting of November, recognising also that the other Section 4 Committees had to be involved. I agree there is an element of reconstruction in that answer. I do not know whether you wish me to go on about the available expertise and how one would decide. Perhaps that is for later.</p> <p>MR WALKER: In terms of expertise on the medical side, the physicians, the person that you identify was Dr Rotblat?</p> <p>DR JEFFERYS: Yes. The obvious person I think to all across the division would have been Dr Rotblat and I would have wished quite clearly, because this was a significant and potentially very serious issue, for this to go before the committees as soon as practically possible, but having to balance a number of other extremely urgent priorities. Obviously I was aware across the division as Gerald Jones has referred to, of oral contraceptives and breast cancer and related HIV matters and the risk that various preparations were rotting condoms. They sound silly, but at the time those were right at the fore of public health concerns and these were being balanced as clear and present dangers in terms defining a priority.</p> <p>MR WALKER: Was Dr Rotblat involved in those?</p> <p>DR JEFFERYS: She was involved in several of the issues with her expertise, particularly with her background in the haemophilia products. She was our haematologist and that is her real area of expertise.</p> <p>MR WALKER: Thank you. You say a little more about this in paragraph 37 to 39 of your third statement. You make the point that there is a paper prepared for the September meeting and you say this would inevitably necessitate a very substantial disruption to the existing commitments of those doing the work. Could I just ask you what the basis is for making that statement that this would inevitably have necessitated very substantial disruption to the existing commitments of those doing the work?</p> <p>DR JEFFERYS: Again this is applying reconstruction to the events, but I think I have outlined earlier today the severe limitation of resources. On the medical side, which is the only area I would deliver a source, we are talking about four available individuals. August for many with young families is also a holiday month and we also have to recognise they had a number of major issues already in the pipeline programmed with deadlines that could not be met. So if we are talking about the period June to July, the work programme at the beginning of July would already be fixed for those applications going to both the September and October</p>
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	<p>meetings. It was our practice then, and still is, to allocate work three months in advance, and remember this was already high prioritised work because we had a backlog of things we were not able to touch at that time. When I am reconstructing here on the medical side, saying there are about four individuals, one of whom had a particular expertise, playing that, those numbers of individuals, it is not very easy to move things without other major items being defaulted upon. On the pharmaceutical side, which I was not delivering the resource, rather Mr Stewart would have been controlling that, but through Dr Purves and his team, again they were equally stretched. They would have had to allocate their resource and therefore I think across the division a decision was made that this should be as soon as possible, but this was the earliest practical date. The Biologicals Subcommittee was of course informed of this by Dr Purves -- not by myself, by Dr Purves -- at their meeting on September 7th, I think, when he informed the committee of the date of this paper being presented, and of course the CSM would also have been informed of that as the programme we were running too.</p> <p>MR WALKER: In paragraph 37 of your third statement you also say this seemed a sensible decision because BSE was not regarded as an emergency. If it had been regarded as an emergency you would have acted very quickly indeed. You would have got action taken in July, if not before the end of June?</p> <p>DR JEFFERYS: No, I think in receipt of the minute which was 24th June, it would have been impossible to put this to the committees in July.</p> <p>MR WALKER: If it had been an emergency, I think you would have dropped everything, would you not, to get action taken?</p> <p>DR JEFFERYS: What I am saying is I think the advisory committees would -- if this was an absolute emergency, yes. If you are talking about normal context, detailed papers have to be put on which informed action can be taken which, this is legal action, can stand the course. If something needs to be banned immediately, action can be taken in that day. That is what you are referring to.</p> <p>MR WALKER: That is the distinction I was seeking to draw. I had understood you to be talking about the fact that if there was an emergency, then people would be told to drop everything and one would act very quickly. I was not suggesting that BSE was not in that category. What I would like to explore with you is whether BSE did not have a degree of urgency which warranted considering whether others could change their commitments, so you could bring it on in time for the September meeting?</p> <p>DR JEFFERYS: I think I would put it another way, that priorities -- and again this is recollection and reconstruction -- priorities were significantly changed from the background I have just outlined to generate this paper by the middle of September, which it was, so priorities were changed. This was given, I would suggest, a high priority in terms of my own four available staff, and by the pharmaceutical colleagues in the division to enable this to be brought forward. Dr Rotblat refers to three to four weeks. I have spoken to Dr Purves who thinks it was nearer five to six weeks of his time with the necessary discussions to bring the paper together.</p> <p>MR WALKER: Can I just show you what Dr Rotblat has said about this? We can put away your statement for the time being. If you can have Dr Rotblat's statement at paragraph 51. We see her saying there that she believes you asked her for the preparation of the paper. She is not able to recall when first asked. Some recollection that a decision was taken to prepare it before the November meeting certainly. She says: "... Dr Jefferys probably told Dr Purves and I to work towards completing in time for that meeting. I believe that when Dr Jefferys asked us to prepare it, he probably told us to prepare it as soon as we could given our existing workloads. I do not believe that Dr Jefferys told us to drop all our other work and concentrate exclusively on BSE or told us that the paper was a low priority. I imagine that the paper was probably put together over the course of three to four weeks." This does not suggest any discussion with her about moving existing work commitments, does it?</p> <p>DR JEFFERYS: This does not, but I do not quite recall it perhaps in that way. Firstly, I think I have explained that we were only doing high priority work in my branch at that time. We had a backlog. A lot of issues were not even reaching the top of the pile. That needs to be recognised. We were only doing high priority work. I think she states quite fairly, I think she was probably not told to drop all our other work, but that other work would have been high priority work with predefined what I would term inviolate deadlines, so it needs to be seen in that context there. Similarly, I do not think she has quite got the structure here. It would not have been me, it is not under my command. It would have been Mr Stewart who had given a similar priority to this for Dr Purves to work together to generate the paper. In terms</p>
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	<p>of discussion, there was always discussion to decide a priority. It was not left for senior medical officers to say, "This is what I am going to do", rather there would have been a discussion at which we would have decided at what is the earliest it can practically be done to achieve this. I make the point that in the context of all the other issues which were not being done at the time, this was given significant priority and things would have been dropped to achieve this. They must have been with only four staff.</p> <p>MR WALKER: Is this your actual recollection?</p> <p>DR JEFFERYS: I would state this is my recollection, that we were giving this a significant priority and I would say, this was a high priority, it is semantics, given the resources and the other competing priorities, so when you have several high priorities then it is difficult, but that was the situation we were facing at that time.</p> <p>MR WALKER: The recollection you have just described is one which differs from what Dr Rotblat sets out here.</p> <p>DR JEFFERYS: I am not sure it is totally different. She says. "... as soon as we could given our existing workloads." I am putting in parentheses that the existing workloads were other all high priorities and that is backed up by extemporaneous evidence which says we had a backlog and were facing litigation at the time. This was Dr Purves who referred it to the Biologicals Subcommittee. I think it would have been discussed with the CSM and at no stage did that Committee say they wished it to be a month earlier. They were happy with that timeframe and I think the --</p> <p>MR WALKER: Pausing there, in discussion with the Committee on Safety of Medicines, I do not believe there is any suggestion that either the committee or the Biologicals Subcommittee were told about your prioritisation until September.</p> <p>DR JEFFERYS: Correct, but they did not in September, as they have done on occasions, write to say they would wish to see this earlier. That is the only point I am making in there. Of course, the Southwood Committee itself, I think we saw we were running in tandem with this, it is my understanding that its next meeting was not until the November. That is my understanding and it was inevitably in some of the influence at the time there.</p> <p>MR WALKER: I am going to turn to the question of consultation with MAFF.</p> <p>LORD PHILLIPS: The question of whether they went to the September or November meeting, was that basically your decision or was it just the way it turned out?</p> <p>DR JEFFERYS: I think this is the way it turned out and would have been a joint decision between myself and the pharmacists, what is the earliest we could practically get this before the committees, assuming this was meant to be, as it was, a fulsome paper which allowed decisions to be made. If it had been decided to go against our normal practice and be a one page paper, then this could go to September. If we practise our analysis, I am reasonably confident that that would have led to the more detailed paper going again in the November. That is the point I am trying to make.</p>
267	<p>[Insert new para 267A]</p> <p>Dr Rotblat said in a supplementary statement to the Inquiry:</p> <p>'I should perhaps also make it clear that preparing a paper (YB88/9.00/3.1-3.37) on the issues raised by BSE for medicinal products was an unusual task that fell outside the normal range of work undertaken by MB3A. The work undertaken by myself and by MB3A as a whole principally consisted of processing product licence applications. I believe that I was chosen to write the paper with Dr Purves not because the work naturally fell within the remit of MB3A (it did not) but because my previous experience, gained before I joined Medicines Division, meant that I was better qualified than other physicians within the Division to do so.' [Insert new footnote 316A: S Rotblat 2 (WS422A), para 5]</p>
267	<p>[Insert new para 267B:]</p> <p>During his oral evidence Dr Jefferys was asked about Dr Rotblat's evidence about the framework for considering BSE: [New footnote 316B: T112 p37 line 8 – p 39 line 19]</p> <p>MR WALKER: Of course, with BSE we are concerned with something where there were no reports of adverse reaction?</p> <p>DR JEFFERYS: Indeed, because of the long incubation period.</p> <p>MR WALKER: It is that aspect, looking at something -- we are not involved with looking at adverse reactions -- that I would like to explore a little further. Looking at what you did in</p>

	<p>relation to applications for product licences, Dr Rotblat has told us that there was a framework. As I understand it, there were two principles which underlay your analysis of advice on the risk of transmission of disease. The first that she has mentioned is that you would look to seek to ensure the safety of the raw ingredients. The second is that you would look for sterilisation or inactivation procedures in the process of manufacture to minimise any remaining risk?</p> <p>DR JEFFERYS: Yes, I agree with both those. Of course, it is interesting to remember that at this time we had just come through the whole issue, indeed, we were still dealing with some of the issues of HIV, which is exactly the process which had been used there. I think when she is talking of framework, I think Dr Rotblat was referring to an intellectual framework, what today we call risk assessment. I don't think it was given that title then. I agree the issue was to look at the provenance of the starting material and then to look at the inactivation and processing procedures.</p> <p>MR WALKER: What I would like to explore with you is, if concerns are being raised about a product, which are not about adverse reactions, then the mental process, the analysis one needs to do, is really the same sort of process that Dr Rotblat has described?</p> <p>DR JEFFERYS: I think it is a common process which is used across the division. The analysis of the issue in this case would be a starting material, but if you are saying would that then fall to a particular branch, what I am saying is that this would normally today have fallen within the provenance of what we call "pharmacovigilance". It is perhaps fair to say that in 1988 that area was more focused, because of resources, on the spontaneous reports through the yellow card system. I think what I was trying to say in my statement there was perhaps we did not have the structure which we had today, the clear division between licensing and post-licensing which allows this to be carried forward.</p> <p>MR WALKER: I follow the point about there being a lacuna. I think the question I am exploring with you is if something arose where there was this lacuna, and the thing that arose was in relation to a biological product, would your branch not be the logical branch to look at the matter?</p> <p>DR JEFFERYS: It might be seen so today, but in terms of the resources at the time it was not a function which was given to us to undertake, although clearly a subsequent decision was made to move towards generating the guidelines which would apply to all products. So I think this was considered by the division as an approach for all products. If you are asking me whether this was a responsibility in May and June of the new drugs group, no, it was not.</p>
277	<p>[Insert new para 277A:]</p> <p>During his oral evidence Dr Jefferys was asked about the Norsk database: [New footnote 321A: T112 p 70 line 20 – p 72 line 12]</p> <p>MR WALKER: I think that Dr Rotblat has told us during the preparation of this paper she and Dr Purves identified that the database was inadequate, because in particular it did not give you data on materials used as excipients or materials used in the production process as intermediates?</p> <p>DR JEFFERYS: I am not sure that is fairly correct. The database held at that time was a complicated database, so-called NORSK database, which was run by our administrative branch under Mr Hagger. It was a complicated database. It is not like the system today with modern technology which is a PC-based system in the building which is interactive and allows staff to have all the information instantly on the products at their fingertips. This needed to be used by a very small number of information scientists who were able to extract the information, but it was complicated to use and you needed to be able to ask the right questions in the right way and sometimes to ask them on several occasions to be able to elaborate that, but with the exception of one or two older products for the review which I think you are highlighting in this paper, which are homeopathic products. With the exception of those, my understanding was that the database would reveal bovine material used as the active and used as the excipient. What it would not do is to reveal in any reliable way those materials used in the distant development of the vaccine. Some of that information would be available and should be available on the various gold files. Those can be in themselves very extensive documents which are submitted at the time of the licence application and then are retained within the division. I think it may be helpful to make that point because that is my understanding of the database. Some of that is with hindsight, because I now have responsibility for our new database, the product licence user system and obviously the</p>

	development of that, and I am rather more familiar than I would have been because I had no use of the issue there, but I am aware of what the database was capable of doing. That is a rather long answer, but it is important to recognise that, I think.
277	<p>[Insert new para 277B:]</p> <p>During his oral evidence Dr Jefferys was asked about the his knowledge as to any information obtained by Dr Purves and Dr Rotblat about the use of bovine materials in manufacture of medicinal products during the preparation of their paper: [New footnote 321B: T112 p 72 line 14 – p 73 line 4]</p> <p>MR WALKER: ... Just before we leave this area though, there is not any real suggestion here that Dr Rotblat or Dr Purves had actually gone out and obtained information about what was happening to supplement what they could not get off the database?</p> <p>DR JEFFERYS: I am not wholly sure that is true either, because if I recall, I think Dr Pickles had referred to a rabies vaccine in her minute and in this paper there is no mention of a rabies vaccine. Why not? Because there was not a rabies vaccine which used bovine material on the UK market at that time, so I think some information had been ascertained. I have actually asked the two individuals concerned very recently, and certainly they do recall making some targeted questions in the preparation of this particular paper. I think that might be helpful to the Committee to know that.</p>
278	<p>[Insert new para 278A:]</p> <p>During his oral evidence Dr Jefferys was asked further about the paper prepared by Dr Purves and Dr Rotblat in September 1988: [New footnote 322A: T112 p 64 line 10 – p 70 line 4]</p> <p>MR WALKER: I think we should have in front of us the Rotblat and Purves paper. That is in our FAD bundle. The reference is YB[88/9.00/3.2. We see from the top corner that is a paper for CMS, SEAR and the Biologicals Subcommittee. The pharmaceutical assessor is Dr Purves and the other is Dr Rotblat. Then we find the paper itself has a section headed “Background”. There is some information about BSE and there is the similar disease, scrapie, and then at paragraph 2, consideration of the BSE agent, its existence and implications for medicines containing bovine material. That makes reference to the Southwood Group. Then over the page we find in the middle of the page four subparagraphs. The introduction to those is that: “It would be prudent to widen the considerations at least in a preliminary way to cover related aspects, namely ...” and then we have: “2.1 The animal species from which tissue is sourced. “2.2 The significance, if any, of the various types of tissue that may be used.” That would be looking at the raw materials, as I understand?</p> <p>DR JEFFERYS: Yes, the safety of the starting material.</p> <p>MR WALKER: Then 2.3: “The ability of the manufacturing and purification procedures to destroy or remove viral or virus like agents.” That is the second part of the framework that Dr Rotblat describes, is that right?</p> <p>DR JEFFERYS: Yes, indeed. I think that perhaps there are two issues here. This is looking at the product itself and how on the pharmacy side and it is a Dr Purves issue, that how the product being manufactured, that in itself, those processes, might have removed any possible risk of contamination, that may be the viral filtration, heat processes, the quantity of material and so on. This is referring to what he has done with the product itself. There is a separate issue which is then picked up later about what other techniques might be applied to inactivate. There are two elements to this, I think.</p> <p>MR WALKER: 2.4 is the products involved, type of tissues they contain, and the relative risk to the patient on administration of a contaminated product and three methods set out there. That involves taking the framework and considering how it applies to the products that are being used for medicinal purposes?</p> <p>DR JEFFERYS: Correct. I mean, remembering that for medicinal products one also has to take into account the efficacy of the product itself, some of which may be used in very specialist circumstances for which there is a very particular benefit to the group of patients or the individual patient concerned. It is classical risk to benefit here, there is an efficacy side which may not be the same if you are looking at food or other materials. That is what comes out from 2.4 here.</p> <p>MR WALKER: In relation to 2.4, do you see this as being a particularly pharmaceutical point or particularly medical point or neither?</p>

	<p>DR JEFFERYS: I think this paper, which was brought by a team, two individuals from across the division, was bringing the expertise of both authors to bear on this. Clearly, 2.4 is the more difficult, because you have for a product a particular efficacy, maybe a very narrow group of patients, and here one is attempting to look at the issues set out previously here, to see what the risks might be of an agent. I use the word without the benefit of hindsight which might be carried forward to different routes. This would be very much here operating in a team manner, the joint paper being produced, but the majority of this derives from the expertise of the pharmacists, because I go back to the point that the inactivation processes and the same starting material are the fundamental issues here.</p> <p>MR WALKER: Equally though there are questions of safety and efficacy which would be for the physicians?</p> <p>DR JEFFERYS: The physician would be very much putting the context of how, for example, bovine insulin would be used in late 1988, and in terms of the risks here this would be a joint conjecture as to how the agent might have carried forward, if indeed it did.</p> <p>MR WALKER: We see the fourth point developed a little over the page at 3.6. After 1, 2 and 3 we see "The fourth and final topic". Do you see that?</p> <p>DR JEFFERYS: Yes.</p> <p>MR WALKER: It continues and relates to the medicinal product and covers three issues. It is clear we need to know which product contains bovine tissues and the type of tissues used in manufacture, so that a database is available for discussion later. If I need to know which products contain bovine tissues, that would be the active ingredients and the excipients?</p> <p>DR JEFFERYS: This is where one would go to say to what extent does one need to know the material used in manufacture, in downstream manufacture and so on, and that is in a sense turning the question around as to what is the level of risk here, how far does one need to go back in the chain?</p> <p>MR WALKER: Can I take you back to that sentence: "It is clear there is a need to know which products contain bovine tissues". That is saying there was a need to know both about active ingredients and excipients, which contained bovine tissues?</p> <p>DR JEFFERYS: Correct. As written there, this would refer to bovine material which the patient would receive.</p> <p>MR WALKER: Then it continues, having begun, "It is clear there is a need to know", it continues: "Along with details of the type of tissue used in manufacture." Would that be referring to intermediates?</p> <p>DR JEFFERYS: It is difficult to say whether the type of tissue here. Applying the benefit of hindsight it might, but also might refer to the source, the country of origin or the source within a particular country. I think it is difficult, not applying hindsight, to say what that would be able to mean, at this distance from the matter of 11 years.</p> <p>MR WALKER: If we go on to page 3.9 we see some recommendations. We see at (vi) the recommendation that there should be an article requesting manufacturers to identify bovine preparations used in the manufacturing process and should come from healthy herds. Do you see that?</p> <p>DR JEFFERYS: Yes, I do, thank you.</p> <p>MR WALKER: Can you help the Committee about bovine albumin and foetal calf serum? Are they excipients or active ingredients or intermediates?</p> <p>DR JEFFERYS: Foetal calf serum and bovine albumin are used in the development of certain vaccines. They would be used in the development of viral vaccines. Those are grown on cell cultures and therefore, put very simply, to enable the cells to be viable they have to be given something to keep them viable, food. Therefore the foetal calf serum is essentially there to allow the development of the viral vaccine, the virus which is inactivated. I think Professor Collee's statement sets this out well, the difference between the bacterial and the viral vaccines here.</p> <p>LORD PHILLIPS: They are intermediates?</p> <p>DR JEFFERYS: Yes, often at an early point of manufacture, when one is going the cell culture.</p>
321	<p>[Insert new para 321A]</p> <p>In a supplementary statement to the Inquiry Professor Asscher said:</p> <p>'2. At the meeting on 17 November 1988, the CSM made a number of recommendations (see paragraph 37 of my first witness statement WS 441). I wish to make it clear that</p>

	<p>the CSM did not intend those recommendations to be final at that time. My recollection is that the CSM saw its November 1988 recommendations as preliminary and envisaged that further work needed to be done on them before they were brought back to the CSM to be finalised.</p> <p>3. My recollection is that we considered that the November 1988 recommendations were not yet in a form suitable to be distributed to product licence holders. I believe that the areas in which we perceived that further work was particularly required were the concept of appropriately certified healthy herds (see recommendation 2) and the question of sterilisation by autoclaving (see recommendation 3) (YB88/11.24/4.1-4.2 at 4.2).</p> <p>4. I remember that the CSM considered it important that, as far as it could, it finalised its policy on BSE before it communicated formally with the pharmaceutical industry. My recollection is that we did not intend the article in MAIL (recommendation 5) (YB88/11.24/4.1-4.2 at 4.2) to be published before clarification of the term “certified herd” was obtained from MAFF and the question of sterilisation by autoclaving was resolved.</p> <p>5. In all this, the CSM was determined to ensure that the substance of its advice on BSE and any formal communications with the industry were right. Failure to do so could have resulted in us being confronted by an angry and confused industry at a time when their collaboration was badly needed.’</p> <p>[Insert new footnote 376A: S Asscher 2 (WS441A)]</p>
321	<p>[Insert new para 321B:]</p> <p>During his oral evidence Dr Jefferys was asked about MAIL: [New footnote 376B: T112 p 108 line 17 – p 110 line 10]</p> <p>MR WALKER: I will turn to the speed with which the questionnaire was issued. I think the starting point is the recommendations of the Biologicals Subcommittee. If we turn on in our bundle to YB 88/11.2/4.1, the minutes of the sixth meeting 1988 of the Biologicals Subcommittee, and we see that you were present as medical assessor?</p> <p>DR JEFFERYS: Correct.</p> <p>MR WALKER: If we turn over the page we find that section 7 is a paper on BSE and a number of recommendations after a full discussion. They are listed as A to G. I was going to draw your attention to E: “There should be an article in MAIL requesting manufacturers identify products in which bovine materials have been used.” MAIL was a medicines information bulletin?</p> <p>DR JEFFERYS: Correct, sent to the 4,500 licence holders worldwide.</p> <p>MR WALKER: What was the nature of it? Was it a confidential bulletin or one which companies were free to publicise?</p> <p>DR JEFFERYS: MAIL is a publicly available document now; as time as moved on it is even on the Internet, but at that time sent to all licence holders, publicly available, which sets out any guidance, guidelines, instructions from -- interestingly at that time it was both human and veterinary, subsequently it was split out, but at that time was common to both areas and that is an interesting point to observe there, and also we set out details of any prosecutions and other legal notices would be required in there. You could say it was our gazette of medicines information matters, both human and veterinary.</p> <p>MR WALKER: An article in MAIL requesting identification of products in which bovine materials had been used, that would be within the normal uses of the MAIL bulletin to seek that sort of information?</p> <p>DR JEFFERYS: No. It would have been an appropriate vehicle to use but to ask for information from more than around 4,500 licence holders would have been very abnormal; the only time in my 15 years that would have been done.</p> <p>MR WALKER: You had not done an exercise of that before?</p> <p>DR JEFFERYS: No, and a major undertaking if you are asking for 4,500 worldwide to respond.</p>
328	[Insert new para 328A:]

	<p>During his oral evidence Dr Jefferys was asked about liaison with MAFF: [New footnote 385A: T112 p 105 line 9 – p 108 line 16]</p> <p>MR WALKER: I want to explore whether it might be right to say that liaison with MAFF should have occurred at an early stage. Go back to the minute of 13th April, YB 88/4.13/5.1. I was going to ask you about paragraph 5 here, the recent requirement that animals from which biological products derived were healthy. Did you know at the time whether the fact that the animal was healthy would have any bearing on whether BSE infectivity might be present in the animal?</p> <p>DR JEFFERYS: I personally would not have had enough knowledge or expertise to be able to comment on this. I was just making an observation here that this had been a requirement which might at that time have provided some degree of reassurance that we were seeking at that time a certificate that the animal was healthy when the product was taken from it. Obviously as the story unfolds one takes a different perception. At the time that was one degree of perhaps minor reassurance but it was a statement of fact as to what we had required, because of concerns about other viral contamination. It had not arisen in the context of BSE, but other prior contamination of products at that time.</p> <p>MR WALKER: This was an area where your colleagues at the Central Veterinary Laboratory were likely to have relevant information, is that right?</p> <p>DR JEFFERYS: So I believe, yes. There was a link between Medicines Division and the Veterinary Products Committee on there, but that again was not a link that was a responsibility in my branch there. It is referred to by others in their witness statements.</p> <p>MR WALKER: Can you recall whether it occurred to you in April 1988 or later, before September, that it was possible that Central Veterinary Laboratory had already been looking at animal medicines in relation to BSE and that they might have something useful to offer you?</p> <p>DR JEFFERYS: I cannot recall at that time -- I did know at that time, and I think it is referred to in the witness statements, that Dr Adams and Dr Diggle, who worked in the review team, were the contact points with the Veterinary Products Committee, so they might have brought information across. Within my own branch that was not an issue where we had discussion on there, but it is something, if I may go back, where the pharmacists might well have had liaison there. It did not occur to me, no, on the medical side at that stage for new products.</p> <p>MR WALKER: If you had made contact with the Central Veterinary Laboratory, I think you will appreciate this is hypothetical, but if you had, your branch, made contact with them earlier in the year before the stage when Dr Rotblat was preparing the paper with Dr Purves, you would have become aware of what MAFF had been doing in relation to veterinary medicines and BSE?</p> <p>DR JEFFERYS: As a hypothetical question the answer to that can only be yes, but I will add I think Dr Purves in his statement does refer to extensive external contacts which he was making during the preparation of that paper, and other papers which I have seen around that time show that the Pharmaceutical Secretariat did have extensive contacts in there. They would be the entry, because we go back to the fact that this was a safe starting material issue, but if you are asking a different hypothetical question of me, I think you need to put that into context.</p> <p>MR WALKER: I want to go back to the context of your initial look at the matter and your response, I appreciate your prompt response, of 13th April. Might it be right to say that because of the obvious interest of the Central Veterinary Laboratory in the matter, you ought to have taken steps to make contact with the laboratory at this time when you are dealing with this minute in April 1988?</p> <p>DR JEFFERYS: I think that could be said, but perhaps the reverse could also be said, could it not, that was contact being made with us? I think interestingly this minute is shared by Mr Wilson with other colleagues in the department which then says, if I have seen the annotations correctly, "Could Medicines Division please be kept informed of other developments"? I would have to turn that one back, speaking for the division, not my own branch. I need to make that point, that I am referring to my division. Most people are taking the division rather than my branch, as it were.</p>
423	<p>[Insert new para 423A]</p> <p>In a supplementary statement to the Inquiry Professor Collee said:</p>

	<p>‘2. I should first of all like to draw attention to paragraph 79 of my first witness statement [WS423] and in particular the sentence “I believe that the purpose of the article <u>at this stage</u> (emphasis added) would have been to discover the extent of the use of bovine material rather than to issue guidelines to industry.” That sentence was not intended to draw a hard and fast distinction between the issuing of guidelines and the seeking of information. Both were to prove necessary, but the way in which they were best progressed had not yet been developed. Although the BSC (Committee on Safety of Medicines, Sub-Committee on Biological Products) and CSM were aware that action on existing products would need to be taken and had begun to consider the criteria which manufacturers should be expected to meet (see recommendation (b)) I do not believe that we had got as far as determining the way in which this information could best be disseminated, nor how compliance with these criteria should be secured. That is what was meant by paragraph 79 of my witness statement [WS423]. Those on the committees knew that the way to take the recommendations forward would be discussed and decided within Medicines Division and after liaison with other agencies such as MAFF. I believe that it was as a result of this that the decision to issue guidelines was taken.</p> <p>3. I should also make it clear that those concerned with this issue on the BSC and CSM appreciated that the recommendations as drafted required further work. A number of the concepts contained in the recommendations needed to be worked through so as to produce an end result that would withstand scrutiny and prove workable in practice. We appreciated that this would require a process of liaison with MAFF, who had expertise in various areas that were not the province of the CSM. It also needs to be understood that the recommendations were seen by those on the BSC and CSM as a composite package. We did not envisage that one particular recommendation could be detached and treated in isolation from the others.</p> <p>...</p> <p>8. The guidelines and questionnaire [YB89/03.00/1.1-1.3], sent together, constituted a comprehensive response to the problem posed by the emergence of BSE in relation to human medicines. Those asked to answer the questionnaire could see precisely why the questions which they were being asked were of relevance. It is my belief that this greatly improved the quality of response to the questionnaire itself. All of the manufacturers reacted most responsibly and most were able to reply promptly. Some needed time and properly received careful advice from informed staff in Medicines Division.’</p> <p>[Insert new footnote 492A: S Collee 3 (WS423B)]</p>
424	<p>[Insert new para 424A:]</p> <p>During his oral evidence Dr Jefferys was asked about the apparent delay in publishing an article in MAIL seeking information from licence holders: [New footnote 493A: T112 p 114 line 2 – p 117 line 11]</p> <p>MR WALKER: In the event this recommendation for an article in the MAIL seeking information was not put into effect promptly after the meeting of the Committee on Safety of Medicines on 17th November. There was no request for information until March 1989. To what extent were you involved in that delay?</p> <p>DR JEFFERYS: I think I have tried to make the point that this was an issue, a team approach, across the division. I am not sure I would accept the word delay. I think rather there were some questions raised by Sir Richard Southwood and perhaps members of his Committee in correspondence with Professor Asscher which needed clarification upon, which Asscher set out in his witness statement, out of which further work was necessary. These were elaborations, as I recall, the paper suggests to me, on the framework guidance which had been issued. The point of the questionnaire was that this was to provide information not just on bovine material but animal materials to be future looking there, and was seeking answers to a series of questions which related, as I would see this, to the guidance which had been put forward. Hence the position on stock, hence the position on when the companies were able to comply with the guidelines and so on. Perhaps I should stop there. Does that help?</p>

	<p>MR WALKER: I think we had better see what happened and to what extent you were actually involved. Can we begin with paragraph 52 of your third statement? You say there was a consideration during this period that all were awaiting sight of the Southwood Report?</p> <p>DR JEFFERYS: That is correct.</p> <p>MR WALKER: "This was of particular importance not simply because it was felt that it would be the most authoritative consideration of the issues raised by BSE, but also because it needs to be remembered that any action taken in respect of individual pharmaceutical products had to be justified on an evidential basis." When you described this are you describing an input that you had into the decision-making process, that these were your views that you were expressing to others about when the request for information should be made saying that it should wait for the Southwood Report?</p> <p>DR JEFFERYS: No, I think this is one of the slight difficulties which I have had during this, that it says there was not a Phase I hearing here. I am trying to set out in 52, and some of these other points, my recollection to help the Committee of what was happening across the division. This was a divisional consideration which I was part of, and very much support what was done, but this is across the entire division at this stage, witnessed by the copy lists on these minutes and the whole division being involved in the different aspects of this.</p> <p>MR WALKER: So far as your own involvement is concerned, would it not have been appropriate for you to say if we are seeking information we do not need to wait for Southwood; we can seek information and that will be a useful thing to do?</p> <p>DR JEFFERYS: I think what was attempted in that period was that we were seeking more -- we were not seeking a questionnaire. What we were seeking was information, if you look at the subsequent questionnaire, as to were the industry now complying with the guidelines? Remember many were resourcing their products, as I outlined earlier. They are very well cited industry, up-to-date with the science. Were they already in compliance and what was the position on stock and how long would it take them to comply with this? Therefore, to have issued a questionnaire one or two months earlier and then to issue a repeat questionnaire to four and a half thousand licence holders worldwide would have been somewhat difficult with the resources available to those who need to receive them. Secondly, this is not something which was going to be just passed by. A statement like this would be picked up by the professional journals and would have to be based on a statement, not least of which because this goes worldwide and to issue without guidance would have raised very important questions back from the industry, back from other regulatory authorities and perhaps in the media as well. So there are a number of factors which fed in there. I was party to those discussions but those were pan agency decisions made above my level.</p>
424	<p>[Insert new para 424B:]</p> <p>During his oral evidence Dr Jefferys was asked about the need to await the report of the Southwood Working Party: [New footnote 493B: T112 p 117 line 19 – p 118 line 5]</p> <p>LORD PHILLIPS: I am just interested. You are waiting to see what Southwood was going to say. What they said was that the risk was remote but they have asked the CSM to take whatever steps are appropriate?</p> <p>DR JEFFERYS: Yes.</p> <p>LORD PHILLIPS: How did that actually help the process?</p> <p>DR JEFFERYS: At that stage we did not know what the Southwood Report was going to say in its final word. In the event the CSM had issued its recommendations in tandem, at the same time as the report was given. I am trying to reflect here what the feeling was that we were operating in tandem with Southwood.</p>
424	<p>[Insert new para 424C:]</p> <p>During his oral evidence Dr Jefferys was asked about the process leading to the issuing of a questionnaire and guidelines: [New footnote 493C: T112 p 126 line 14 – p 129 line 10]</p> <p>DR JEFFERYS: Again, this is very difficult 11 years on without reconstruction, which may sometimes lead one into errors of construction, but I think this was an evolving process here. I think if you look at the flow of events, there was detailed consideration by experts in the Biologicals Subcommittee, the SEAR Subcommittee and the CSM and in the other two Section 4 Committees, and then Sir Richard Southwood formed his group, and subsequent to the meeting of his group raises one or two issues which had not arisen in the discussions as I</p>

	<p>understand them, but had come forward which Dr Purves had had with the colleagues in MAFF, when these were being elaborated, and they had raised some issues over the healthy herd on one side, but on the other side of the equation, saying that maybe the recommendations are too strict in the requiring of hardy virus studies and so on there, and that was an issue which then needed to be taken back with the CSM with those experts to look at those issues again. If those questions had not been raised, very proper and right they were, this was an iterative process, the guidelines might have been issued earlier in which case, perhaps as you are alluding, the questionnaire might have been issued earlier but this is an evolving matter as the two were brought together. I think on the informal point here, it was already seen and is borne out by what was happening at the time, that the industry -- let us be clear, what we are talking about here are those making parenteral products. That is a very specialised area of the pharmaceutical industry involving a great deal of expertise to bring together those high technology advanced products. Those small group of companies, the majority of whom are based outside the United Kingdom but are very familiar with the science, would have already been there by informal channels that I alluded to earlier here. I think it is interesting but I am not quite sure to be frank how you informally consult with those who might not know about this whom you do not know who they are. It is a little naive to believe that way. I think that those who knew about this were aware through the usual channels, and indeed several had already resourced their products because they had their own very eminent scientists advising them, some of whom were advising other bodies in here. But I am not sure you can give something in MAIL informally. The MAIL in those days was only issued every three months, from memory. It was quite a major undertaking. It would not have been possible to issue an informal notice in MAIL. Equally -- and I think senior lawyers were present at the committee in November -- the Licensing Authority finds it very difficult to offer informal advice when it is a Licensing Authority. So just to put that into the context again, we were working towards getting the guidance out as soon as possible, and the questionnaire happened to run alongside that. In the event that the guidelines had been further delayed, the questionnaire might have been issued earlier or vice versa. Sorry to give a long answer, but I am trying to explain what was in the mind of the division and my own mind at that time. I do not know whether that helps or not, but I am trying to be helpful.</p> <p>LORD PHILLIPS: Did MAIL go to all companies that had current licences for products in this country?</p> <p>DR JEFFERYS: It went to everybody who had any form of licence in the country. Obviously anyone outside the country -- it went to everybody who had ever had or had a pending licence, or a Clinical Trials Exemption Certificate. It was a very wide, and still is, a very wide audience there. And to all regulatory authorities worldwide as well. It is not a minor issue.</p>
531	<p>[Insert new para 531A:]</p> <p>Dr Minor has said in relation to the CSM Working Group on BSE: [New footnote 613A: S Minor (WS 576) para 27]</p> <p>27. I was invited to join the CSM Working Group on BSE. I believe I was invited to join as Head of Virology at the NIBSC in order to provide expertise on biological products. I remained a member throughout the WP's existence. I attended the first meeting on 6 September 1989[YB89/09.06/10.1-10.12]. It appears from the minutes that I attended each of its meetings, except those of 10 January 1990 [YB90/1.10/3.1-3.3] and 8 July 1992 [YB92/07.08/14.1-14.2]. I do not recall why I missed those meetings. I cannot now recall the detail of any of these meetings. Looking at the minutes now I believe I would have been happy with the WP's work at the time, and considering the matter again now, I remain so. By way of general observation, I note that the minutes reflect that the approach taken to eradication of bovine materials from medicaments was essentially to see them phased out. That in fact happened rapidly. As far as I am aware at that time there was no evidence that BSE was transmissible to humans; this approach was adopted to ensure that the proven clinical benefits of those materials were not lost in the face of an unproven risk.</p>
531	<p>[Insert new para 531B:]</p> <p>Dr Schild has said in relation to the meetings of the CSM Working Group on BSE: [New footnote 613B: S Schild (WS 575) paras 50-56]</p> <p>50. I can remember nothing about the details of the meetings themselves but have</p>

	<p>reconsidered the minutes, and would make a number of general comments about their contents.</p> <p>51. The minutes reflect an awareness of the need to strike a balance between the risks posed by BSE and the benefits of the use of bovine material in medicines and vaccines; see for example paragraph 3 of the minutes of 6 September 1989 [YB89/09.06/10.1-10.12], and para 6.3 of the minutes of the meeting of 10 January 1990 [YB90/1.10/3.1-3.3].</p> <p>52. The bovine material is most commonly used in the form of calf serum employed in the manufacture of viral vaccines and in addition, other bovine materials were used in bacterial growth medium in the production of bacterial vaccines. Based on studies of other animal TSEs (such as Scrapie) in the 1980s and subsequently, serum was and still is considered a very low risk material. Any potential risk is further reduced by sourcing from young animals where there is a low risk of BSE contamination of any tissue. The time needed in order to phase out UK sourced bovine materials completely from such products would be substantial. An unchanged and standardised manufacturing process is the key to ensuring a consistently high quality product; a change from bovine serum could potentially have had a significant effect on the quality and efficacy of a vaccine. Any such change could require research and development work and clinical studies to confirm the quality of the product.</p> <p>53. Even a switch to the use of bovine materials sourced outside the UK could not have been made “overnight” without major disruption of the availability of vaccines. Typically, manufacturers make seed and bulk vaccine preparations which remain potentially useable for many years. Replacing vaccine stocks using a new seed which had not been in contact with any UK bovine materials would take time and effort on the part of manufacturers and was, in the event, undertaken expeditiously.</p> <p>54. Self-evidently, vaccines are of vital importance in preventing the spread of diseases such as measles, polio, whooping cough. There is a danger these diseases would spread rapidly if vaccines were discontinued, even for a short period of time. It must further be born in mind that at this time, as far as I am aware, there was no evidence of transmission of BSE from bovines to humans.</p> <p>55. The strategy adopted was therefore to seek to ensure that the source of bovine material used would be switched to BSE-free countries as soon as possible without interruption of vaccine supply. In fact, the manufacturers moved quickly, and I believe that by 1991 all bovine materials for vaccines were sourced from outside the UK.</p>
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