Friday, 14 October 2011

(9.30 am)

(Proceedings delayed)

(9.43 am)

THE CHAIRMAN: Good morning. Yes, Ms Dunlop.

MS DUNLOP: Thank you, sir. I'm obliged to you for allowing a little bit of time for the resolution of one or two minor issues. There remains, however, a matter which I need to draw to your attention.

Professor Ludlam is not yet in the room because there is an issue about what questions are going to be put to him by counsel for the patients, families and the Haemophilia Society. A set of questions was intimated timeously and indeed, I have tried to include a number of them in my own questioning but some of them are very specific to two particular individuals.

You have the list, sir, and the questions I'm referring to are questions 18 to 23 and then also questions 51 and 52, which relate to a second individual.

Normally, when counsel for one of the core participants intimates questions in advance, it's possible for the lists to be discussed between counsel and a common position reached, but on this occasion I have taken the view that whether these particular

questions may be posed should be a matter for you, sir. I would therefore suggest that it might be best to invite counsel for the core participants to address you on whether these questions are appropriate.

THE CHAIRMAN: Right. As a formal matter, can I be sure that I understand the scope of the potential dispute. Gentlemen, do you agree that these two groups of questions, 18 to 23 and 51 to 52, are the contentious areas?

MR ANDERSON: Sir, those are the questions and the only questions to which I would object in this list.

THE CHAIRMAN: And you are content that that is the position also?

I should say, gentlemen, that in the case of the questions 18 to 23, the list of questions that I have seen name an individual and I'm not anxious that the name should appear as an aspect of any debate that takes place here today. On the other hand, does the individual in question, or do the individuals in question, know that they are being discussed in this way?

MR DI ROLLO: Yes, they do. I don't think it's necessary for my purposes that they should be named or identified in any way.

THE CHAIRMAN: They have to be identified in some way to

make sense of the discussion.

Application by MR DI ROLLO

Submissions by MR DI ROLLO

MR DI ROLLO: I suppose so. But there are two specific instances which require some examination, in my respectful submission. It is not necessary to identify or to name the individuals.

THE CHAIRMAN: Is there a protocol that we can adopt that will make it sensible, distinguish between the two and make sure that the transcript can be read?

MR DI ROLLO: I believe they are already called A and B, I'm being told.

THE CHAIRMAN: They are in some contexts being called A and B, but I have to know here in public that that's the way we are going to do it. Is the individual in questions 18 to 23 to be called "A"?

MR DI ROLLO: Very well, yes.

THE CHAIRMAN: And the individual in questions 51 to 52, "B"?

MR DI ROLLO: Very well, indeed.

THE CHAIRMAN: I think that I can go about this in a number of ways but in order to keep matters within reasonable bounds, it might be best, Mr Di Rollo, if you would make a positive application to have these heard.

As you know, you are departing from my protocol as

to how these applications should be made but since the questions were intimated, I understand in good time, and Ms Dunlop has had a chance to look at them, I'm not going to take any procedural point in this case, but please don't take that as an indication that I will relax the strictures that I have sought to lay down in any other case.

Would you like to take them, I think, group by group, Mr Di Rollo? So deal with questions 18 to 23 first, and you can tell me how these fit into my terms of reference and why I should explore them in the way they are put.

MR DI ROLLO: 18 to 23 concern the circumstances in which patient A became infected with Hepatitis C as a result of the administration of a concentrate in May 1986.

THE CHAIRMAN: Yes. Okay.

MR DI ROLLO: And your terms of reference, of course, do encompass the circumstances generally in which patients became infected as a result of the administration of concentrates.

THE CHAIRMAN: Yes, well, I think I should say that the generalities on that seem to me to have been very widely explored already and, as at May 1986, I would incline to the view at the moment that the evidence probably establishes that by that date, everyone getting

Factor VIII concentrate already was, if they had been treated in the past, or would immediately become infected. Is that not so?

MR DI ROLLO: Yes, it does.

THE CHAIRMAN: What is particular to this person, patient A, that affects the generality of that view?

MR DI ROLLO: The circumstances are whether or not he, as a previously untreated patient --

THE CHAIRMAN: Whether he, as a previously untreated patient?

MR DI ROLLO: Yes.

THE CHAIRMAN: Yes, okay.

MR DI ROLLO: Should have received a Factor VIII concentrate at that time.

THE CHAIRMAN: That appears to me immediately to be a question of clinical practice and not a question of the infectivity of the product or the general issue of vulnerability of patients to infection if they got it, Mr Di Rollo.

That's as far as I'm going at the moment, Mr Di Rollo. I want you to be alert to that as a problem. I would like this to focus on my terms of reference, not on what might be the subject of proceedings elsewhere. Are these issues the subject of proceedings elsewhere?

MR DI ROLLO: They are the subject of proceedings elsewhere.
THE CHAIRMAN: Then you will be conscious of the question as to whether any power of mine should be exercised in a way that is ancillary to the pursuit of litigation outside of this room, rather than in pursuit of my terms of reference.
MR DI ROLLO: I can assure you that I'm well aware of the need not to use this as a vehicle for pursuing in litigation, and it's not my intention --
THE CHAIRMAN: Mr Di Rollo, it's not you I'm concerned with here, with the greatest respect. I understand you are carrying out your instructions and I'm not suggesting the matter shouldn't have been drawn to my attention. I accept that it should. But I think I have to be aware that I have powers that have been prescribed to enable the recovery of documents, the citation of witnesses and so on, to instruct this Inquiry as to matters of fact relevant to the disposal of the terms of reference.

If I can't be sure that that's why I'm being asked to do something, that becomes a factor in itself.

Anyway, I'm going to let you get on and tell me what it is. You know I have been thinking about this and I have been looking at it, but I want you to tell me, in a way I can write down and be sure that I understand, just exactly what it is that makes this relevant to the

Inquiry.

MR DI ROLLO: What makes it relevant to the Inquiry is an examination of the systemic issue of the decision-making relative to whether previously untreated patients should or should not receive factor concentrates during the relevant period, ie the period between the end of 1985 and the middle of 1987.

THE CHAIRMAN: Just pause on that so far. It's systemic issue of the decision-making. Now, these are clinical decisions, are they?

MR DI ROLLO: There are decisions to be made in relation to the ordering or not ordering of the 8Y concentrate from England and then there are, beyond that, on guidance to be given in relation to the circumstances in which previously untreated patients should receive concentrates.

THE CHAIRMAN: Mr Di Rollo, I can see some general questions implicit in that, for example, whether there were established protocols for addressing the question. That's not what you are asking. But there are other points, you see: the ordering of 8Y. Maybe I should draw to your attention right away, because it occurred to me when I saw this, that in the UK Haemophilia Reference Centre Directors' analysis of possible forms of treatment, [SNB0015606] of 16 May 1988,

paragraph 5.2.3:

"For patients in Scotland and Northern Ireland with Haemophilia A, NHS 8Y is not available and we recommend either Z8 or [something else]."

That's when 8Y was in production. The period we are concerned with now is the period when it was being tested and there are records as to what the CTX was for, and if you are going to raise questions about the availability of 8Y in Scotland, it seems to me that perhaps a necessary prior step is to establish that there was indeed an availability of the product other than on the casual basis, perhaps, that we have heard about from Professor Ludlam already. There is no use in asking about protocols for the use of a product if it's not available.

Could you just tell me then what your researches have shown as to the availability of 8Y for general use in Scotland at this time?

MR DI ROLLO: As far as I'm aware, the only way in which this item could be obtained would be in the way in which it was dealt with in the middle of 1986, after this particular event.

THE CHAIRMAN: Then the answer, I am afraid, is that you do not know, Mr Di Rollo. With great respect, where is the factual substratum if you have not researched the actual

availability of the products? I know this is extremely important to patient A in another context, and I know that it's something that patient A wants to be ventilated.

MR DI ROLLO: And this is the only opportunity that he will have for it to be ventilated.

THE CHAIRMAN: So what? The fact that I am here does not create an opportunity. That is a quite inappropriate way to approach it. My question is how, within my terms of reference, I can deal with this, where the substrate of fact is not set up?

So, Mr Di Rollo, I'm not here to exercise sympathy and this is a matter of strict competence from my point of view. I'm not trying to be too hard on you but I think I really must know the basis, and with the greatest respect, to tell me that this is the only time is not part of the answer.

MR DI ROLLO: Well --

THE CHAIRMAN: If it were, it would apply to every single individual in Scotland who thinks that they have something that they want to find out.

MR DI ROLLO: The circumstances in which this occurred were mentioned yesterday in a letter which the -- it was mentioned in the preliminary report as -- the critical letter, I think, is the letter which -- just give me

a moment --

THE CHAIRMAN: Where is the preliminary report reference, Mr Di Rollo? I'll look that up.

MR DI ROLLO: The preliminary report references are paragraphs 10.197 and also at paragraph 11.318.

THE CHAIRMAN: Thank you. And the letter?

MR DI ROLLO: The particular letter that I'm interested in is the letter dated 27 June. It's [SNB0075871].

THE CHAIRMAN: Where do you want to go first?

MR DI ROLLO: If we could go to the letter and just look at the paragraph:

"A young haemophiliac --"

THE CHAIRMAN: Can we wait until it's brought up, please.

(Pause)

MR DI ROLLO: "A young haemophiliac, who previously had minimal therapy with Factor VIII, received an infusion of the current heat-treated product a month ago. He now shows signs of liver enzyme rises indicating non-A non-B Hepatitis. Christopher is a bit ruthful with his own staff about this because he feels that this patient should have received 8Y or an equivalent product."

THE CHAIRMAN: Right. You have looked up in the dictionary, I hope, about "ruthful"?

MR DI ROLLO: I have, I have a copy of it.

THE CHAIRMAN: I was hoping for some help in understanding

its general application.

MR DI ROLLO: I don't, having looked it up in the dictionary, know what "ruthful" is meant in the context it is used in this particular passage, I have to say.

THE CHAIRMAN: You do not know?

MR DI ROLLO: I don't know what was meant by Dr Boulton, and I don't know whether Dr Boulton is using his own word or using Christopher Ludlam's word.

THE CHAIRMAN: I can see the problem; I don't see the solution.

MR DI ROLLO: I have to say the word "ruthful" wasn't one that I had ever seen or used.

THE CHAIRMAN: "Ruthless" is one that occurs more often in a judicial context.

MR DI ROLLO: Indeed, and it seems to be the opposite of that. But the use of the word, I think, when it was explained yesterday in evidence by Professor Ludlam -- he said:

"I think I felt a bit sad that we did not have 8Y to give the patient."

Is what he said. And that use of the word "sad" in that context would seem to be one meaning of "ruthful".

THE CHAIRMAN: It might suggest that the word should have been different and be "rueful", or something like that.

MR DI ROLLO: It might be, or it might not. I don't know.

It's one of the things I would like to explore, and what I would like to know is whether or not Professor Ludlam was upset with his staff because this patient got Factor VIII on that occasion, or whether he was defensive of his staff because he felt his staff had no opportunity to avoid infecting him because the 8Y wasn't provided.

THE CHAIRMAN: Well, now, Mr Di Rollo, could you, please, tell me where that aspect of clinical practice and Professor Ludlam's response to it fits into my terms of reference?

MR DI ROLLO: Well, in terms of reference 8, you are required:

"To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS boards and SNBTS, their officers and employees and associated agencies, to prevent the provision of infected blood and blood products."

In terms of reference 5:

"To examine the circumstances generally in which patients treated by the NHS in Scotland became infected with Hepatitis C, HIV or through the use of blood products in the course of their treatment."

THE CHAIRMAN: I have five specific individual deaths specifically referred to me. Do you say that that

requires me to investigate specific instances other than those deaths?

MR DI ROLLO: No, it doesn't require you to investigate specific instances, but you are required to investigate the circumstances that a number of specific instances potentially gave rise to and may have been avoided.

THE CHAIRMAN: I'm not sure I understand that.

MR DI ROLLO: I will try and explain myself.

THE CHAIRMAN: "Required to investigate the circumstances that a number of specific instances potentially gave rise to and may have been avoided."

Please, you have to break that up a bit and help me.

MR DI ROLLO: Well, we are here concerned, in this particular section of the Inquiry, with a particular problem. We are here concerned with the problem that arose in a period during which it was known that there was a severe danger, or serious danger, that if someone received a concentrate for the first time, they would be infected with non-A non-B Hepatitis.

THE CHAIRMAN: But this is not that sort of case in the light of the clinician; this is someone who has had minimal therapy with Factor VIII but has had some.

MR DI ROLLO: Precisely, and there may well be patients, that we don't know who they are exactly, but there may well be patients out there somewhere who are going to

present to their GP or at Accident & Emergency during this period, who have lower than normal levels of Factor VIII or potentially IX, or some other problem, which means that when they present to casualty, those treating them may well take a decision to administer a concentrate to them. If they were to do that during this period, that would result in infecting them with non-A non-B Hepatitis.

THE CHAIRMAN: Not necessarily. This is a person who has had Factor VIII, in the understanding of the writer. Now, we are talking about clinical practice. That's absolutely clear, and therefore the fact that must be assumed to be in the mind of the person writing this letter was that the individual had had Factor VIII.

MR DI ROLLO: Well, that's an error.

THE CHAIRMAN: With the greatest respect, that simply draws attention to the particularity of this, that has got nothing to do with generality.

Let's take a hypothetical case in which the clinician is confronted with a young man like this, who is believed to have had Factor VIII. The information at the time would be that, really, almost inevitably -- unless he is in a very special category, such as the hyperimmune -- he is going to get hepatitis. So if he is a hyperimmune person, he is not going to get

hepatitis this time. If he is not hyperimmune, he has already got it.

Mr Di Rollo, we must be more precise about this. If this is clinical, the hypothesis is set out in the letter, and it is the hypothesis of a person who has been treated with Factor VIII.

MR DI ROLLO: I see that that's what the letter says. The systemic issue I want to look into is the circumstances as to what should happen in relation to someone who had never previously received Factor VIII, Factor IX before their presentation at Accident & Emergency.

THE CHAIRMAN: That's not this case.

MR DI ROLLO: It is this case.

THE CHAIRMAN: No, with respect, it is not this case. This case is one that is defined by the contemporary correspondence, and what you are saying is that the hypothesis on which the correspondence proceeded is wrong, but that's not an issue for me. And I don't think it can be an issue for me. If this is wrong, it's just irrelevant. The issue that you have outlined, the systemic issue as to what one does with PUPs, is something that can be asked without reference to this case at all.

MR DI ROLLO: This whole section arose as a result of me putting a hypothesis to Professor Ludlam last time

round.

THE CHAIRMAN: If it was with this in mind, perhaps the hypothesis was not sufficiently clear for me to understand what you were about.

MR DI ROLLO: I don't know the answer to that. I would have thought it was pretty obvious what I was about at the time then, and it's also pretty obvious what I'm trying to do now.

THE CHAIRMAN: Yes, it is pretty obvious, and it is becoming obvious, that what you are instructed to try to do is to obtain information that will be of primary significance in a litigation which is not my affair.

MR DI ROLLO: With respect, you should give me more credit for understanding what I do. That's not what I'm trying to do. I'm actually trying to explore something of real significance here.

THE CHAIRMAN: Well, please, is it in relation to previously untreated patients?

MR DI ROLLO: Yes.

THE CHAIRMAN: Is it of a general nature?

MR DI ROLLO: Yes.

THE CHAIRMAN: Then it has got nothing to do with the facts understood by the medical profession at the time in relation to patient A, and it can be asked without reference to patient A.

At least it seems to me at the moment, you would be perfectly entitled to say to Professor Ludlam, "Professor Ludlam, were there, as at this date in" -- 1987, is it, or 1986? -- "between 1986 and 1988, were there in position within your area, protocols for the treatment of persons presenting for the first time with indications of haemophilia, which ought to have been enforced" -- or however you care to put it -- "in order to protect PUPs from risk of infection?" Something perfectly general. And the answer to that will either be, "Yes, there were protocols," or, "No, there weren't protocols," and I can't see why you shouldn't explore whether there should have been protocols if there weren't. It has nothing to do with patient A. It's a general issue.

The problem here is that, with respect, these questions are focused in such a way as effectively to avoid the generality and concentrate it on the particular, when they could easily be asked -- and perhaps there would be no objection; Mr Anderson might object but he might fail. Perhaps there would be no problem about getting an answer to the generality.

MR DI ROLLO: I think it goes beyond simply the issue of protocols available to staff because what I'm also interested in is what could and should have been done to

protect the previously untreated patients during this period.

Some questions were asked yesterday about when it occurred to Professor Ludlam to order the 8Y or to try and get a supply of 8Y for this very purpose, and we had some limited answers in relation to that.

It respectfully seems to me, a possible situation is that it only occurred to him to order 8Y after this particular incident in May 1986, and it is worthwhile, it seems to me, exploring the issue as to whether or not it could have occurred to him before that event.

THE CHAIRMAN: It didn't occur to people in Glasgow at all, Mr Di Rollo.

MR DI ROLLO: Well, I'm not sure how that makes any difference. That makes it even worse for the people in Glasgow, perhaps.

There is material which we have which indicates fairly, in my submission clearly, so far so good as far as the English 8Y product was concerned, and that it would not have been unreasonable to have anticipated, I would suggest, that and steps could have been taken to prevent by having such a supply available at an earlier stage. So the issue then arises as to what it was that caused Professor Ludlam to order the 8Y. Was it this particular event or was it simply an appreciation at

some point during the course of 1986 that there had been a change of situation or a -- there was a better development in terms of the information that was available.

THE CHAIRMAN: You say Professor Ludlam ordered the 8Y, did he?

MR DI ROLLO: He didn't order it but I think there is a letter -- that he asked Brian to see if it was possible for it to be obtained and then there was then a -- put into -- he went through the PFC in order for it to be ordered.

THE CHAIRMAN: And he gave an undertaking about applying a protocol if it were used? Or Dr Perry did?

MR DI ROLLO: I think Dr Perry --

THE CHAIRMAN: Because it was part of ...? Or was made to appear to be part of the CTX process?

MR DI ROLLO: Trial.

THE CHAIRMAN: Yes.

MR DI ROLLO: If the point is not obvious to you or if it's something which you don't think that it requires to be looked into, then there we are.

THE CHAIRMAN: I can see that there are points here that can be made the subject of general questions that could be relevant, Mr Di Rollo. What I can't see is how the particular issues that you have focused on actually bear

upon the generality, and if we look, for example, at question 21, that's an attempt to recover something that's of no real significance in this Inquiry at all. That's my problem. I'm looking at the questions you have posed to get the flavour of what's happening, and really, as you have tried skilfully to expand it and make it general, you seem to me to be taking it further and further away from these questions without formulating issues or questions that I might be able to deal with more sympathetically.

MR DI ROLLO: Well --

THE CHAIRMAN: Anyway --

MR DI ROLLO: The difficulty that one has is I don't know what Professor Ludlam's answers are going to be in relation to a lot of the questions. The point is that --

THE CHAIRMAN: None of us know that.

MR DI ROLLO: Well, exactly, and I have to give notice of specific questions that I may want to ask in advance and the issue as to -- first of all, the circumstances surrounding this event, one would have thought, may well be in the forefront of his mind, and one wants to test the extent to which he was influenced by this event in relation to the decision to have available the 8Y product.

That is why I feel that it is necessary to give notice that one would want to know whether or not there was an Inquiry made by him into the circumstances surrounding this particular incident and whether he was satisfied by the explanation that he was given in relation to that. If he felt that he had not provided his staff what they should have had available to them, then that seems to me to provide a background to what he then does next, which is to seek the provision of this material, whether it's just for Edinburgh or for the whole of Scotland. That leads us on to the next issue, which is whether or not, even when more information becomes available, and when it becomes obvious that the English are prepared to make the material available, more should have been done to make this material available for the rest of the potential population, ranging from the very severe haemophiliac to the person with a very slightly lower than normal Factor VIII or IX level, all of whom may be required to be treated for the first time before the Z8 comes in. That's where we are going with this.

THE CHAIRMAN: Who is the very severe haemophiliac, patient A or patient B?

MR DI ROLLO: B.

THE CHAIRMAN: B? I see.

MR DI ROLLO: We know that the administration of Factor VIII is potentially lethal and therefore there has to be a system in place --

THE CHAIRMAN: Do we know it's potentially lethal in that language, rather than being liable to transmit a disease that could, in the long run, involve a higher degree of morbidity. "Potentially lethal" is a very harsh expression to use unless you are going to give me examples of it.

MR DI ROLLO: They knew it was progressive liver disease leading to cirrhosis of the liver.

THE CHAIRMAN: I would have thought that "potentially lethal" would be a better description of the two young people who tried to cross the railway track yesterday and were killed. What you mean is: capable of transmitting a disease that might, in some cases in the long term, give an increased morbidity and mortality to the patient.

MR DI ROLLO: I think I would put it a bit stronger than that and maybe somewhere between "potentially lethal" in your language.

We know that it was known in 1986 that the product was potentially harmful to a patient and therefore there would require to be systems in place so that only those patients who strictly required that item would be given

it, and it respectfully seems to me that the system, if there was a system -- and I'm not sure we do know there was a system -- broke down in this particular case and if a system breaks down, then that, in my submission, is something which this Inquiry is entitled to look into.

THE CHAIRMAN: Every system can break down. You know? No system is infallible. You know, I don't need evidence to tell me that systems can break down.

I think this system, if there was a system, as you say -- and you have not explored that yet -- may have broken down in thousands of cases throughout the United Kingdom, millions of cases throughout the world.

We are talking about human beings. You see, this is where one reaches the cusp, as it were. The generality is that the product can transmit infection. There are a few exceptions to that, and therefore one might infer that unless a person falls within the scope of an exception, administration of the product for the first time is going to infect him.

There may be, then, a question whether, knowing that, one should have in place what I have called, "protocols", but basically a series of systemic rules that have to be applied by any clinician confronted with the need to deal with a patient who is showing signs of damage related to a blood disorder.

The answer to that may be, "There is a need for those", "There is no need for those", "There was a need but we didn't have them". That's a real systemic issue. "There was a need; we did have them". But, from time to time, problems are going to arise that are not dealt with. When you reach that stage, apart from the generality that problems are going to arise, exploration of the particular doesn't increase one's knowledge of the systematic points. It becomes personal to the person who is going to allege a deviation from the system that may or may not be negligent, give rise to claims and so on, which are properly the business of a different tribunal from this.

This is my worry, that, so far, I can see loads of good grounds for pursuing the general. I see lots of grounds for acknowledging human fallibility. Goodness, I have probably displayed plenty of it in the course of this Inquiry myself; perhaps most of us have. But if you look at your questions, they are not of a level of generality. You are actually looking for a report into the particular case.

What has that got to do with my terms of reference? That's the reason I'm pressing you on this.

MR DI ROLLO: Well, I can see that questions number 18 and 19 are specific in a way which is perhaps unnecessary to

explore the sort of issue -- I have tried to explain to you what it is that I'm trying to do in relation to this. It is quite difficult in advance of a piece of examination to know exactly what one would want to ask in relation to answers where one doesn't know what one is going to get.

THE CHAIRMAN: Yes.

MR DI ROLLO: What I have done in the questions, I suppose, is put the questions in as extreme a form as one would hope to be able to ask, so that everyone knows the extent to which I'm seeking latitude.

What I am seeking to do is to be able to examine Professor Ludlam with a view to trying to get an understanding of what it was that those who were on the front line in May would be expected to do with such a patient, and what they were instructed to do and whether or not those instructions could be expected to be complied with.

If there was a failure, which I think there may have been, why did it fail?

THE CHAIRMAN: You see, again we come near -- as I have tried to say, I have very little concern at the moment, subject to what Mr Anderson has to tell me, about the generalities, about the need for instructions and so on, as questions that can be asked. But one should step

across the boundary from the general into the particular. You are not using the particular to instruct the generality in this case; you are using it to explore something quite different.

Anyway, I have heard what you have to say. Mr Anderson has no doubt heard it all too. Is there anything else you want to say about the first class of case, the questions 18 to 23? I think I would like to deal with them in stages so that I get a proper feeling for each group of questions.

MR DI ROLLO: I would say that it is reasonable for me to be allowed to ask why it was that letters were written to Dr Ludlam about what happened in --

THE CHAIRMAN: What letters are these?

MR DI ROLLO: Both the houseman and the registrar wrote letters to Dr Ludlam about what had happened. They were asked for an explanation, as I understand it, from Professor Ludlam.

THE CHAIRMAN: This is of general importance, rather than relating to the particular case?

MR DI ROLLO: It is of general importance because again it is a question of exploring the system that was in place. Was there a system and did it break down and why did it break down? If somebody goes to casualty and is given Factor VIII and they don't need it at all and if that

was happening on a regular basis, is that not something that should be looked into?

THE CHAIRMAN: Was it happening on a regular basis? Are you alleging it was happening on a regular basis?

MR DI ROLLO: I don't know.

THE CHAIRMAN: Well, with the greatest respect, that will not do, Mr Di Rollo. You are introducing pure speculation in support of this. Now, the reality is, if you had known about a number of cases, these questions wouldn't have been asked in this case. These questions are asked with reference to a specific case.

MR DI ROLLO: All I know it what's contained in the preliminary report in relation to numbers, which is that, as we explored with Professor Lowe, there are 31 people that were previously untreated patients who received concentrates for the first time during this period.

THE CHAIRMAN: Yes.

MR DI ROLLO: I actually don't know whether in fact patient A is the person referred to in the documents that we have.

THE CHAIRMAN: Nor should you because we are trying hard to protect individuals' identities.

MR DI ROLLO: Even I don't know the answer to that.

THE CHAIRMAN: I know. Again this is because of my concern

that what we are doing now is moving to the particular as the focus of attention, not as an illustration of a wider problem.

MR DI ROLLO: I can quite see there are a large number of questions that you do not need to know the answer to in order to conduct or to fulfil the terms of reference arising out of this specific case, but there are some questions arising out of this specific case that do inform those terms of reference and those questions relate to the explanation that was given to -- whether an explanation was required, what the explanation was and whether he was satisfied with that explanation as against the system that was in place or not, as the case may be, in relation to dealing with this particular problem. I hope that makes it clear what I'm trying --

THE CHAIRMAN: That's your submission.

MR DI ROLLO: -- to explain.

Question 21 obviously deals with the conclusion of that investigation. I'm prepared to depart from questions 22 and 23. I don't require those questions to be answered in the specific sense. But I would perhaps want to ask some general questions about the volume of product that might be required and also the levels of Factor VIII in a person's bloodstream.

THE CHAIRMAN: Well, I'm not going to deal with issues of

that kind casually, Mr Di Rollo. I think the discussion already is developing to the point at which the wisdom of requiring proper formal applications with support is becoming clearer and the departure from questions is just as bad as the proposing of them in the first place.

Anyway, should I hear what Mr Anderson has to say about questions 18 to 23 at this stage or do you think it would be better from your point of view to cover the questions at the end, 51 and 52 as well?

MR DI ROLLO: Questions 51 and 52 -- I'm content just to deal with that -- are really to explore in general terms how one would look into or how one would deal with preventing someone being infected with concentrate at a later time. It's 1986 to 1987. It's obviously after patient A. There is other material available in relation to that I will submit makes it clear that it was even more important by that stage to cater for the previously untreated patient as time went on.

THE CHAIRMAN: This again is focused on a particular individual, is it not?

MR DI ROLLO: When we say we were focused on a particular individual, I can't proceed on the basis of things in the abstract; I have to have something in mind. As I understand it, two core participants were selected as examples, as I understand it, of a large number of

potential individuals, and one has to have in mind specific circumstances in order to make meaningful any general questions that one has.

THE CHAIRMAN: In some cases that's undoubtedly so.

MR DI ROLLO: The questions I'm asking are general questions and I would submit that there is nothing specific -- I have someone specifically in mind, of course, but there is nothing specific about questions 51 and 52.

THE CHAIRMAN: No, 52 is a question of such generality that I'm not sure I understand what it's all about:

"Why should an infant from outwith the central belt given Scottish Factor VIII in 1987?"

What? Why should the infant what?

MR DI ROLLO: I think it's, "should be given".

THE CHAIRMAN: "Why would an infant from outside the central belt then be given Scottish Factor VIII in January 1987?"

I suppose one answer is because he was here.

MR DI ROLLO: The purpose of this exercise, I think, is to try to give notice to other parties as to the sort of issue that may be raised. My understanding is that if there is a problem, it's because it's too specific. You, sir, have just indicated clearly that if the question has a problem, it's not because it's too specific and therefore I don't think it requires much

more input from me.

I think I would be in a position to ask general questions about this particular matter and I don't think --

THE CHAIRMAN: Without identifying patient B?

MR DI ROLLO: Of course not.

THE CHAIRMAN: Yes, and without going to circumstances so particular to patient B that they cease to be illustrative of the general point and really came to focus on patient B, because that's my worry.

MR DI ROLLO: The only witnesses I can deal with for this particular matter are Professor Ludlam and Dr Colvin and of course I have to put some sort of general hypothesis to them.

THE CHAIRMAN: Right.

MR DI ROLLO: The essence of it, in relation to both patients, is to do exactly the same thing. The problem that arises with Professor Ludlam is that one of the patients happens to be potentially -- or could be -- I don't know, in fact, as a matter of fact -- could be one of his own patients, and why I'm constrained to putting specific questions is because I don't know what he is going to say in answer to questions about systems. That's the reason why the questions have been put in the specific way that they have in relation to patient A.

THE CHAIRMAN: Mr Anderson?

Submissions by MR ANDERSON

MR ANDERSON: I'm much obliged, sir.

Sir, the existence of these questions was brought to my attention by Ms Dunlop on Sunday. There had been no prior information, either to myself or those instructing me, and consequently there has been no investigation into the questions in dispute.

As I said earlier, I have no objection to the vast majority of the questions, which seem to fall to a greater or lesser extent cleanly under the topic C3A and indeed some have already been answered, but I have concern about the particular questions. But I should make clear that my objection is not based simply because of the fact that they have come somewhat late in the day, although there is an element of that.

THE CHAIRMAN: I wouldn't rely on that, Mr Anderson. The procedure is flexible and if it's time that's a cause of concern, I'll make sure that you are given the time to prepare properly to deal with any issue that arises. I'm not concerned to listen to purported problems of that kind.

MR ANDERSON: I was seeking to make clear that I was not relying upon that but there is an element of the fact that the individual cases have not been investigated;

rather, I object as a matter of principle and I simply seek to make that clear. In my submission there are good reasons for this.

Sir, these two individual cases, or at least one of them, involve named doctors and one can see that, I think, in question 19. These doctors may be impliedly or explicitly criticised. Neither of these doctors knows anything about these questions or indeed this inquiry, neither being still within the employment --

THE CHAIRMAN: Could you just pause a moment? Douglas, have you got the regulations with you? You have just raised something which I would like to be clear about. I may be using one of my own witnesses for this purpose. (Handed)

Why I'm raising this question is that, of course, if indeed lack of notice were to become important, rule 12 of the Inquiry Scotland Rules provides that:

"The chairman may send a warning letter to any person where the chairman considers that (a) the person might be or has been criticised during the proceedings at the Inquiry."

Now, at the moment my concern is "might be". If you are right that there is a risk of criticism, direct or indirect, being directed towards the individual named doctors, it is just possible that I don't have the

flexibility to deal with this at my own hand and relax the rules, as I might otherwise be inclined to do, because I would be obliged to send a letter to any of the doctors. If indeed they are being sued, as appears likely to be the case, it would be wholly inappropriate to allow questions to be asked without their getting service of a formal notice under rule 12.

MR ANDERSON: Indeed, I did not have in mind, I confess, the rule itself but simply as a matter of principle --

THE CHAIRMAN: We are dealing with a statutory construct, where principle is perhaps less obvious from time to time.

MR ANDERSON: One might like to think that the regulations have their provenance in a good and sensible principle, sir. But, as I say, although neither remain in the employment of -- at least as far as we know -- health boards -- one is thought to be working in the south of England and the other one's present whereabouts are unknown -- I have a grave concern about former employees being directed to a discussion about their clinical judgment in individual cases in a situation in which they are not represented, they know nothing about it and they have no ability to have any input into the matter, and this is a discussion about them and about their professional judgment, their clinical judgment, which

will apparently be disseminated on the World Wide Web.
THE CHAIRMAN: Yes.
MR ANDERSON: The second reason, sir, is that, as you have suspected, there are extant civil actions in respect of these two questions, albeit they have been sisted for some considerable period of time. I think the position was that they were raised in order to defeat the time bar.
THE CHAIRMAN: A perfectly proper course of action, Mr Anderson.
MR ANDERSON: Perfectly proper. I don't suggest otherwise.
THE CHAIRMAN: But again, because it's on the World Wide Web, I would not for one moment anyone to get the impression that it was inappropriate to raise an action to stop a time bar running.
MR ANDERSON: I think everyone is at one on that, sir. I simply, by way of background, the summons were served and then sisted and, as I understand it, there has been no further procedure. The point is that there are civil actions extant and I'm very unhappy about a witness, in particular Professor Ludlam, who is likely to be a material witness in one of the litigations, being questioned in this forum, particularly when he has not investigated the matter, and I have grave concerns about the appropriateness of using this forum in this way.

I don't for one moment, of course, question my learned friend Mr Di Rollo's probity in this matter and it may very well be, as he says, that this is not the purpose of his asking these questions, but the result of asking these questions is almost certainly to influence in one way or another the litigation which is currently sisted and in my submission that's simply not appropriate.

It may be said that those individuals are simply looking for answers and I heard my learned friend use the phrase "the only opportunity". I have two things to say about that, sir. The first is, of course, that those instructing my learned friend, if they are looking for information, can simply write to the relevant health boards with questions of fact, which those health boards will be happy to answer and indeed, as I understand it, would be obliged to answer. That is something which has not been done hitherto, as I understand it.

Secondly, I have a suspicion that this is an attempt essentially to extract some sort of opinion evidence from Professor Ludlam and again I have very grave concerns about that, and one can see in question 21 where that concern arises from.

In brief, sir, it's a matter for you but I would suggest that these mini inquiries, which is essentially

what they are, will be of no assistance to you. They are unnecessary, inappropriate and this is simply not the apt forum to discuss questions of clinical decision in individual cases. That, sir, is not part of your remit, I would suggest, and it is particularly inappropriate to discuss questions of clinical decision in individual cases, when the matter has not been properly investigated and the whole background facts are not known.

The final thing I would like to say is this: if, as a general proposition, it is accepted that the treatment of choice for a particular class of persons is X and the treatment in one particular case is Y, then in my submission no significant inference can be drawn from that fact and in particular no adverse inference can be drawn from that fact, especially when we don't know all the facts, we don't know the background and, as Professors Lowe and Ludlam said yesterday, matters of choice of treatment require you to assess the patient individually.

Until one knows everything one needs to know about the individual patient, it is quite wrong to embark upon a discussion as to the rights or wrongs of treatment in any particular case. But in any event, as a matter of principle, I suggest to you, sir, that it is not within

your remit and for that reason alone these questions should be disallowed.

Now, much of what I said, I think, relates to questions 18 to 23 but, when one turns to 51 and 52, the difficulty there -- if one looks at 52, there is a problem with that, firstly, that it clearly is a reference to patient B, but at the same time the question is posed in such general terms as to give rise to a question as to its usefulness in any event.

It's a matter for you, sir, but I would suggest to you that whatever answer were to be given to that will take this Inquiry no further at all. So for those reasons, sir, I object to those questions.

THE CHAIRMAN: Mr Di Rollo, do you have anything to say about the application of regulation 12?

MR DI ROLLO: The questions, if one looks at them, are not intended to lead to any criticism of anyone. What's being asked in relation to question 18 is who gave the instruction to administer, so there is no criticism in relation to that. Was there a misunderstanding --

THE CHAIRMAN: Mr Di Rollo, I think that you have already gone far enough for me to give you my decision. I think that the discussion has made it abundantly clear that the formal procedure for intimating issues that are to be investigated should be followed, that you should set

out afresh, looking at these questions in the light of the discussion we have had, some way of presenting them as a matter of generality that seeks to avoid some of the inherent difficulties that we have discussed, that that is intimated to Mr Anderson's present clients, that I will then consider it on its terms and explore whether regulation 12 has to be applied.

So in hoc statu I'm going to refuse permission to examine Professor Ludlam today. I have got an interest in completing this Inquiry. I have got no interest in excluding matters of substance. But I am determined now to ensure that if matters of substance are to be explored that are arising afresh, as it were, proper steps are taken to ensure that everyone who could be affected by the material is properly apprised of what is involved.

Now, I really do think that your attempts, successful attempts in many ways, to tell me what the generality is point the way to how you might do this. At the moment I'm left with the concern, focused by Mr Anderson, this is far too particular to individual cases and it's far too open to the representations that we have discussed that at times focused on them to the exclusion really of the generality, and I think also you should be aware that I have got a real concern, not just

for this Inquiry but for any others that might, if anyone is ever minded to instruct such an inquiry again, follow as to the risk of intentional or accidental abuse of the powers by exploring matters in relation to civil litigation.

I think I might well recommend to the cabinet secretary that there be a specific instruction to any other reporter ever instructed to ensure that where a generality is focused, individual cases are not explored.

Anyway in the meantime I'm refusing the questions in hoc statu but I want to you consider very carefully what it is that you are interested in obtaining. Put it in an application. We will have it intimated and circulated and I will consider the need to apply regulation 12 in relation to the circumstances as they emerge.

I think regulation 12 is very important in the context that Mr Anderson has focused. If you just look at the structure of the questions, the risk of criticism emerging is so great that I don't think it can be ignored, whatever intentions one has. Therefore, this has to be thought through and I give you the opportunity to do that.

I suggest that you make the application within

four weeks, which is the date I gave yesterday for all such applications, but that we then take matters forward as best we can.

Now, I think as far as I'm concerned, it's time for a break.

(10.50 am)

(Short break)

(11.42 am)

THE CHAIRMAN: Yes, Ms Dunlop?

MS DUNLOP: Thank you, sir. This morning's discussion has made me realise that there are some further questions which I ought to ask and I wonder if I might be allowed to pose some further questions to Professor Ludlam.

THE CHAIRMAN: Is that acceptable to others?

Yes, certainly.

MS DUNLOP: Perhaps Professor Ludlam should return.

THE CHAIRMAN: Yes.

PROFESSOR CHRISTOPHER LUDLAM (continued)

Questions by MS DUNLOP (continued)

THE CHAIRMAN: Good morning, Professor Ludlam. I hope you have found the accommodation acceptable during --

A. Thank you, and the coffee's particularly good.

THE CHAIRMAN: Yes, Ms Dunlop?

MS DUNLOP: Thank you, sir.

Professor Ludlam, I'm going to ask you one or two

more general questions about the period from the end of 1984 to the middle of 1987.

Can we start by going back to the December 1984 document from the reference centre directors. That's [SGF0012388].

Can we go to page 2 of that, please?

We remember actually that the structure of the document is that at the foot of page 2 it outlines firstly a list of options, options in probable decreasing order of safety from AIDS for Haemophilia A, and we see that option number 1 is shown as "heated UK concentrate", but with the caveat that there is still an NANB hepatitis risk. And then number 2:

"Single donor cryo or fresh-frozen plasma."

Number 3:

"Heated imported concentrate. Note: still NANB hepatitis risk."

Then there are recommendations. Number 1, the need to continue to use concentrate because of the risk of bleeding causing disability or death; number 2, DDAVP. Then on to the next page, please.

Number 3:

"For Haemophilia A needing blood products."

We have a divide between virgin patients, those not previously exposed to concentrate, and children:

"use cryo or heated NHS Factor VIII (if available)."

And then severe and moderate patients are discussed also. Haemophilia B is section 4.

Perhaps a similar sort of ethos as between haemophilia A and Haemophilia B, which seems to be being particularly careful with patients who are "virgin", those not previously exposed to concentrate, and children are mentioned specifically in 3(a).

Now, this is December 1984, so the factual position is that screening of blood donations has not yet been introduced and I think we have established that that does make a difference in one's assessment.

Next I would like, if I could, please, to go back to the transcript for yesterday, and towards the beginning, can we look, firstly, please, at page 59 from yesterday's transcript?

This is a part, Professor Ludlam, where you and I are still discussing generalities at the outset of your evidence. As far as the number for the page with the four pages, it's 15, if that helps. If that makes sense. Thank you.

Do you see there, at line 8 on page 59, I'm saying to you that:

"The concern that one has, obviously, in relation to this matter is that treating someone for the first time

with a blood product during this period means that you are exposing them to the risk of hepatitis -- non-A non-B, as it was then known ... "

THE CHAIRMAN: I'm slightly concerned, is this Professor Ludlam's evidence or is this Mr Di Rollo's questions directed to Professor Lowe?

MS DUNLOP: Sorry, I may be in the wrong bit.

THE CHAIRMAN: I think this is Mr Di Rollo's questions to Professor Lowe that started around about 56.

MS DUNLOP: Sorry, I'm in the wrong bit. Yes, I can see that. If you will allow me a minute, sir, we will find the right bit.

THE CHAIRMAN: It is probably exactly the same point.

MS DUNLOP: It is the same point but it's the wrong witness.

THE CHAIRMAN: The summary starts around about page 72, I think. Look at TRN0010054 at page 74.

MS DUNLOP: Yes, thank you. Sorry about that. Yes, there we are, 74:

"I wonder if it would be fair to say however, that the therapeutic policy generally over this period would be guided by a desire to avoid the use of blood products unless there was no alternative.

"Answer: That, I think, is fair, yes."

We will just look at the top of 75 to make sure there is nothing else we need to look at. Right.

Now, Professor Ludlam, the guidance, I suppose, might be described as being deceptively simple in its terms, in that the sorts of choices between individual products that may fall to be made with any one patient could be very difficult. So I suppose the thinking behind providing the guidance is that it will be a starting point for clinicians, but the finishing point will obviously have to involve an assessment of the circumstances of the individual patient. But you personally, as a director at that time, and a reference centre director at that, presumably saw the provision of guidance as helpful?

A. Yes.

Q. Yes. Can we then start with you as a centre director at that time. You had been at the meeting, which had discussed the issues, and you will have received the document too. So, yes, it will have been in Edinburgh Royal Infirmary?

A. Yes.

Q. Yes. I just wondered what steps were taken in Edinburgh Royal Infirmary to ensure what I might term "vertical dissemination", so you are at the top but obviously you are not always there. So what steps were taken to communicate the thrust of the guidance to other staff who might be encountering patients with haemophilia?

A. Well, I think the guidance given in this document, leaving aside, if I can, the heat treatment, is what our therapeutic practice was.
Q. Right.
A. In other words, it was standard practice to use DDAVP if that was suitable. Very much so. Because we were aware of the risks that we have all been discussing here.
Q. Yes.
A. If DDAVP or desmopressin was not suitable for whatever reason, then it was a question of considering cryoprecipitate or heat-treated concentrate, and we were particularly fortunate in Scotland in having heat-treated concentrate. We didn't have to make some of the awful decisions that some of the clinicians had to make early in 1985 in England.

So there was still the policy, depending on the circumstances -- and every patient is different -- we were still using cryoprecipitate for small children and babies around that time and moving on to the concentrate, as I hinted yesterday or stated yesterday, often when they came to go on to home treatment. That was the way we arranged things.
Q. Yes. What actually happened in the department? Was there a folder with guidance documents in it? Were there charts on the wall? Was it all done with verbal

instruction? How was guidance disseminated?
A. We had a small team of people: myself, a lecturer, a registrar and a haemophilia sister, and our policy was -- policies for all sorts of things were, I think, generally accepted and well-known within the team.
Q. There has to be something that leads to their being generally accepted?
A. Yes. I am afraid I can't remember at the moment. Now we have large numbers of written policies. I can't remember at this time. I know two or three years after this we certainly had written policies. I can't remember at this stage whether there were written policies for -- guidance policies in general, locally produced. I'm sorry, I can't remember.
Q. Right. The most difficult decision, it seems to me as a layperson, is the choice between heat-treated concentrate, NHS heat-treated concentrate, certainly, and cryoprecipitate. Now, I suppose the sense of risk that attached to cryoprecipitate must have been different before October 1985, from what it was after 1985. Am I right about that?
A. Yes.
Q. Right. So the introduction of screening in October 1985 must have made cryoprecipitate a more attractive choice than it had been before October 1985?

A. I think so, yes, with the caveats that you mentioned yesterday about false negative results on screening and the window period. We really didn't know how much safer cryoprecipitate was for that screening that started in September 1985.

Q. Right. But I think we understand that cryoprecipitate, even before October 1985, is still seen as having a part to play. It's mentioned in the December 1984 guidance document, and perhaps slightly more so. It's difficult to quantitate that but slightly more so after October 1985. That's the really hard choice, isn't it, between heat-treated concentrate and cryoprecipitate?

A. Yes.

Q. And the factual scenario in which it's going to crop up is the patient with no previous exposure?

A. Or little.

Q. Or little. No or little previous exposure. Having established, as we have, that plainly the circumstances of any one individual are relevant, did you take steps to go a little beyond the guidance for your particular staff, so as to give them, as it were, a bit of a steer as to the general policy that you might want to see applied in Edinburgh Royal Infirmary for patients in that category?

A. I think it would be quite clear that patients in that category should be discussed at a senior level, because it's not just a matter of cryoprecipitate versus concentrates being, if you like, very equal; it might depend on the clinical circumstances of the patient.
Q. Right.
A. At one extreme a baby comes in, a new child with a major intracranial bleed, life-threatening. I think my judgment would be that child should receive a concentrate because you could make it up quickly, you knew exactly how much you were giving, it was easy to give, it hopefully would be effective treatment.
Q. Yes.
A. So there is an instance where I would have given Factor VIII concentrate to, if you like, a previously untransfused baby.
Q. Yes.
A. Because cryoprecipitate, as I think has been explained here, takes time to make up, the dose is unknown, the volume greater, harder to give to a small baby. So there's an instance where I wouldn't have given cryoprecipitate for that particular situation.
Q. Yes.
A. So these situations, as you see, arise uncommonly and it's difficult to make up categorical guidance, if I can

put it that way.

Q. Yes.

A. And each has to be considered on its merits and that's why we have senior doctors who are available to discuss these issues, and sometimes I have difficulty deciding what the best thing is for a patient and I telephone someone else, who I think can offer me better guidance.

Q. I think we understand the point you are making, professor, and other professions don't confront it in such stark terms perhaps because what's at stake is uniquely difficult in medicine, but other professions do have a similar issue, which is for senior people, do they try to be prescriptive as much as they can to assist junior members of the team, or do they say, "If this sort of situation arises, contact somebody more senior?" And I think we can understand that both of these are reasonable solutions to that sort of situation.

How do you think staff would appreciate that in that situation it was their responsibility or your expectation that more senior support would be sought?

A. For a patient who has not been treated before?

Q. Yes.

A. That's a very unusual situation.

Q. Yes.

A. And I would almost certainly be contacted.
Q. Right. But I think I'm interested in how practically it actually worked. I mean, when a new doctor arrived, either a junior member of staff or somebody who had worked elsewhere, did they have some sort of induction? Did you say to them, "Here are my policies?" We have established, I think, that it's difficult to recall, and I understand why, it's a long time ago, how much use was made of written material, but do you have any memory of sitting down with more junior staff and explaining to them some of the more important expectations you had of them?
A. I think a lot of the day-to-day knowledge about the patients, knowledge about our policies, was known to the haemophilia sister, who was, if you like, the constant feature, very much at the front end of our service. Unlike now, when trainee doctors, trainee registrars, are on very formal rotations and come to work for us for just a few months and it is quite a short period, at that time our staff were with us for often several years, so there wasn't a large turnover of staff like there is -- of junior staff like there is now. Coupled with that, we had a lecturer post that was a more permanent post. So there were people who were conversant with treating haemophilia. There wasn't

a large turnover of staff and the need to have an induction programme like there is now.

Q. Right. So I think what I'm picking up then is just that, that new people would pick it up; they would pick it up from staff who were already there and had absorbed the way you worked?

A. It was very easy for them to enquire if they didn't understand something, didn't know something as well.

Q. Well, what about a slightly different event then? What about something like the introduction of screening of donated blood in October 1985, which is going to have an effect on the assessment of the relative merits of different blood products? What happened then? Did you gather the staff together and say, "This has now happened. You will all appreciate that that makes a bit of a difference"? Did you do something like that?

A. I don't think so, because it was a difficult time and there was discomfort in using cryoprecipitate, sufficient discomfort that some haemophilia centres didn't use it at all.

Q. Right.

A. They didn't have it on the shelf for treating haemophilia. They were treated with Factor VIII concentrates or DDAVP.

Q. You are answering in relation to my specific example.

Let's pull back from that and just think in the general that any event in haemophilia care which is happening, has happened, a new product or a new piece of research or something of that nature, did you have team meetings or any sort of gatherings where you would discuss that with the staff?

A. We had weekly educational meetings, at which we would discuss our internal arrangements, our internal policies, we would have outside speakers. I seem to recall a speaker from the blood transfusion coming to talk about developments in clotting factor concentrates.

Q. So these were a fixture?

A. These were a fixture, yes.

Q. And during the day?

A. Yes, they were at half past eight on Friday mornings.

Q. Right. Did you sometimes discuss issues of this nature, treatment dilemmas?

A. Yes, they were meetings to keep us up-to-date and to introduce us to new topics, new issues. There were clinical presentations of a patient with a particularly interesting story or medical condition. So that happened every week.

Q. Right. So in terms of assisting more junior members of staff -- and everybody is junior to you -- more junior members of medical staff to respond to these patients

who present particular difficulties, I think we understand that they might have been discussed at the weekly meetings, but your general expectation was of junior staff contacting more senior staff if such a patient should present. Is that right?

A. Absolutely, yes.

Q. Yes. And in response to the question about how junior staff would know that that was expected of them, you are telling us that they would learn that from others around?

A. 99 per cent of people who come up to the haemophilia centre, it's all very straightforward.

Q. We are talking about the 1 per cent.

A. Yes, and the 1 per cent does stick out as being different.

Q. Right. What about giving assistance to other staff in defining that group, making sure that other staff understood that this is indeed the 1 per cent, that this is the group with whom these difficult decisions arise? How did junior staff actually learn that?

A. Because these are likely to be patients that aren't in our records.

Q. Right.

A. We have case notes for all our known and registered patients. So that was all very clear from the case

notes and the general expectations. If we had the sort of people who came as unknown to us, which were mostly visitors coming to Edinburgh on holiday or on business and they had a bleed and they needed treatment, and they come to the haemophilia centre and they will have a haemophilia card saying they have got haemophilia, where they are registered, what kind of haemophilia it is they have got, what the severity is of their haemophilia, and it may or may not say what they are treated with. So it's a sort of an introduction. Whoever sees the patient would look at this, probably ask the patient, apart from what was wrong and so on, what they were normally treated with, and most patients knew what they were treated with and we took it from there.

Q. And did junior staff always just have to speak to the person on the next rung above or can they come straight to you?

A. They would come straight to me.

Q. And that would be true in the mid-1980s as well?

A. Yes, I made myself very available.

Q. Right. So I think we understand the position to have been that there were no set guidelines that, as it were, refined the UKHCDO document and that you preferred to see the 1 per cent, if we can call them that, as people

in relation to whom specific issues would arise and should be resolved with the involvements of senior medical staff?

A. Yes. I can't recall whether there were written documents or not.

Q. Right. I should say that when I'm asking you about these sort of policy questions, I am meaning the whole of our difficult period, notwithstanding that there was quite a significant change in October 1985. We are thinking about the years 1985, 1986 and the first part of 1987, and I think the answers you are giving are your best recollection of what happened around that time. Is that right? Is that correct?

A. I think so, yes, sorry, I was just reflecting on --

Q. Sorry, I didn't mean to interrupt your thought.

THE CHAIRMAN: Take your time, Professor Ludlam, if you want to answer it more fully.

MS DUNLOP: Excuse me a moment. (Pause)

A. I think in general, although as you were asking the questions, I was thinking more in terms of 1985.

Q. Right. So do you think it changed in 1986 and 1987?

A. That's what I was thinking about.

Q. Right. (Pause)

A. I don't think so, no.

Q. No. I just wanted to pick you up on your answer about

junior staff having the right, as it were, to come straight to you.

You said, "They would come straight to me". Now, they could come straight to you, we understand. They would come straight to you is perhaps slightly different. Are you saying that in a particularly difficult situation, that would have been your expectation and if so, how would they know that?

A. If they have got a situation that they are not quite sure how to deal with, they would ring me up and I would walk down the corridor and see the patient.

Q. What about the over-confident?

A. If I perceived someone was being over confident, I would offer them some tuition.

Q. All right. But all of this is, with respect, a little bit reactive. If someone has gone beyond the reach of their learning and competence and dealt with a patient on their own initiative without seeking help when they should have, the damage has been done, has it not?

A. Mostly. The queries came to me and there is a fine line about giving people responsibility and them being able to manage, to practise as a physician. They are in training. I personally -- someone in my position can't oversee everything they do, but when someone comes to work with me, I very quickly get an impression of their

general level of competence and understanding and I say to people when they first start with me, "Please, if you have a query, get in touch with me. I keep my door shut to keep the noise out, not to keep people out." I try and make myself very available, because it is -- some of these patients, even though they are known patients, come up with a medical problem that may not be entirely straightforward. So I'm not only consulted about the 1 per cent, there were lots of more percentages which -- there are shades of grey and different ways of potentially responding, and my responsibility is to give as much responsibility as I can to my staff in training, as I feel comfortable and as they feel comfortable.

Q. Right.

A. But with an understanding of the sort of areas and topics that I like to be informed about anyway, even though they may know what the right thing is to do, there are certain situations I would like to know about anyway.

Q. Professor Ludlam, because this is an Inquiry, I think I have to probe just a little bit further and put to you that the sort of scenario we have been discussing -- that is the patient with mild haemophilia who needs treatment, who has had no or minimal previous exposure to concentrates, needing treatment, where there is

a continuing risk of hepatitis, which is a very significant adverse consequence and the treatment decision is a very difficult dilemma -- that whole package is something that called for specification, so a written document or an advance instruction from you communicated to all staff.

Looking back, even just in retrospect, what's your response to that?

A. Well, it could give rise to the wrong therapy. Let me caricature. A patient with mild haemophilia is involved in a road traffic accident, comes into hospital unconscious, may have an intracranial bleed. The recipe, the guidance says give DDAVP for mild haemophilia. That would be totally inappropriate for many reasons I could go into, if you wanted to.

Q. I was wondering perhaps about a simpler response. What if the guidance said in block capitals "phone me". Would that not help?

A. That is, in a sense, what the guidance was. Here is an unusual situation.

Q. But you didn't see the need for making that kind of provision in advance, as it were, for putting down in writing, so there wasn't debate, what you expected the response to be?

A. I expected people to get in touch with me if it was not

clear how they should proceed with the medical care of patients. That applied not just to mild haemophilia. I looked after patients with leukaemia and lymphoma and a whole range of conditions, and if one of my staff had some doubt about how to proceed, then they asked me.

Q. Right.

Professor, this has all been about what I was terming "vertical dissemination". I would like to turn to horizontal dissemination because we mentioned that a little bit yesterday. By that, I mean getting the current thinking distributed around Scotland, in particular to the more geographically distant areas. Would I be right to deduce from what you said yesterday that you didn't see yourself as having a role in ensuring that that happened?

A. As I think I clarified yesterday, the haemophilia centre in the Royal Infirmary in Edinburgh was one of, I think, six in Scotland, and they were seen, particularly by the Scottish Office, as very much sort of equal and all services should be provided at all of them. That is how the original health circular was set out and defended.

We had meetings with the Scottish Office blood transfusion and haemophilia directors about twice a year from the early -- I think they may have been at the end of the 1970s as well but certainly in the early 1980s,

and reference has been made to those here in this Inquiry.

It was -- and I had no managerial responsibility, financial or otherwise, for haemophilia centres in the other hospitals.

It wasn't really until, I think, 1988, when the Factor VIII working party was established for a whole range of reasons, that brought us together regularly. The arrangements between Edinburgh Haemophilia Centre and the other haemophilia centres in Scotland was much the same as it was between other reference centres in England and other non-reference centres or haemophilia centres. But there weren't regular meetings. They were given guidance, if you like, centrally from UKHCDO, and if there were any queries that needed discussing, the directors of those centres would either phone up the chairman or the secretary of UKHCDO or they might have phoned me. I'm just trying to recall.

When I arrived in 1980, the other three haemophilia directors in the East of Scotland were very senior, experienced clinicians. Dare I say it, much more experience in looking after people with haemophilia than I had.

Q. Yes.

A. I was an even younger man in those days.

Q. So you exercised humility?
A. Well, you know, they had been around for a long time.
Q. Yes.
A. And were, I think, good clinicians.
Q. Right.
A. In their different ways.
Q. Obviously we are thinking about this difficult period and if it were to be thought that it would have been a good idea for somebody to try to make sure that all hospitals in Scotland had some assistance with the current thinking on how to deal with patients with haemophilia presenting for the first time, say, or patients with mild haemophilia who hadn't had previous exposure to concentrates, the patients who present the particular dilemmas. If it had been thought that it would be a good idea for all the hospitals in Scotland to know what the thinking was, whose job would it have been to make sure that that sort of information is sent round?
A. Well, I suppose it's a medical policy decision. It perhaps should come from the chief medical officer.
Q. Excuse me a moment. (Pause)
Just one more thing, Professor Ludlam. What was the arrangement for when you were on holiday? I'm sure you did -- no doubt, occasionally -- go on holiday. What

was the senior support for staff then?

A. That was my colleague, Dr Alistair Parker.

Q. The other haematologist who was on the headed paper at that time?

A. Yes. He had had a lot to do with looking after people with haemophilia and I think understood therapeutic policies and knew a lot of the patients, the regular patients, and he would know -- it would be brought to his attention if there were new patients, different patients.

Neither of us were averse to phoning up someone else if we didn't know what to do in a particular circumstance. It's slightly more tedious then than it is now because you would have to go through the hospital switchboard and it was a very lengthy process but, you know, you could get advice from people in Glasgow or Oxford or London.

Q. Just one last matter, professor. When this supply of 8Y was obtained in the summer of 1986, was it for Edinburgh patients or was it for everybody in Scotland?

A. Well, as I think is clear, I requested it and it was held primarily at the protein fractionation centre and therefore it was available for anyone who wished to apply to use it.

Q. Yes. And Dr Perry didn't sent you all 50 vials?

A. He sent me 20, I think.
Q. But as matters turned out, I think you used the whole 50 vials. Did you ever mention to any of your colleagues in Scotland that that stock existed?
A. I assume that would be a responsibility for Dr Perry. He had a new product available for patients.
Q. Right. Is that a "no". Do you have any memory of ever saying in a conversation, "Oh, there is a stock of 8Y at PFC?"
A. I'm sorry, I can't remember.
Q. You can't remember. Right. Excuse me. (Pause)
It has been pointed out to me that the other question, I suppose, that arises in relation to 8Y as well, is that when that development occurred in the summer of 1986, did you mention that to the staff?
A. I'm sorry, which staff?
Q. When the 8Y arrived in Edinburgh, some vials you have and the balance is at PFC. I think it's the 20/30 split. Did you specifically speak to your staff about that?
A. I'm sure I must have told them about that, yes.
Q. But you don't have an actual recollection?
A. I'm sorry, I don't, but it was an important new product available and I'm sure I would have told my staff.
Q. Right. And would you have given them any instructions

as to the sort of patients for whom this precious commodity might be used, or would you have asked them if they were considering using it to talk to you?

A. I would have told them that it was for people who we thought either hadn't been exposed to blood products or had little exposure and might not have hepatitis.

Q. So would you have led them to understand that they should speak to you or were they free to give it if they saw fit?

A. Oh no, it was a very precious product.

Q. So they are expected not to do it on their own initiative?

A. Correct.

Q. Thank you very much, professor.

THE CHAIRMAN: Mr Di Rollo?

MR DI ROLLO: I'm not sure exactly what we should do next because --

THE CHAIRMAN: Can I tell you that I think that a lot of questions have now been asked by Ms Dunlop that raise issues that I would have thought that if you wished you could pursue. For example, there has been no reference to departments other than Professor Ludlam's own, but do you want him to leave and raise an issue with me?

MR DI ROLLO: No, it's just that, in view of this morning's discussion, I wasn't entirely sure whether it would be

better to ask some questions now and then deal with matters later or to come back again and deal with this witness all in one go. That's what I'm unsure about.

THE CHAIRMAN: It did occur to me that what has now happened might change the focus quite a bit for the future. And if there is anything you think you can ask at this stage, then I would be content. I have to tell you, I would quite like to know the answer myself at this stage to the horizontal dissemination of instructions within the East of Scotland and not just throughout Scotland.

MR DI ROLLO: I'm quite happy to try and explore that. I was going to ask him quite a number of questions in any event, as --

THE CHAIRMAN: I know that.

Questions by MR DI ROLLO

MR DI ROLLO: Perhaps, professor, can I deal with one point that emerged from your statement? Can we have your statement up? If we go to paragraph 10, we see what we are dealing with there:

"The number of patients not infected with non-A non-B Hepatitis virus(es) and requiring treatment in the period December 1984 to May 1987 was very small (in Scotland during this period it might be as few as ten individuals or less). It comprised of new patients

(mainly small children) with severe/moderate Haemophilia A and an occasional adult with mild haemophilia or von Willebrand's disease."

Is that right? What I was wondering is, if we look at the preliminary report at paragraph .9.326, we have there the statement that:

"The number of people treated for the first time in Scotland with a blood product during the period from 1 September 1985 to 30 June 1987 was ... 18 in the East of Scotland and 13 in the West of Scotland."

I'm just wondering how we marry up those two statements, yours and it. Is there some reason to think that what's contained in the preliminary report is inaccurate?

A. No, I think that is a reasonable estimate from -- I think this was from the Scottish Office investigation in the year 2000, these figures.

Q. I think you played a part in providing the figures for that?

A. I did, yes. I think perhaps what my statement in paragraph 10 is -- clearly it does not match that and I think it is an underestimate. I think I was more thinking in terms of patients per year who might turn up. The number of people with severe haemophilia turning up each year in Scotland is only about three or

four. I have to accept the figure in paragraph 9.326 as being the best estimate. I'm sorry, mine is perhaps a little misleading.

Q. Looking at systemic issues then, if we could just anticipate what could happen, stepping back for a moment, the patient, the potential patient, what those on the ground, as it were, the casualty officers and all the rest of it, might have to worry about might be the person who has not come to the attention of the haemophilia services before. This is the unusual patient. Babies, you are going to be referred to, and presumably it's possible or likely that you were going to be around, but the one that the casualty officers are going to be concerned about are the ones that are not in the severe category potentially, the milder end of the spectrum. They might not even be haemophiliacs, in the strict sense of the word, at all. You are nodding. Is that correct?

A. Casualty officers see a lot of bruised people and they have to make an assessment as to whether the bruise is in keeping with what seems to be the injury or whether it's a bigger bruise, more extensive. And we do quite a lot of clotting screens for patients who turn up in casualty with some sort of haemorrhage. With a bit of luck, the casualty officer will have enquired about the

past history of bleeding. So we do a lot of clotting screens; bruising is a common presenting situation in a big casualty department.

Q. So just from the point of view of the worrying about what could happen and giving instruction as to what you should do in certain types of situation, one of the kinds of patient that one might have in mind is the patient at the mild end of the spectrum who could, potentially at least, have a clotting problem that would require some sort of clinical intervention?

A. Yes.

Q. Now, just following that through then, I think we have heard that from your evidence to my learned friend this morning, your position on this is that you would expect those that were dealing with the problem at the ground level, if you like, if they were unsure what to do and had a doubt about what to do, they would refer to you for advice?

A. Yes, if a patient turned up in Accident & Emergency with a large bruise, and we did -- we were asked to do some clotting tests and the results showed that the patient had mild haemophilia, then that would be a very unusual event and one that -- we would go down and see the patient in casualty ourselves because it's very unusual.

Q. You have mentioned twice there, in the course of my

asking you questions, doing clotting tests. Obviously, before administering Factor VIII or IX or any other kind of course of action, presumably the cryoprecipitate as well, you would have to have a clotting test carried out. You would have to do a screening, a clotting test of some kind?

A. For a new patient who wasn't diagnosed with haemophilia.

Q. Yes.

A. Yes, you can't make a diagnosis without measuring the clotting factor levels.

Q. You can't make a diagnosis but you wouldn't treat with Factor VIII or a concentrate without that information, that specific information?

A. I wouldn't treat a patient unless I knew what the diagnosis was.

Q. All right. And you can't making a diagnosis, and the diagnosis obviously depends on the results of the clotting test?

A. Of a clotting test, yes.

Q. So it follows that the questioning of the person on the ground, that person would have to be instructed or would have to know not to give or administer Factor VIII without a clotting test having been performed?

A. If they had never been investigated before. If they had been investigated before, then one would ask them what

the results of the blood tests were.

Q. Can I just ask you about what being "investigated before" actually means? We know that haemophiliacs carry a card and that card has information on it, and that immediately gives a treating doctor, whoever it happens to be, specific information about that person that tells them a lot about what to do next, and in that situation the problem doesn't arise in the kind of situation that we're dealing with here, which is the previously untreated patient. So can you give us some content to the information that they would get, apart from this haemophilia card?

A. There are sometimes patients who have actually very good histories suggestive of bleeding disorder, and either you can't find a laboratory abnormality or they have got a sort of borderline abnormality, and those individuals I'm often hesitant to label as having a disorder because I may not be quite sure what it is, because once you have put a label, a diagnostic label on someone like that, it's very difficult to erase it if tests in future show it's actually not the case.

There are all sorts of other implications for labelling patients having bleeding disorders, for example life insurance and so on.

I have a small number of people who I say actually,

"I'm very sorry, I think you have got some sort of bleeding disorder. I can't quite put my finger on it. If you find yourself seeing other doctors, mention that you may have a bleeding disorder. We have your records in our haemophilia centre. The doctor can phone us up and we could look at them."

Q. What I'm interested in, I think, is the instructions given to staff in a situation like this. I'm not asking what you would do yourself. What I'm interested to know is to what extent they would be instructed, that you can rely on what they tell you about their history, which may or may not be informative, in the absence of a card, or you must perform a screen before you do anything next. Do you see the problem, potentially?

THE CHAIRMAN: Could we just pin down whether you are talking about staff within Professor Ludlam's department or staff in Accident & Emergency?

MR DI ROLLO: I appreciate that. I would be interested to know how it would work with the Accident & Emergency, and then if they then referred to your staff, who would be on duty at the particular time. So it is both in fact, that I'm interested in how they would be instructed to deal with a situation like this.

A. This is a patient -- can we just clarify --

Q. What we are talking about is the potential problem that

arises in this period, to give it a timescale, of an individual who presents, unannounced, with a problem, that you do not have any specific information about the level of clotting factor in their bloodstream?

THE CHAIRMAN: When you are considering this, professor, bear in mind that I have an interest to know whether there was anything parallel to the system you operated with your own staff, of weekly educational meetings, or whether there was any other mechanism by which the views of the haemophilia clinicians were made available to non-haemophilia doctors within the wider hospital set-up.

I think it may be that how the A&E man on the spot responded might be influenced or affected by general guidance you had already given or not. If you could bear in mind the wider context, please, when you are dealing with specific questions that are being put to you.

A. Thank you, I will.

MR DI ROLLO: Is it reasonably clear what I'm asking?

A. A patient turns up.

Q. Yes.

A. With a haematoma, a large bruise.

Q. Yes.

A. With or without a history --

Q. You get a history of some sort. I mean, I suppose potentially, you might get a history that, "I bleed easily," or something like that. What instructions do you give to your staff to deal with a situation like that?

A. Well, the doctor concerned would send some blood off for clotting tests. They have a very low threshold for doing that.

Q. That's really what I'm interested in. The doctor would have to have information about what the clotting level was in order to make a diagnosis. Is that the standard practice?

A. Yes.

Q. Unless you had a clear history in the form of specific information about the person's history, such as a haemophilia card, or that they were registered as a haemophiliac, something along those lines, and they were able to give you reliable information about their history, about what their clotting factor level was, otherwise you are not in a position to make a diagnosis?

A. No, you are absolutely correct. Before offering treatment, one has to be very clear as to what the condition is, what the level is of the potentially deficient clotting factor.

Q. How was it that staff were told what you have just told

me? How were they told, "You have got to be very clear about these things"? How did you do that? Not just you but we are talking about systems here. How was it done during this period?

A. The system was that clotting tests came -- we get a lot of requests for clotting tests from Accident & Emergency and if one turned up with an unexpected abnormality, as might occur in haemophilia, then that result was reported back to the person who requested it, and our duty registrar was informed and our duty registrar would then use his judgment as to whether or not to follow it up, and certainly if there was a question of a screening test potentially identifying a patient with haemophilia, then he would make sure the Factor VIII and Factor IX levels to start with were measured, and he would go and liaise with the doctor in the Accident & Emergency department.

Q. What I'm interested to know is how did the Accident & Emergency staff, referring perhaps for advice to your department -- how were they instructed how to deal with this situation? Who instructed them and how were they instructed?

A. Well, in one sense you would need to ask the people in charge of the Accident & Emergency department, but I would say that it was also part of general medical

education. If someone turns up with what looks like a bleeding state, a bit unexplained, that they might have a bleeding disorder.

Q. Right. Now, in the management then thereafter, the question then is what to do as to how to treat them, if it's discovered that they have a Factor VIII deficiency, for example. I think you are telling me that at that point a decision might be made by the registrar as to whether or not to administer Factor VIII without reference to any higher up the chain?

A. The haematology registrar?

Q. Yes.

A. It would be an unusual situation and they would almost certainly make some rather detailed enquiries, and I would have thought might well have reported to me.

Q. "Might well have" suggests that they may not?

A. I appreciate that. I can't say categorically they would. It depends on their level of experience and their training. But any new person with haemophilia that appeared in Accident & Emergency I would probably expect to hear about.

Q. Before any decision is made as to what treatment to give, is the question.

A. It might depend on the severity of what the clinical problem was, whether I was immediately available to

offer an opinion. So it depends a little bit on the circumstances.

Q. Well, that seems to be the system in your hospital. Was that the system in other hospitals that you know about in your area? Is that how it would generally be done? It wasn't just the Royal Infirmary that has an Accident & Emergency in Lothian and South of Scotland. Is that how it would be dealt with otherwise, do you know?

A. I think in other hospitals, if they thought they had a patient with mild or any sort of haemophilia, they are very ready to pick up the phone to us and ask what they should do.

Q. And do you know, did they?

A. We occasionally get calls, yes.

Q. But it would be a matter for them to decide whether to pick up the phone or not. It's up to them really?

A. Yes.

Q. If it was generally not known or not disseminated that there were particular issues with the use of a particular blood product during this period, how would they be informed about that?

A. Any patient who crossed the threshold into the Accident & Emergency department we would hear about. The Accident & Emergency staff, as soon as they identify either an existing patient or a new patient, they get in

touch with us directly.

Q. Presumably blood concentrates were available to be used in these other areas, were they?

A. They were.

Q. And decisions made to use them could be made without reference to you particularly?

A. Could be.

Q. Or even your department?

A. Could be.

Q. And so the problem then might be that they might use them in situations where you, on reflection, might think that perhaps wasn't such a good idea for that particular patient?

A. They might do but many people have very low threshold for phoning us for advice when a patient turns up unexpectedly with a bleed situation.

Q. To what extent were they informed of the particular need, perhaps, to avoid giving this product to someone who had never been given it before, during this period?

A. They would be -- a haematologist would be alert to that, and they are the people who would be in the position of having the information from the blood test if it was a new patient, but -- it possibly had haemophilia.

Q. There is a tension, is there not, between solving the immediate problem of stopping the bleeding in the

quickest and simplest and easiest way possible, against the long-term consequences that using a particular method might involve?

A. Entirely. But --

Q. And the question is how this decision-making on the ground is informed by a specialist, up-to-date, clear information and how that's disseminated down the chain, as it were. That's really what we are interested in.

A. Well, the way that the system works is, as I say: as soon as a patient appears in a casualty department, we are invited to offer advice as to how they should be managed.

Q. I mean, I appreciate your point that this sort of thing won't happen that often, of course. It is a relatively unusual event but it is a predictable event, isn't it? It's one that one can anticipate occurring. Is that right?

A. It does occur, yes.

Q. And the question is, if Factor VIII is available or Factor IX is available during this period to be used, what is or who is ensuring that it's not being used in situations where it isn't really necessary?

A. Yes, I thought I had been fairly explicit that there is a very low threshold for us being consulted about such patients when they turn up in other casualty

departments. Mostly they are known patients who turn up in other casualty departments. So we know about them; we can offer advice over the phone. If it's a new patient who looks like they have got haemophilia and it's not immediately life-threatening, we would probably get them sent over to our hospital.

Q. The question about whether you are a haemophiliac or not as defined -- and there are all sorts of definitions about that -- the two things that really matter are the nature of the bleed that needs to be stopped and the ability of the body's system to stop that bleed by itself without assistance, whatever this happens to be. Those two things have to be assessed, presumably?

A. Yes.

Q. One thing that you have to do is work out what ability of the body has to stop the bleed and that requires detailed information.

A. Yes, it requires a Factor VIII or IX level, or whatever the disorder might be or potentially be. Yes.

Q. All right. I want to ask you about another matter --

THE CHAIRMAN: I would like to follow up on some of these areas myself.

Professor Ludlam, we have, I think, a fairly clear picture of how your department operated, and I think also a fairly clear picture that from time to time

patients would present at other departments of the hospital with signs and symptoms that could give rise to a suspicion that they might have clotting deficiencies.

The response to that might be prescribed by a written protocol and handed down or it might depend on practice or a combination, and it might depend on experience and all sorts of other things.

Did you ever, as a haemophilia director, issue anything in the way of written instructions or advice to the Accident & Emergency department as to how they might respond to possible clotting defects generally?

A. Yes, we have.

THE CHAIRMAN: At this time, had you done that, 1985 to 1987?

A. Not at this time, I think. Subsequent to this time, for other reasons I'm happy to go into, if you want.

THE CHAIRMAN: At the moment I want to stick to this bit. Other people later will ask why there were changes perhaps, but just concentrating on this period, there wasn't a written instruction, directive, advice or anything of that kind?

A. There was advice that was given to the people in charge that if a patient came in to Accident & Emergency, to contact our service immediately.

THE CHAIRMAN: Could I explore that just a little?

A. Yes.
THE CHAIRMAN: The person in charge would be, what, A&E senior consultant, or something of that kind? How would that be done? Was there a meeting of heads of department, or some other way for disseminating information of that kind?
A. No, but that was what was known. If a patient came in to casualty and was known to have haemophilia, the automatic response was to phone up the haematology --
THE CHAIRMAN: The critical case is not the patient who is known to have haemophilia; it's the patient who is displaying signs and symptoms that might lead to an inference of haemophilia.
A. Yes.
THE CHAIRMAN: Can we concentrate on that one, please?
A. Certainly.
THE CHAIRMAN: What was the established practice or protocol or whatever, if any, in respect of them?
A. I think if a patient turned up with either a haematoma or something bleeding, particularly if it was out of context in terms of injury, then the casualty officer would ask them about previous events that might have given rise to bleeding, like dental extraction or tonsillectomy, or any other operations, and even if the answer to all those was negative and the bruise or

bleeding seemed a bit out of context, they would send us a blood sample and we would assess it.

THE CHAIRMAN: This happens at 2 o'clock in the morning in the hypothetical case and the A&E officer hasn't seen the problem before but sees swelling, let us say, or bruising that seems disproportionate to the history of trauma that he has received. At that point, I suppose one possibility is that he would think of clotting disorder. Are there other circumstances that he ought to have in mind among the range of possible causes of a disproportionate bruising? Leukaemia, for example; is that a possibility?

A. Some disorder of the blood clotting system, which has many components, and there might be an underlying malignancy, for example, or a fracture that hadn't been diagnosed after an injury, a tumour on the bone, something of that sort.

THE CHAIRMAN: And is it, at that stage, that the haematologist comes into the picture or does the haematologist get information about it after a lab test or what? What triggers the next step?

A. Usually blood tests and then the blood -- and another investigation. An X-ray might be very appropriate. The blood tests would be the next investigation. The results of these would be phoned back to the requesting

unit and we had a system where, if the results were outside certain limitation or were unexpected, our laboratory staff knew to phone the duty doctor.

THE CHAIRMAN: That's two contacts by the lab staff so far. One is back to the requesting A&E doctor, who clearly is entitled to know what's going on. One is at the initiative of the lab technician to contact you. Might the lab technician also contact the haematologist on duty at that point or not?

A. Yes, the duty haematology doctor, yes.

THE CHAIRMAN: So these things are things that happen always? Are they things that are prescribed or what?

A. This is how we run our service. One of our major responsibilities is to keep a watching brief on the results that go out from the laboratory, to try and pick up those that are abnormal and unusual in that particular clinical context, and that's the tricky thing because if you have, for example, a renal unit, the haematological indices in people with chronic renal failure are different from normal people or from people who are getting cardiac surgery. So you have to have some system for filtering out what's expected and what isn't expected, what's unexpected.

Some of this is done by computer screening these days, because we get over 1,000 blood samples a day.

But clotting tests that are unexpectedly abnormal are one of the things we take a particular interest in and get in touch with the clinicians because often, when we report the results back as being abnormal, they are not picked up by the clinician who saw the patient, or they don't understand the significance of it, and that's why our laboratory staff get in touch with our registrar, who then gets in touch with the clinical unit and asks them about the patient.

THE CHAIRMAN: Mr Di Rollo, we are going to rise now since it's 1 o'clock but you may wish to come back on some of that before you go on to your other material.

MR DI ROLLO: Thank you very much.

(1.07 pm)

(The short adjournment)

(2.00 pm)

THE CHAIRMAN: Mr Di Rollo?

MR DI ROLLO: Thank you, sir.

Professor Ludlam, we were talking before lunchtime about systems, and I think we have heard a little bit of evidence about that. As I have understood it, this is a pretty basic and standard situation, that you rely on Accident & Emergency to refer to haematology anything which they feel requires consideration and haematology, within that department, if it's someone at a low level,

if there is something that requires to be considered as unusual or out of the ordinary, you would expect that person to go further up the chain, and the next level up the chain would be to registrar and then to you. That's the situation, as far as systems are concerned?

A. That is correct and I wonder if I could use this as an opportunity just to correct some incorrect information I gave to the chairman just before lunch.

I was asked about protocols in the Accident & Emergency department for referring patients and I said that there were protocols recently, and I indicated that at this time I thought there probably weren't. I was thinking about that over lunchtime and I clearly remember that we, every two or three years, met with the A&E consultant in charge and brought up-to-date a protocol that we had that was in -- they had got a book of protocols and guidance for their doctors and we did have a guidance sheet in there as to how the staff in A&E should respond to someone with haemophilia, or potential haemophilia presenting.

Q. What I want to know, Professor Ludlam, is in the course of this critical period that we are talking about, between 1985 and 1987, did you, with a particular concern about this type of previously untreated patient, instruct your staff that if they were informed about

that patient, that they were to get in touch with you so that you could then take the clinical decision as to what sort of treatment they were to get?

A. I don't think it was a specific instruction for this two or three-year period but I think there was a general understanding that when a new patient presented, I or someone senior in my department should be consulted about treatment, because all the other patients -- the patients who were known to us -- we had records of how they should be treated. It was in their case notes, it was in our computer system register, so if a patient turned up and there was someone who was new, then that would be a decision for someone with some experience and reasonably senior in the department.

Q. Can I just understand what you mean by "reasonably senior" then. Do you mean consultant?

A. Consultant, or in those days we had senior registrars, who will have been in training in those days for five or six years perhaps, coming up to consultant status. Some of them may have a special interest in clotting. And again, depending a bit on the circumstances, if they felt comfortable making the decision, then they might make a decision; but new patients with haemophilia turn up very infrequently. They are quite an event, and so if I was there, or even if I wasn't there, my colleague

Dr Parker was there, we would almost certainly get to hear about them unless the person who was acknowledged, as it were, was confident about what was appropriate to do.

Q. Were you ever aware of that situation in the period that we are talking about, where a new patient was given Factor VIII without you being informed about that?

MR ANDERSON: Don't answer that, please, professor, unless instructed or directed to do so by the chairman.

I do have a concern, sir, that we are going from the general to the particular. I don't think I have to say any more about that because it's clear to all of us in this room after this morning's decision.

THE CHAIRMAN: I think that is so, Mr Di Rollo, and I would prefer you to follow the other course that I suggested, if you wish to pursue that type of question.

So again, I think that the proper answer, although this is not the particularly appropriate place to be doing it, is to say that I won't allow it in hoc statu.

MR DI ROLLO: Very well.

THE CHAIRMAN: I want to talk to you later about whether we are going down that route and how far to go, but I think, as a straight matter of form, that's what I should do right now.

MR DI ROLLO: There is another one or two matters that

I want to explore. One matter I would like to have guidance on is whether I may go -- in my list of questions there is reference to the letter which was --

THE CHAIRMAN: A letter that has been in the evidence before?

MR DI ROLLO: Yes.

THE CHAIRMAN: Well, if it's in the evidence, I don't think --

MR DI ROLLO: But I do want to explore what might have been meant and what was said and the history of that.

THE CHAIRMAN: I think what was meant, what was said and then adding or "and the history" may be quite difficult. I'm conscious that questions are being asked about what was said and what was meant but I think the history had better stay subject to the general reservation at the present time.

MR DI ROLLO: Very well.

I think you were shown yesterday, Professor Ludlam, a number of letters. This is in connection with the request that was made for Factor 8Y, in the middle of 1986, and what I want to do is to put before you a number of specific letters.

Could we have [SNB0075871] on the screen?

This is part of the correspondence that followed -- am I right to think -- you said this morning it was your

request for Factor 8Y?

A. Yes.

Q. So it was you that requested it?

A. After discussion with my colleagues in blood transfusion, yes.

Q. Yes. And who did you actually make the request of initially?

A. My recollection of the correspondence is that I asked Dr McClelland or Dr Boulton and they wrote, as you see, to Dr Perry, I think it was, to try and --

Q. I think it was you initially put the request -- or at one stage you put the request in the form of a letter. It is referred to in some correspondence. Do you remember doing that, that you did write a letter about this?

A. I don't remember writing a letter but the correspondence states there was a letter so I presumably did write a letter.

Q. I just want to try and understand, leaving aside the history that's given. The passage that I'm interested in is the passage that says:

"Christopher is a bit ruthful with his own staff about this because he feels that this patient should have received 8Y or an equivalent product."

Do you remember discussing this matter with

Mr Boulton?

MR ANDERSON: Again, I'm hesitant keep jumping up to object but with the greatest of respect, this seems to be an investigation into a particular set of circumstances involving a particular clinical decision by particular clinicians who are not involved in this Inquiry.

I appreciate, it may be difficult in certain circumstances to distinguish the general from the particular but in my submission this is verging over that line into the particular and is not in the general.

THE CHAIRMAN: Again, I think that's correct.

Professor Ludlam, when did you get to know that there was a product that was known, or came to be known as "8Y"?

A. I knew that the Blood Products Laboratory at Elstree was developing a new product called "8Y", that they were hoping to heat at 80 degrees for 72 hours, some time in 1985. I think that was generally known. I would have known that.

THE CHAIRMAN: You would hear about it at meetings of the UKHCDO reference doctors, apart from anywhere else?

A. Yes.

THE CHAIRMAN: What was your understanding of the procedure that would be followed in relation to the development and introduction into use of such a product if it were

to be introduced?

A. In England?

THE CHAIRMAN: No, at all.

A. At all? It would require to be given as test infusions into a number of people, probably with severe haemophilia, who hadn't been treated for several days, to assess the post-infusion Factor VIII level and the half-life, the time that it remained in the plasma, the rate at which it disappeared from the plasma, to make sure that you got the expected therapeutic rise. That will be done in a number of patients. Nowadays, I think, the regulations are that you have to do it in about ten or 15 patients. You would then have to study those patients later to ascertain whether or not they had developed an antibody, an inhibitor to the Factor VIII, to see whether it had altered its antigenic structure.

It would then be necessary to give it -- if that was all satisfactory, to give it to patients who were bleeding with conventional bleeds, to make sure that it stopped the bleeding. How that is assessed has changed over the years.

THE CHAIRMAN: Can we just pause at that stage then.

At what stage would the basic clinical trials on a CTX come to an end? Would it be before or after the

final comment you have just made, that it would go to patients who were bleeding with conventional bleeds? Is this a separate step?

A. That's a separate step but it would be part of a CTX.

THE CHAIRMAN: It would be part of the CTX?

A. Yes.

THE CHAIRMAN: I want to ask you a little about CTXs.

I know that one would apply to get one and specify the product and indicate what was going on and make proposals for the scope. Was there a regulatory constraint on the scope of CTX work?

A. My understanding of the CTX arrangement was that an application was made to do a study. The conventional -- the full, if I can put it this way. The full way to do it would be to apply for a clinical trial certificate, and in that I think there was then a very formal assessment of the protocol. That took up quite a lot of time. It was very lengthy. So, as a sort of, as I understand it, short cut, someone who wished to -- usually a manufacturer who wished to conduct a trial under the CTX regulations, put in their proposal and if there wasn't an objection within six weeks, they could then get on and conduct the study.

THE CHAIRMAN: If we can come from the general to the particular, when you heard about the development of F8,

of the English product, what did you understand was going on?

A. My understanding is that they applied for a CTX.

THE CHAIRMAN: And did you have any understanding at all about the geographical or other scope of the clinical trials that were anticipated in that application?

A. No, I have merely seen the front sheet with the signatures on it.

THE CHAIRMAN: Were you asked, asked, by anyone to take part in those clinical trials?

A. No.

THE CHAIRMAN: A stage came when you made an intervention, as it were -- and I'm trying to choose some sort of totally general word that carries no implication with it -- into the process and asked for some of the material. What was the state of play at that point, as you understood it? Had the clinical trial process ended or was it still current?

A. It was still current.

THE CHAIRMAN: Did you understand that you were making this request at a time when the trials were still current and before they had been completed and before any question of general release would have arisen? Have I run too many things together?

A. No, I think I appreciated -- I certainly appreciated it

didn't have a licence and I think I knew it had a CTX -- was there another part to your question?

THE CHAIRMAN: Yes. It was merely to define the time period and if it was still unlicensed then, that answers my final point.

A. Yes, it was certainly unlicensed at this time, is my recollection.

THE CHAIRMAN: Can you remember now what it was that prompted you to make the request for some 8Y?

A. I think it was the appreciation that it was perhaps less likely to transmit non-A non-B Hepatitis than the NY product, Factor VIII product, that was available in Scotland, the 68 degree, 24-hour material.

THE CHAIRMAN: I think we know a whole background to the question of the effectiveness of the Scottish product, but Mr Di Rollo, that takes me to a certain point. If you think that you can ask any further questions now on this topic, please do and we will see what Mr Anderson says. Otherwise, I think I would prefer you to adopt the alternative route and consider whether you want to pose them in another way.

MR DI ROLLO: Very well. Can I just ask you this, and it is relevant. It's about your relationship with Brian McClelland. In terms of geography, he was next door to you in the Royal Infirmary.

A. He was down a different corridor but they almost abutted, a short distance away.
Q. He was somebody you would see on a regular basis?
A. Yes.
Q. And have conversations with all of the time, and exchange information with all of the time and throughout your professional working life?
A. At that time, yes.
Q. And if he was aware of something of interest to you, it would be very likely that he would pass that on to you, in relation to developments in this area of treatment of patients, haemophilia patients?
A. Yes, I think that's right. If he thought -- particularly if he thought I wasn't aware of it.
Q. Indeed. If we go to [PEN0161152], these are minutes of a meeting, the Central Committee for Research and Development in Blood Transfusion, the Central Blood Laboratories Authority, and present at the meeting we can see a number of people. That includes Dr McClelland. Obviously, I appreciate you were not present at this particular meeting. Were you aware of this particular organisation, its existence?
A. I'm not sure that I was. It was part of the blood transfusion arrangements -- they had various committees and meetings. I didn't know exactly what they were, who

went to them.

Q. Those that were present, not those in attendance, not the civil servants, but the actual doctors that we see there, did you know all of those individuals or had met all of those individuals?

A. I know who they all were apart from Dr Gibson.

Q. If we look at paragraph 14.3, which is on page 1153:

"Dr Rizza reported upon further trials carried out with heat-treated Factor VIII, which he had now been using for approximately nine months. He confirmed that none of his patients, including children, had become clinically ill and therefore the immediate signs were encouraging."

There is other information that you were shown yesterday about developments relative to the English product and I'm not going to go back over them. I'm just interested in this particular item at the moment. What's interesting about this is that, first of all, Dr McClelland was at the meeting and secondly, it is being reported that the trials have been going on for approximately nine months.

From my limited understanding of these matters, the fact that a patient had been exposed to Factor VIII -- if hepatitis emerges, it may well emerge at a relatively early stage. So the fact that there are no clinical

signs after that period seems to be encouraging in respect of the clinical trials so far. So it's a case of so far so good, but these signs are encouraging. Is that right? That's what it says.

A. That's what it says.

Q. Did Dr McClelland share with you that information?

A. I don't think so, no.

THE CHAIRMAN: Do you know whether Dr McClelland would have been free to share with you information about a research and development committee?

We have been over this area before, Mr Di Rollo. I think that one has to be clear whether this is an open meeting or a private and confidential meeting.

MR DI ROLLO: I don't know, is the answer to that.

A. If I could say that the minutes that I was shown yesterday by Ms Dunlop and the meeting in March 1986, it said "Confidential" at the top, and that was some information about this trial.

THE CHAIRMAN: I don't think it does say "Confidential" on these.

A. No.

MR DI ROLLO: I don't think that was an issue that was explored with you yesterday, in fact. I thought the point about the minutes of March was that you weren't at that meeting but you were meant to be at the meeting.

Is that not right?

A. In that case there were two sets of minutes. There was a meeting of the Scottish Home and Health haemophilia directors and blood transfusion, that I was sorry not to be there and sent my apologies. There were some other minutes from a central blood transfusion research meeting or something -- I forget what it was -- that had handwritten at the top "Confidential", just off the top of the screen.

Q. Yes, "In confidence"?

A. In confidence.

Q. Yes, that's a different one. I think that's at an earlier stage. I think the question that I asked was whether Brian McClelland did indicate or you were aware of information about how things were going down south, and the supposition that he didn't share that information with you, whether it was confidential or not.

A. I don't recall him sharing it with me and even -- there are a number of issues that are raised by this. Even if initial results, treatment of the first few patients looks encouraging, that is not a reason to presuppose a successful outcome to the study. Medicine is full of examples of drugs that look promising to begin with and patients -- it applies particularly in the cancer

field -- are desperate to get hold of the drugs and then when all the results are pulled together at the end of the study, the drug is found not to be useful.

I think the issue here, one of the very pertinent issues is how many patients have to be studied before you can be reasonably certain that 8Y is a hepatitis-safe product.

MR DI ROLLO: Can I just take issue with that in this way: Obviously, if you are going to present it as a hepatitis-safe product, then I can understand that matter. The question we are dealing with, the context of this, is adding that extra element of safety, which is not there currently with the product that you have, which is why, as I understood it, an order was made in May/June 1986 -- so it's not a case of it being hepatitis-safe or guaranteed as hepatitis-safe or scientifically proven as hepatitis-safe, it's a case of having sufficient information to take the view, "Well, we have got these people that may have to be given it for the first time. They are very rare but what about catering for them?" As I understand it, that's essentially your approach in June of that year, and what I'm trying to get at is what has changed between the turn of the year and June?

A. More patients will have been recruited and studied. So

there will be more information on more patients that looks encouraging.

Q. You didn't have any specific information to that effect in terms of a document or -- as I understood it yesterday, what has prompted a change of decision to make a request is information that you have been given by a colleague, isn't it?

A. Yes.

Q. So somebody has told you something about this English material, which you have then said, "We should get some of that".

A. Yes.

Q. Does that bear any relationship to treating a previously untreated patient in May of that year?

A. It became clear in May 1986 that the NY 68-degree, 24-hour concentrate that we were using could and did cause non-A non-B Hepatitis.

Q. You knew that anyway. You knew that it could, maybe that it did, in that particular case.

A. All right, it did.

Q. But you knew that?

A. It did, yes.

Q. So the question is what has changed between the information that was available to you or your colleagues -- I mean, you had the good idea of trying to

get some material in June. The question is that there were those responsible for the provision of material to hospitals in Scotland who had as much information as you had at an earlier stage.

THE CHAIRMAN: Sorry, I think that you may be running more than one thing together there again. Do you want to look at the question as it is put, Mr Di Rollo. I'm not sure it's easily answered.

MR DI ROLLO: I'll take it out.

THE CHAIRMAN: No, no. I don't want you to take it out. The question is that:

"There were those responsible for the provision of material to hospitals in Scotland who had as much information as you had at an earlier stage."

That's what's confusing me and I'm just inviting you to think whether you want to rephrase it, not take it out.

MR DI ROLLO: Perhaps I can rephrase it. Let's break it down.

In June, you have been given certain information by a colleague about the effectiveness in preventing non-A non-B of the English 8Y. There were others that had that information before June in Scotland. That's right, isn't it?

A. It seems to be.

Q. And the information that you had in June, if it was available to them at an earlier stage, the question that I would like to know the answer to is: why did it not happen that a request was made for 8Y to be made available for previously untreated patients at an earlier stage?
A. I understand your question and I think you need to put it to someone from the Blood Transfusion Service, because they were responsible for providing National Health Service Factor VIII for use in Scotland.
Q. Did you ever speak to Dr Rizza at UKHCDO meetings?
A. Yes.
Q. Did he ever mention how things were going with Factor 8Y?
A. I can't remember, beyond what's in the minutes of the meeting, I'm sorry.

I don't know if it would help but the first, as far as I know, bringing together of the 8Y data for consideration was in September 1986. Before that it was just being gathered patient by patient. There is the possibility that it was also presented at the WFH meeting in Milan in June. We thought about that yesterday. I certainly wasn't at that meeting.
Q. You seem to have known a few weeks earlier. These letters, dated 27 June, talk about you having

a conversation with Brian -- that's what's referred to, using Christian names, obviously -- with Dr McClelland, concerning obtaining this material for a specific -- it does look, does it not, Dr Ludlam, that it was for a specific reason, that something had happened that had made you think that it would be good idea to get some of this stuff?

A. There had been a transmission of non-A non-B by the Scottish Factor VIII NY product and therefore it seemed appropriate to think about what other products might be available that wouldn't have this.

Q. The point I'm making is the prompt for that seems to be that particular event. Is that not correct? The event of the transmission of non-A non-B Hepatitis.

A. I can't be absolutely certain at this time but it must have been part of the discussion.

Q. Which is why, when we look at Dr Perry's letter, he talks about just concluding these discussions. It's a specific reference to that event as well. The whole context of the request is the context of this event, isn't it, not the information that you were given about the relative safety of Factor VIII, do you see what I mean, of 8Y?

A. There was clearly a general discussion. I'm sorry, I can only speculate as to what precipitated it.

Q. We've talked about September, now go to the BPL annual report. It's dated March but it's actually published in September, I think, and that's [DHF0021590].

It would be misleading to say that the date of this is March 1986 because I believe the publication for this to be at a later time. Look at the next page. It's September, I think. But it's covering the period. The specific page I want to go to is page 5 of [DHF0021590].

This says at paragraph 2:

"The 'AIDS-related' problems at BPL had been addressed at BPL and PFL the previous year so that by April 1985 all Factor VIII intermediate concentrate leaving the laboratory was heat-treated at 70 degrees centigrade for 72 hours and a new high purity concentrate, designated 8Y, entered clinical trial. Factor 8Y replaced the older concentrate after August 1985 and, dry-heated to 80 degrees centigrade for 72 hours, set the international standard for products of this type. After 12 months' use, there were no reported cases of ... HIV and, more important, no evidence of transmission of non-A non-B Hepatitis virus to recipients at risk of infection."

That would be a public document, or at least it would not be confidential.

THE CHAIRMAN: I think it is, with respect, if you look at the first page you looked at. It's a confidential document. First page of text.

I'm sure I saw somewhere that it was confidential. I can't read that. Yes:

"The report is from the director of BPL and PFL to the CBLA and is confidential."

MR DI ROLLO: Does that mean that that information would not be available to those people in Scotland? You are shaking your head, professor.

A. I have never seen this document before. We don't get the annual report of BPL.

Q. This information is available somewhere and I suppose the question one has to ask is: it's obviously significant information relative to the issue that does arise; why is it that, following your intervention in June, a request is made? Why is it that Factor 8Y is not available to deal with previously untreated patients in Scotland even in September of 1986?

What is the reason why this material is not provided, not just in Edinburgh but throughout Scotland?

A. I think the answer to that partly -- you would perhaps need to address this to representatives of the Blood Transfusion Service but the anticipated plan was that Z8, heated at 80 degrees for 72 hours, was going to be

available in either August or September 1986, and in fact the first two batches, I think, had been made in July and then they ran into a bit of a problem, is my recollection, and production got put back two or three months.

Q. Right, so the question then is what about getting some English material in the intervening period?

A. I think you should put that question to the Blood Transfusion Service and they would say that there was some available at PFC probably.

Q. Can I ask you what steps were taken to alert physicians throughout the country what they could do, that this material was available and would be useful for previously untreated patients?

A. I think you would need to ask Dr Perry, who was holding the stock of this at PFC, which is the national centre for NHS blood products.

Q. Although this document is described as "confidential", does that mean that PFC would not be privy to this annual report or would it be circulated to them at all?

A. I can't answer that question, I'm sorry.

If I can just say, I think -- I think this discussion is a bit viewed with hindsight of 8Y, which we now know to be a very safe product and this was very early days in it being assessed. We considered this

yesterday and there were some examples where in a sense, the thresholds were breached for it potentially being labelled as transmitting non-A non-B Hepatitis. These were very early days in the assessment of a new product.

Q. Yes, but, Professor Ludlam, it is not hindsight for you. You were there, you ordered it.

A. Yes, but for -- but I think there has been -- the view in some of the consideration of it recently, in the last day or so, is that it was safer than I thought it might be; in other words, I thought it was perhaps a little bit safer but not completely safe.

Q. The trouble is obviously, clearly you thought it was a better option because there is less risk. Let's put it like that. Is that fair? It is a lower level of risk for non-A non-B as far as you can tell?

A. Yes, and it's a question of how much better.

Q. Well, anything that's materially better, which is obviously you thought it was sufficiently, materially better because that's why you put in the request that you did, clearly.

You say this discussion is affected by hindsight but I don't know if that's really correct, given that we are in a situation where increasingly, throughout 1986, it became clear that all -- the signs were encouraging even in 1985. They were even more encouraging in 1986 and

there was nothing that was discouraging, and we had already passed the point by the middle of 1986 where someone had thought it sensible to have this material available. Is that not a reasonable summary?

A. I think that's a reasonable summary, yes.

Q. I'm not getting at you personally in relation to this, it just happens that you are the person that I'm asking questions, but the question is: why is it that nothing was done to make this material more generally available for patients throughout the country?

That's a legitimate and reasonable question, isn't it?

A. I think the response to that would be the trial was ongoing and in a sense I had perhaps jumped the gun a bit by asking for it when I did. Perhaps it looked like the right thing, if you like, to have done in retrospect but supposing in fact 50 or 75 per cent -- there was 50 or 75 per cent chance of it transmitting hepatitis, then my idea wouldn't have been quite so clever.

Q. It would still have been clever because it was still less of a risk than the existing Scottish material.

A. Well, we didn't actually know what the risk of the Scottish material was. We knew it had transmitted non-A non-B Hepatitis on an occasion.

Q. Presumably, the increased heat and increased length of time is designed to give a greater level of protection from that point of view?
A. Yes.
Q. I don't see how you can have it both ways, Professor Ludlam. It was either a good idea or it was not a good idea to order the material or request the material in the middle of June, and if it was, then presumably, as time went on, it would become an increasingly good idea to order the material as time went on, or make it available for more than just patients at Edinburgh or patients that might come into Edinburgh Royal Infirmary?
A. Perhaps the distinction could be drawn between what I thought was a good idea and what should be national policy in Scotland. If we had had a discussion about what should the national policy be in Scotland, that might or might not have come up with the same answer.
Q. The problem about national policy is that there doesn't seem to have been anyone in charge of assisting or instructing those in the regions, if you like, apart from outwith the central belt, as to how to deal with this particular problem during this particular period of time. As I understand it, no one seems to have had the responsibility to change the guidance that was given

between 1984 and 1986, given that there had been a change in the relative merits of the different options available.

A. I think that's fair comment. It's always difficult to know when to rewrite guidelines, how much has to go and change before guidelines are rewritten.

It was quite a fast-moving area, this, as you can see. Particular months when decisions were thought about or made differed from month to month. Things were moving quite rapidly. It was a very, very confusing period to be working in and there were many meetings as -- I have learned about more meetings in the last two or three days than I knew took place. It was a very confusing time to be working in this area, for the Blood Transfusion Service, for the fractionators, both in Scotland and in London, and in an international context, particularly in relation to the safety of dry-heated products.

We were bereft of guidance from -- perhaps from the Committee On the Safety of Medicines. They are responsible for licensing the products and offering guidance on therapy. It was a very difficult area and it might have been helpful to have had some high level guidance but it wasn't forthcoming.

Q. It does seem to have been a practical possibility for

Factor 8Y to have been made available in Scotland to deal with a specific problem, which is the previously untreated patient. That does seem to have been practically possible. Is that right?

A. Clearly it was practically possible but if I can say, my English colleagues were desperate for NHS, heat-treated Factor VIII. They had been through an awful period in 1985 when there was a paucity, and if I can go back a few years before that, haemophilia physicians in England had campaigned vigorously and repeatedly through the 1970s to get an adequate supply of NHS Factor VIII, and the unfortunate things that rolled out in the 1980s, and particularly acutely in a sense in 1986, was because of inadequate funding for the preferred product; in other words, a National Health Service product, and my physician colleagues in England were desperate to have 8Y and it still only fulfilled a third of their need, and the sort of word on the street was that I would be jolly lucky to get some.

Q. There was word on the street then? People say, "You can try it if you like but you might not get any"?

A. Yes.

Q. That's a good reason for perhaps not even asking, but it is a reason for not asking. "We didn't want to ask for the English Factor VIII because we didn't want to

deprive the English of a heat-treated product which they didn't otherwise have." Is that why you didn't ask before June?

A. No, I don't think that's why I didn't ask before June but if I wrote to BPL, I was very unlikely to get any and that's why I went through these rather formal channels, because I thought that he had more influence and leverage than a mere physician in Edinburgh.

Q. It does appear that somebody who is aware of the facts and has all the information, such as yourself, sees a gap and appreciates the need to fill that gap. Is that right? And what I'm wondering is that that gap, as it was at Edinburgh in June or May or whatever, remained throughout the country right up until the point at which the Z8 became available and produced in Scotland.

A. No, because there was some 8Y at PFC available, and as it emerged yesterday, I managed to wheedle some out of Newcastle.

Q. Provided the person was smart enough to know to ask for it, they would get it. The trouble is there might have been one or two doctors throughout the country who didn't have their finger quite so much on the pulse as you did?

THE CHAIRMAN: It's all right. I think actually that might have been a compliment, professor. You don't need to

hesitate quite so long --

MR DI ROLLO: It was meant to be a compliment with a slight sting in the tail.

THE CHAIRMAN: I thought so. It's the "et dona ferentes" bit. So you have got to look out.

MR DI ROLLO: Which is why he was hesitating perhaps.

I think that's probably as many questions as I can ask at this stage.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: I'm in a slight quandary when my learned friend finishes by saying "at this stage".

THE CHAIRMAN: He knows that there is the direction I gave earlier that if he wishes to raise any other particular matters, he should adopt a particular approach to it; adapting slightly what was concerned with a different matter yesterday, of course, but following broadly the same procedure and give notice. I think that's what "at this stage" means in this context.

If I'm wrong, Mr Di Rollo, you had better tell me.

MR ANDERSON: Well, I have one or two questions. It seems to me appropriate that I should ask Professor Ludlam those questions. If it be the case that my learned friend wishes and is able to ask further questions of this witness, no doubt I will be allowed to ask question that may arise from that.

THE CHAIRMAN: I do anticipate that further matters would follow a rather tighter procedural course and you will have a chance to make representations about the scope of questioning before we got to questioning at all.

MR ANDERSON: I'm much obliged. In that case, I will proceed, if I may.

You will be relieved to hear, Professor Ludlam, I have only one or two questions, I hope.

Questions by MR ANDERSON

MR ANDERSON: Could we have up to the screen two pages from your report. Pages 2 and 5 of [PEN0171798]?

What I'm interested in, professor, is in the main body of the report at paragraph 3, and although it's entirely plausible I'm being slow about this, there is a possible dislocation between that and paragraph 8 in your appendix. If we can take them one by one. In paragraph 3 you say in the second sentence:

"It was not until mid 1986 that evidence started to be reported to suggest that it might be a hepatitis-reduced concentrate. This concentrate was only available to meet approximately one third of the total use of Factor VIII in England. The majority of patients were treated with commercial concentrates which were likely to transmit hepatitis."

Do you see that?

A. Yes.
Q. So we appear to be talking about a period in mid-1986 and a third, which I take it would have available to them the new 8Y product. Is that correct?
A. Yes.
Q. If we look at paragraph 8 in the appendix, it says this:
"In early 1985 at BPL the initial batches of 8Y, heat-treated at 70 degrees/72 hours, were available for use in patients, however, it was not until October 1985 that 8Y at 80 degrees for 72 hours was in full production. At that time it only represented about one third of Factor VIII concentrate used in England, the other two thirds were of commercial origin (of unproven viral safety and likely to transmit non-A non-B virus(es))."
I just wonder about this period between mid-1986 and October 1985. Do you see the possible dislocation? When was it that a third was available to the English population? Do you know that?
A. I think that was actually addressed in the report from BPL that we had up on the screen a few minutes ago, which I think suggested that the predecessor to 8Y was heat-treated until about April 1985. 8Y was introduced -- now, 8Y may have been treated at the slightly lower temperature initially, and I'm not sure

when the 80 degrees came in, whether it was in the spring or in October 1985, but overall, during this two-year period, approximately a third of the Factor VIII that was used in England was of NHS origin and two thirds was commercial.

Q. Right.

A. The proportions didn't change very much over this two-year period. So the majority of patients, or the majority of infusions being given in England all transmitted the commercial -- would all have transmitted non-A non-B Hepatitis.

Q. All right, thank you.

THE CHAIRMAN: I think in due course, Mr Anderson, Professor Ludlam, I will be looking at a whole series of answers here, including paragraphs 9 and 10 and so on. I rather suspect it's quite difficult to work out precisely the sequence of events in England. But it clearly took place over a long period of time right into 1993 before there was a full evaluation of 8Y.

A. That's correct but I think the original production was certainly in existence by October 1985. The period I'm a little uncertain about is the first two thirds of 1985. What the temperature was and which product was being issued, and I know that they had at one stage intended to heat-treat NHS Factor VIII in early 1985 and

I think they ran into difficulties. You would need to ask the blood transfusion experts about that.

THE CHAIRMAN: We have Dr Smith coming and I'm sure that he is the person who will tell us exactly what the sequence of events was.

MR ANDERSON: I think that's right, sir. I'm quite happy to move on from that and we will wait until we hear from Dr Smith.

Professor, could you look with me, please, at the letter, which is [SNB0075914]? This is a letter we have looked at on a number of occasions before, from Dr Boulton to Dr Perry at PFC. This is the letter that makes reference to the letter you wrote, which we haven't been able to find. It says:

"Last week Dr Ludlam wrote to Brian asking if it would be possible to obtain some of the BPL products for use if a previously untreated haemophiliac presented for replacement therapy."

It then goes on to say:

"He said it would be difficult to estimate its potential use accurately but I understand that he has no haemophiliacs on his books at the moment who have not been treated."

This is, of course, second-hand and there is a quoting of what you have said to him, but when it says

"he has no haemophiliacs on his books," is that a reference simply to Edinburgh Royal Infirmary or is that to the East of Scotland?

A. Edinburgh Royal Infirmary.

Q. All right. Then it says:

"He has no haemophiliacs on his books at the moment who have not been treated."

What does that tell us about how pressing you saw the need to obtain this material?

A. You never know when a new baby is going to be born with haemophilia or a new patient is going to appear. Sometimes, yes, one does know. One makes a diagnosis for some reason or other before treatment is necessary and then you have someone you know hasn't been treated. But usually patients present because they bleed and the diagnosis is made after they have bled. And therefore you need to have something -- you need to have treatment available for them.

Q. You see it says here that:

"There are no haemophiliacs on his books at the moment who have not been treated."

I think you told us yesterday that in fact the 20 vials that you got did not, in fact, go to a previously untreated patient. Is that correct?

A. That's correct, yes -- at least I think that's correct,

yes.

Q. But rather they went to someone who had suffered an allergic reaction?

A. That's correct, yes.

Q. Having used up those 20 vials, did you make any request for any further supply of 8Y?

A. I can't honestly remember. I don't know whether I used up the other 30 vials that were at PFC, assuming those hadn't been used by someone else, or whether I went directly to a colleague in Newcastle to scrounge some.

Q. You see, this is more than a year before the Scottish product became available, but I don't think we have seen any record of you making a subsequent request of BPL. Is that right?

A. I certainly used some more 8Y, which I obtained from Newcastle, and I can't remember whether that's because I couldn't get any more -- BPL wouldn't give me any more. I can't say whether we went back or whether the blood transfusion went back to BPL and asked for more and was told they couldn't have any. It wouldn't have surprised me because the supply that I had been given actually was on the understanding I would use it for PUPs, previously untransfused patients, and actually I had breached that; I had used it for someone else who needed it for a different reason. So it's just possible

they may have had said, "Well, he didn't use the original product under the conditions in which we gave it." I'm sorry, I can't remember.

Q. All right. But you said yesterday that you used the auspices of PFC to get the product because you thought that as a lone physician from Scotland writing to BPL direct, the request would have been unlikely to have succeeded. Is that correct?

A. That's correct because there was quite a lot of difficulty in England in allocating stocks of 8Y. Without going into the details, which I'm not familiar with, each English region had an allocation of 8Y, depending on how much plasma it supplied to BPL. As Scotland didn't supply any plasma to BPL, it had, in a sense, no right of access to 8Y. So it was a concession that had to come out of somebody else's supply, one of the English health authority's allocation.

Q. Yes. I take it that you thought it was unlikely that you, as an individual practitioner writing to BPL, would have been successful on your request and that problem would have been the same for any other physician in Scotland writing?

A. I imagine so, yes.

Q. Just before we leave this, the 20 vials you used, as you

say, not in a previously untransfused person but the one who had an allergic reaction; can you remember when that was? When did you use up your 20 vials?

A. I think it was the autumn of 1986.

Q. Can you remember when it was that you tried to obtain further supplies from Newcastle?

A. Well, I think it was at that time. So it came out, in a sense, of the Newcastle allocation.

Q. Yes. On this question of the efficacy of 8Y and what was known about it at the time, I say that deliberately to distinguish it from what we now know about its efficacy; we now know it was very safe. But in June/July 1986, your appreciation as I understand it, is simply that there was less risk attached to it than there was to the existence of Scottish product. Is that correct?

A. Yes.

Q. At the time, had you any idea how much less risk it might have represented?

A. No, and that's a point I was on the point of making. Mr Di Rollo and I were having a discussion about this. Because trying to allocate risk in this situation is very difficult. There is an intriguing paper published in 1983 entitled, "If nothing goes wrong, is everything all right?" subheaded "Interpreting zero numerators".

And this offers guidance as to when it is reasonable to say that something is safe if nothing goes wrong when you are testing it, and in the context of -- we are talking here about 8Y, which -- you must remember we were looking at a surrogate marker for hepatitis. We couldn't measure the virus at this stage. It became much easier when we could measure Hepatitis C virus. We were using a surrogate marker; in other words, a touch of liver damage as assessed by the plasma level of the ALT, the enzyme that comes out of liver when it's damaged, and a very precise protocol for assessing it.

And we saw on the screen yesterday, some of the results of patients in which there were raised levels of ALT -- in a small child who didn't appear to have other reasons for having a raised liver function test.

So you needed to have studied about 30 patients before you get down to the 5 per cent risk level, which is the conventional risk level, and by June it seems that a handful of patients had been studied and the handful that were shown on the screen, about half of them were in fact previously transfused patients, some of whom had -- at least one had a raised level.

So the number of patients who had been assessed by June or even September 1986 was small, in a study that, when it was completed, was defined as inadequate

and hence a further study was undertaken. So in June 1986, if we had applied the rule of three that comes out of this paper on zero numbers, zero numerators, it might only have been a reduction from 90 or 100 per cent to perhaps 60 per cent.

Q. Would it be right to say that your individual request for 8Y was more in hope than in expectation, or is it partly in hope and partly in expectation?

A. I'm always hopeful. Dr Perry is a very influential man, a very persuasive individual, and he was obviously successful on this occasion.

Q. I'm much obliged to you. Thank you, professor.

THE CHAIRMAN: Ms Dunlop?

MS DUNLOP: Mr Johnston.

THE CHAIRMAN: I do apologise.

MR JOHNSTON: For once I do have one point I would like to raise.

THE CHAIRMAN: I have no excuse. I should not have passed you by.

Questions by MR JOHNSTON

MR JOHNSTON: Please don't apologise.

Professor Ludlam, it's just one point that arises out of something you discussed at the end of answering questions from Ms Dunlop. She put to you, if I may just remind you, that if it were thought a good idea for

somebody to make sure that all hospitals in Scotland had some assistance with the current thinking on how to deal with patients with haemophilia presenting for the first time, or patients not previously exposed to concentrates, whose job would that be, and you said you supposed it would be a matter of medical policy, and perhaps it would be for the chief medical officer.

What I was wondering really is, if we are talking about how to deal with a particularly tricky patient, as it were, is it right to think of that as a matter of medical policy or isn't it really something that the clinician is going to have to assess for himself?

A. I think it's a matter of public policy. Every now and then there are circulars issued by the health departments, for example in relation to infectious diseases, people returning from other parts of the world where there are infectious diseases that doctors might not think of when they are seeing a patient in this country.

If I remember rightly, the health departments have put out circulars to alert particularly general practitioners to this situation, and particularly to ask patients if they have been to particular parts of the world where there have been little outbreaks of these rather unpleasant conditions.

Q. So if you are thinking of guidance from the chief medical officer, for example, I take it you are not thinking that the chief medical officer will say, "In this instance, use cryoprecipitate; in this instance, use Factor VIII concentrate," or are you anticipating that that sort of level of detail would be prescribed from government?

A. It would be very helpful if the chief medical officers would give that advice.

Q. But if they were to give that advice, do you not think that they would in turn be taking it from those who would have the appropriate expertise, namely the clinicians?

A. It would give an opportunity for a very considered opinion to be developed, a more general -- you would have the benefit of more than just, for example, me as an individual, providing an opinion.

Q. Isn't it right that, in any event, there was more than that available; you looked at a document from mid December 1984, the document from the haemophilia centre directors, where they have spelled out a number of things and then they set out the options for treatment in a particular order of preference, and then they made recommendations. I take it that would be a document that would be helpful because it came from

those with the appropriate expertise. Do you agree with that?

A. Yes, we were doing the best we could. Can I remind you that there was a lot of -- there could have been more guidance perhaps earlier by the Committee On the Safety of Medicines about what therapeutic policy might be. It was an extremely difficult time for us as clinicians and it might have been useful to have people -- more than just us to look in the broader context. It was a bit left at our door, is how we felt. A very difficult time.

Q. Yes, of course, everyone appreciates that but ultimately, I suppose what I'm thinking of is that in much of your evidence today and yesterday, you have been talking about what happened where particularly difficult issues arose with new patients presenting, for example. Now, in that sort of situation, as I had understood your evidence so far, you have squarely said that that is a matter where, if it's me, I have to apply my own judgment as to what the appropriate treatment is. If it was somebody else, they would be in the same boat, wouldn't they? You have to assess the particular patient with the material you have?

A. You do, but to have some guidance, I think, and potentially to address some of the issues that we have

been thinking about between England and Scotland by the health ministers, the chief medical officers, I'm sorry, might have been helpful.

Q. The document I just referred to with the various options for treatment, you were asked about that this morning, whether you disseminated that further and then you said, "Well, actually this is what we were doing in my department anyway". I just wonder, that being the case, how much difference would it have made if somebody else had given you what they thought was best practice, given that you are yourself an expert in the area?

A. Well, as we have seen, things change fairly rapidly and it would have been, I think, helpful to have had some more input from the Department of Health.

Q. All right, thank you.

I have no more questions, sir.

THE CHAIRMAN: I think that we really must give the stenographer a short break.

MS DUNLOP: Absolutely.

THE CHAIRMAN: And I would also like your help with the rest of the day.

MS DUNLOP: Yes, I don't want to waste any time discussing it. I want to press on. Dr Colvin has sat all day waiting to give evidence. So if we can have perhaps five minutes and start at half past three.

THE CHAIRMAN: Have you any further questions for the professor.

MS DUNLOP: No, no. I think it's time Professor Ludlam had a rest.

THE CHAIRMAN: I'm not sure about that. These questions about the role of the CMO have really come out of the blue and you clearly have views about the balance that there might have been between general guidance and the role of the clinician. If you think about it and want to submit any later comment on that, I would be quite happy to hear it.

(3.27 pm)

(Short break)

(3.33 pm)

DR BRIAN COLVIN

Questions by MS DUNLOP

THE CHAIRMAN: Ms Dunlop?

MS DUNLOP: Thank you, sir.

Good afternoon, Professor Colvin.

A. Good afternoon.

Q. You haven't been here since March, so to remind everybody that your CV, which we do have, tells us that you were at The London Hospital for 40 years. I think, you were a consultant haematologist and the director of the haemophilia centre there between 1977 and 2007.

Initially it was just The London Hospital but, as you put it last time, there was a regimental merger and it became Bart's and the London, and that was from the early 1990s.

A. Yes.

Q. Good. Can we have your statement on the screen, please, your report, indeed. [PEN0171674]. Thank you.

Professor, because we are slightly short of time, I think we can take the first couple of pages as read. They are introductory. They outline the questions posed to you and your own introduction about knowledge of risks in general. So if we have a look at page 1 and then page 2 perhaps.

I don't think anything you say on page 2 is unfamiliar to us. There is perhaps only one point to pick up and it is in 2.1, where you say:

"It is well-known that there was insufficient Factor VIII concentrate derived from donors within the UK to meet national demand."

I have to point out that the situation in Scotland was better than the situation in England, and we have had a lot of information that illustrates that certainly in 1983, Scotland was close to self-sufficiency or at self-sufficiency, whatever quite that means.

A. I'm certainly well aware of that. We were well aware of

it at the time and we were slightly envious of our Scottish colleagues at the time, I think.

Q. Right. Can we look at the next page then, please.

You refer to a UKHCDO haemophilia working party report for 1986 to 1987. That document is [SNB0017706]. I don't, I think, want to go to it but you extract the relevant points from it. You say that the report acts as a snapshot of the position in September 1987. It makes clear that the incidence of symptomatic hepatitis related to blood products is falling. It mentions eight cases of non-A non-B Hepatitis related to Armour heat-treated Factor VIII. It concludes that pasteurisation of Factor VIII and IX, using current techniques, is unlikely to be completely effective in preventing transmission of infection, and it also mentions the cases of HIV infection, and I know that you want to correct the reference to "4.1" so that it in fact reads "3.1"?

A. Thank you.

Q. Yes. Because it's in paragraph 3.1 that you have mentioned the transmission of HIV by Armour heat-treated product.

The working party report also suggested that surveillance of hepatitis-related blood products should be enlarged to include all infections, including HIV, so

that information regarding the relative risk of infection related to different products can be collected. Your personal experience; you were obviously well aware of the risks from fairly early on, and you tell us that in 1986 you published "Heat-treated Factor VIII Concentrate in the United Kingdom: a Preliminary Study". That was a series of case reports undertaken with colleagues at the Middlesex Hospital and at BPL. If we have a look at that, that should be [PEN0171782].

There it is. What's the full title of the journal, please?

A. Clinical and Laboratory Haematology.

Q. Right, thank you. That's a fairly staple magazine for haematologists, is it?

A. A general haematology magazine, perhaps not in the first flight of magazines compared with the New England Journal of Medicine or the Lancet, but quite widely used by haematologists at the time.

Q. We can see your name obviously, also the name of Dr Smith and Mrs Winkelman, who I think we recognise from PFL and BPL. And we can see that it relates to three patients given intermediate purity NHS heat-treated Factor VIII:

"None had previously received more than six donor

units of blood products."

On the first page there is reference to papers at which we have already looked, namely the papers by Fletcher et al and Kernoff et al. And you go on to observe, by way of background, that hepatitis is asymptomatic in many cases but if patients are followed carefully, there is often evidence of chronic hepatic inflammation which can lead to permanent liver damage, and one of the references for that is the article that for shorthand we can call the "understated problem article" or the "Sheffield article" perhaps.

There is then a reference to AIDS. If we look on to the second page, we can see that in fact the product that was being used there is a product heated at 60 degrees for 72 hours. Is that right?

A. Yes, indeed.

Q. And you call that, I think, a prototype product, and in the rest of the paper you outline the characteristics of the patients.

Can we just perhaps move through it on to the next page, page 3. We can see who they were. Page 4, details of the batches and then details of the results, and then on page 5 we find the discussion. You are pointing to the fact that three patients had not previously been exposed to large-pool concentrates, and

then on to the next page, they had previously been transfused with less than six donor units.

They would normally have been expected to develop non-A non-B Hepatitis as a result of their treatment after first exposure to large-pool concentrates, and you refer to the Fletcher paper, in particular, and the Kernoff paper, and you say:

"The continuing normality of our patients' transaminase levels therefore implies that heat treatment of the concentrate may have been successful in neutralising non-A non-B Hepatitis virus, although this approach has been previously disappointing."

Then on to the next paragraph. We can see some references to heat treatment against HIV, and then on to the final page of text, you are obviously saying that this is work in progress, that there was ongoing research. So I think you referred to this just as an early piece of work on the likely success of heat-treated product.

A. I think even perhaps just to demonstrate that we were all looking at different concentrates to try to demonstrate whether or not it was possible to neutralise the non-A non-B Hepatitis virus. It was more to show that we were looking into the problem.

Q. Yes. To go back to the report, please, in the next

paragraph, 1987; you published a study which related to cryoprecipitate. The reference for that is [LIT0010640]. This time it is dealing with six patients, we will see. Again, patients who had never received large-pool concentrates. You say:

"No evidence of hepatitis or HIV infection was detected in a follow-up period of one year."

You say:

"Following the introduction of screening of blood donors for anti-HIV in the UK in October 1985, the use of cryoprecipitate in selected cases should be reconsidered."

And the narrative of background is perhaps unsurprisingly that the association of HIV with the use of NHS Factor VIII concentrate had provoked reluctance to use cryoprecipitate as well, and you are reporting a study which you had carried out between October 1982 and July 1984, looking at the risk of transfusion hepatitis in the group, and you had already looked to see evidence of HIV infection.

Then "Patients", "Methods" and "Results", the second page, please. You tell us under the heading "Discussion" that in your small study, admittedly small, but in your study you had found no evidence of infection with hepatitis or HIV viruses after careful follow-up of

each patient for one year, and you refer back to the Kernoff paper. We have looked at that already this week and I think we can perhaps recollect the table in that, which occupies almost the whole page, and there is a chunk of patients, perhaps two thirds of the way down, who had been given cryoprecipitate and none of them had developed hepatitis.

So these findings in the Kernoff paper were consistent with your experience, as reported here? Yes.

Then can we just go on to page 3, please? Essentially you are saying not to write off cryoprecipitate, to reconsider its possible usefulness, as you say, in selected cases.

So the point you are making is that even with the screening that has been introduced in October 1985, some of the perceived danger of cryoprecipitate has been alleviated and it's available as a product and should be considered for some patients?

A. I think that's true but I think, as time moved on, since the study was for patients looked at in 1982/1984 and since it was published in 1987, by that time really the world had moved on, and I think by that time we had really given up using cryoprecipitate. So in those days particularly, it took a long while to get things published, and I think by the time we published it,

probably the world had moved on.

Q. So it might have been more useful if it had been published in 1985?

A. It's a question whether it was useful ever in a way, but I think that it seemed a good idea at the time, but then many things do. And I think it was worth publishing the data. But the difficulty with cryoprecipitate was that since it wasn't going to be heat-treated or otherwise virally inactivated, then, if you did get a single donor unit which was infected with Hepatitis C, or even conceivably HIV in the infective window before seroconversion, then, of course, you would be very reliably infected with Hepatitis C or HIV.

So I think, once it became really apparent that viral activation was going to be effective, then cryoprecipitate became much less attractive. Again, the reason that I presented this paper to you was to show you the uncertainty of this period and the fact that we were looking at various options in a scientific, or quasi scientific way.

Q. Certainly, Dr Colvin, don't be too modest about it because the factual position in Scotland in the 1985/1987 gap was that the heat treatment protocol that was being applied to Factor VIII was not as severe as what was being applied to the NHS product in England.

So cryoprecipitate certainly has been mentioned to us as something that was on people's menu of products at that time.

A. I think it's worth pointing out that the 8CRV product, which you referred to in the previous paper, which was less severely heated, may not have transmitted non-A non-B Hepatitis because of the donor pool and the heat treatment, and so I appreciate that it looks as though that level of heat treatment wasn't fully effective in neutralising the virus.

I think one would have expected a product like 8CRV to transmit Hepatitis C in retrospect, and that's what we thought, unless it had been heat-treated. When it was heat-treated, it seemed that that did reduce the infectivity, but one has to remember that the donor pool, which contributes to the concentrate, probably makes a difference in terms of the weight of virus that has to be neutralised.

So I make no specific claims about the 8CRV material. It may well have been that had you studied enough patients with a particular donor pool that would be treated in that particular way, then infectivity might have been demonstrable.

Q. It's actually quite difficult, Dr Colvin, to arrive at what appears to be an accurate sense of what might have

been the prevalence of HCV in the donor pool in the mid-1980s. Extremely difficult, in fact. We have various different figures. I think the last time you were here, there was some discussion about whether the prevalence might have been about 0.1 per cent. You said you used to use 0.3 per cent when you were reckoning such matters in England. According to Professor Howard Thomas' map as at 1999, the prevalence in the United Kingdom is shown as under 1 per cent. Phil Minor in a paper in the Lancet in 1990 has 0.4 per cent.

So quite a lot of different numbers, and we do know that in -- I think it's the six-month period immediately after screening was introduced in Scotland in 1991, the prevalence in the Scottish donor population was 0.088 per cent. So plainly it depends on the particular population group you are looking at.

A. And of course, donors are likely to be less infected than people who don't present themselves as donors.

Q. But certainly, when one tries to arrive at a rough estimate of the infectivity risk of cryoprecipitate, that question presents itself, well, what was the rate, the background rate of infection in the population, and it's rather difficult to answer.

A. Yes, indeed.

THE CHAIRMAN: Of course, there is another problem, isn't there, that the rate in the general population cannot be attributed to any particular subgroup of the general population? It is an overall percentage, which may have a very wide range of variation within the totality.

A. And of course, globally the variation is huge, so that the prevalence in Egypt, for instance, is very high indeed. 20 or 30 per cent, so we are told.

THE CHAIRMAN: I'm just thinking for a moment of the background to your own papers, that the fact that there may be a 1 per cent or a 3 per cent risk overall doesn't mean that in respect of any particular batch, the donors contributing reflect that overall percentage.

A. No.

MS DUNLOP: Next, Dr Colvin, in your report, which we should look at again, please, if we could go back to 1676, 5.4, you are telling us that you contributed the largest number of patients to the UKHCDO study, which concerned possible virus transmission in previously untreated patients and related to 8Y and 9A.

Can we have a look first, at the interim report on that study, which is [SNF0011123]. We need to go into the next page, please.

We looked at this yesterday and Professor Ludlam pointed out that there are some flaws in it, I suppose.

I think we know it was difficult to find patients, suitable patients, on whom to try new products and that must have been one difficulty and perhaps a temptation to relax the criteria here and there to get enough people. But this talks about circulation of a protocol in relation to the 8Y and 9A research in spring 1985.

Patient selection. The analysis which is collated in this paper is restricted to patients who had had no large-pool concentrate before 8Y and 9A but possibly had had variable amounts of cryoprecipitate.

Then frequency of testing, and I suppose one can set a desire for how frequently measurements might be made, but you are obviously dependent on compliance by patients turning up to have certain biochemical measurements taken?

A. Indeed.

Q. Yes. Then the products tested. We can see a desire, reflected here, to expose patients to many batches. I suppose so that an over-optimistic verdict on the safety of the products is not arrived at. Both concentrates were heated in the freeze-dried state at 80 degrees for 72 hours.

Then the results. Doing the best the researchers could to measure whether any NANBH had occurred, we see that none of the patients in the group had any ALT or

AST above two and a half times the upper limit of normal.

Then on to the next page in relation to HIV.

A larger number of patients is discussed, and here it's rather easier perhaps to be definitive about whether or not transmission of HIV had occurred. They say:

"No case of HIV seroconversion has been reported in over 100 patients."

Then "what next?":

"It's acknowledged that the present data are inconclusive ... data are currently being more rigorously assessed by a statistician."

Then there is the reference to the rule of three, to which Professor Ludlam alluded.

So I suppose in very simple terms, this is cautioning against extrapolating from small measurements, I suppose, in trying to allow for the picture that might be presented if a larger number of subjects had been studied, and that's why the infectivity rate is shown as possibly being zero to 14 per cent.

I suppose this is taking account of the fact that if you look at 25 patients, you might get one result, but if you looked at 75, the infected patients might all be

between 26 and 75, as it were; is it something like that?

A. Yes, I think that the difficulty really is that the numbers are very small, the patients are not truly untreated; they have had previous treatments, albeit in small-pool concentrates, and the distance between the sampling is not entirely satisfactory.

Just to give an example, had one of these patients been infected with Hepatitis C, cleared the infection and therefore developed evidence of normal liver function tests, then they wouldn't have shown up as being infected because they had already been infected, and there could be susceptibility to infection which was being masked by the fact that the patient had already been infected and recovered from the infection.

So the smaller the number of people you are looking at, the greater the level of uncertainty, and the rule of three is quite carefully discussed in the paper that I referred to later in the account by Mannucci and Colombo, which you may want to discuss. But the point is that it's very unwise to make claims for a product when there is still a level of uncertainty.

Q. Yes. And this is addressed, really, in the last paragraph. I think this is actually pulled together by Dr Smith. It looks as though he has prepared this

summary. He says that:

"The proposal is to follow this pilot study with a more formal prospective clinical trial with a stricter protocol."

So that's really addressing the very points you are making, Dr Colvin.

A. Clearly there was, at this time, a great urgency to know what the best concentrate to use was. So it seemed to those of us who were investigating at the time that the use of patients who were not truly untreated was a risk worth taking to get the data that one needed to be reasonably confident that a particular product was safe.

Q. Yes. And we have seen a number of references to "relative safety" as well, or "relative infectivity", and I suppose that concept must have been crucial, that one might not have achieved perfection but, so long as a new product was better than the current product, it might well be worth changing to the new product?

A. It was indeed important to try to get this data because there had been a number of disappointments at various points. There was the disappointment over the product -- the Hyland product, which was referred to in the Colombo paper, which I'm sure you have seen. There was the disappointment over Alpha Profilate, which was a heat and heptane product, where, despite the lack of

HIV conversions, there were some non-A non-B Hepatitis cases.

So there was a number of cases where the use of heat treatment to inactivate Hepatitis C or non-A non-B, as it was then, had been disappointing. So there was a great deal of interest in trying to be as confident as one could and not making unjustified claims for any particular product.

Q. Yes. You go on to point out in your report, if we can just go back to that then, please -- and we are at paragraph 5.4 -- that the fuller study was published in the Lancet on October 8th 1988, and you give us the title of that paper.

Perhaps I'll just give the court book reference for it rather than going to it. It's [LIT0010330].

You have, I think, neatly abstracted for us, Dr Colvin, the key features, and we can see that on the screen now. 32 patients treated with a total of 30 batches of Factor VIII, ten batches of Factor IX, and insofar as the Factor VIII product was concerned, it was 8Y and the paper found no evidence of hepatitis transmission and suggested that the viral inactivation process had reduced the risk from about 90 per cent to a statistically determined rate of 0 to 9 per cent, and I think from memory there is some further discussion of

the statistical angle in that paper.

Rule of three or similar.

You go on to tell us that you are quoting these publications to illustrate that in the period 1985 to 1988, active investigation into safety was going on. There were still cases of non-A non-B Hepatitis and HIV even due to heat-treated Factor VIII concentrates, and no claims had been made that any concentrate was free of the risk of virus infection. So that's the landscape.

A. Yes, indeed.

Q. And you share with us your memory of telephoning from Milan back to your own unit in 1986 because you were very concerned when you heard about the transmissions of HIV by the Armour heat-treated product.

A. Really, I think just to illustrate what a sort of fevered time it was, where rumours would spread, if you like, at conferences and one had the responsibility of deciding what to do about such rumours. And being a long way from home without mobile phones in those days, I remember it was a particularly shocking thing to learn and difficult to know what to do other than to phone home and say, "Don't use this product".

Q. Yes. Section 6 is dealing with that very paper that you mentioned. I think it's the Mannucci and Colombo paper?

A. Yes.

Q. In 1988, and even then some reticence demonstrated by the authors, who say that the most they are willing to conclude is that the products described are only presumed innocent.

A. It's interesting to note that in the table 3 from that paper, Mannucci --

Q. Let's get it up, so that we can see what you are talking about. I think we should. [LIT0010456].

A. So this paper was published one week before the 8Y study, and in this table you can see that Professor Mannucci refers to patients studied, 16 under the NHS. So that's the less than 20 patients. So 16 patients were studied by dry heat, whereas in the publication which appeared the following week, there were 32 patients studied, although some of those had Hepatitis B.

So again, there was the problem of information dripping out, if you like, and it was -- the numbers were constantly increasing. So the perceived risk was gradually falling. So whereas in the interim study report I think they quoted 0 to 14 per cent, by the time we had got to the final study report, we were down to 0 to 9 per cent, whereas in the publication from Mannucci a week before, in the Lancet, the risk was regarded for that particular product as 0 to 19 per cent. So it was

really very difficult to know what the true risk was, even as late as 1988.

Q. Yes. Of course, our primary focus is on the period between the end of 1984 and 1987, when Scotland achieved its own product heated at 80 degrees for 72 hours. The achievement having been before, but in terms of the issue to clinicians, that was achieved in the spring of 1987. And that interval obviously creates some treatment dilemmas for clinicians dealing with patients with haemophilia in that interval.

Can we go back to the report, please, and look at the final page. So [PEN0171674] at 1678.

We asked you to put yourself in the position of a haemophilia clinician in Scotland in that interval. You mentioned DDAVP and I think we all understand the logic of that. Becoming more difficult, however, are the questions you answer in the ensuing paragraphs. You say:

"Where necessary, I would have used the concentrate that I believed, on the evidence available to me, was least likely to transmit NANBH or HIV."

"Where necessary"; does that mean that you would have been trying to avoid the use of concentrate if you could?

A. I think that where there is elective procedures that

could wait for a year or two, you might want to avoid a procedure altogether. I think that where you had a patient who could have responded to desmopressin, then one would have used desmopressin, and then I think the reality was that in many cases you couldn't really postpone a procedure or it was necessary to get on with it fairly quickly, and desmopressin simply wouldn't be suitable. So that's what I mean by "where necessary", it's where necessary.

Q. Yes. Fine.

In the next paragraph you say you would have considered the possibility of using cryoprecipitate. We have looked several times, and we are not going to look again, at the UKHCDO reference centre directors' report from December 1984, and it does talk about using heat-treated NHS product or cryoprecipitate; easy to say, difficult to apply, one imagines, in the field --

A. Yes.

Q. -- but you are saying you would have considered cryoprecipitate for patients whose exposure to blood products was likely to be very limited. I wondered if you meant past exposure or were you including future exposure?

A. Very much future exposure. To take up the point that Lord Penrose just identified, that if we are talking

about the risk of donor infection, then the more units of cryoprecipitate you give, the greater the likelihood of one of those donors having Hepatitis C, and this is like, sort of playing Russian roulette, which I think we discussed the last time I attended the Inquiry, that once you have, I don't know, 100 exposures, you are getting pretty close to the point where one of them is probably going to have Hepatitis C in it.

So if you were just going to take a tooth out, where you knew you wouldn't need to use very much material or do some very minor procedure, then maybe cryoprecipitate might be an option, at least in the period 1984, rather than 1987. But one knew that if one was going to use a large amount of cryoprecipitate, then you were running a greater risk of transmitting hepatitis because if there was a unit of cryoprecipitate that you used that was infected, then you would transmit it.

Q. So just to take that on a little bit, if you had a patient who -- and I think for these purposes we have to assume a small child, who has plainly had no previous exposure because of their youth but whose Factor VIII deficiency is severe, then are you saying that one might reason that this child is going to have, in future, extensive exposure so there isn't really anything to be gained by trying to stick to cryoprecipitate?

A. Well, this is very tricky. My policy at The London, until 1984, was for children to use cryoprecipitate if I could. I think I may have said this at my last appearance. That wasn't necessarily a very widely-held view, but I am afraid to say that many of my severely affected children with haemophilia simply weren't manageable with cryoprecipitate, which is quite difficult to use in many ways, did receive factor concentrates and died of HIV infection.

So I make no claims at all to have protected my children against Hepatitis C or HIV, but there were one or two patients who were actually quite heavy users of concentrate, who we did manage to get through with cryoprecipitate and who didn't develop Hepatitis C infection. So I think it was a really difficult decision, and the reason I used cryoprecipitate in those children, as and when I could, was that I appreciated that certainly up to the period probably in 1984-ish, those bags of cryoprecipitate that we used were very, very unlikely to transmit AIDS.

Q. Yes.

A. So it was extremely difficult to know what to do. But I think that for very small usage in adults, where you were going to really have quite a small number of units and then not use any more, for instance for very mild

haemophilia, where you couldn't use DDAVP, it was an option. I think that for very small children, where tiny volumes of cryoprecipitate would achieve haemostasis, it was also an option but it was an option with diminishing benefits as the number of units went up.

Q. Yes. And I suppose the other consideration that struck me is that in this period, even with a child who has severe haemophilia, you could reason that a better product might be going to come along, so you are not talking about trying to assess how much cryoprecipitate this child will require for the next ten or 20 years. It might be for quite a short period?

A. That is exactly when my reasoning was in carrying on with cryoprecipitate until 8Y became available for the children.

Q. Finally, if we just move down the page, we did ask you whether you would have been concerned if you had been in Scotland and you had heard that there appeared to be a hepatitis-safe product available in another part of the UK that wasn't available for your patients. In your answer you have said that there was no evidence that any Factor VIII concentrate was hepatitis-safe and you have talked about evidence emerging in 1986.

I think I'm wanting to press you perhaps on the

concept of a concentrate that was hepatitis safer; so rather than absolutely safe, a concentrate that was safer than what had gone before, and I know today you have had a very lengthy opportunity to look at some documents that I gave you this morning that are the straws in the wind. Without going to them, because we have only got a couple of minutes, the documents that were emerging in England -- there is a CBLA set of minutes, there is the product sheet 8Y, we then have the --

We don't have a couple of minutes, we have slightly more than that.

THE CHAIRMAN: "A couple" is such an indefinite expression that I am not prepared to sign up to it.

MS DUNLOP: I want to go to this because we have an unredacted version of it, which I should have used yesterday, and that's something to celebrate. It's [PEN0161142]. This is the unredacted version of [DHF0017386]. As luck would have it, nobody from Scotland was actually at this meeting. This is 9 July 1985.

A. Good Scottish names, and Charles Rizza is very much a Scot but he wasn't working in Scotland.

Q. He doesn't count then. And Dr Fraser, we know, was in Bristol. Dr Forrester had sent his apologies as had

Dr McClelland. But this one has information on the third page, so 1144, about progress with 8Y. We have looked at this before but I think you maybe recognise this whole page, which is devoted to a new virus safer Factor VIII concentrate and is, albeit in relation to very small numbers of people, quite optimistic.

It's much the same information as is given in the product sheet, which we won't go to but is also from later in July 1985; [DHF0030476], just for reference.

Then the other two documents that we have looked at in this regard are [SNB0015469], which we will look at, if we could, please.

This is Dr Perry writing his report in January 1986 for a joint meeting in Scotland of blood transfusion directors and haemophilia directors. If we could go through it, I think it's page 3. No, it must be the next page:

"Directors will be aware ..."

The penultimate paragraph:

"... that the Blood Products Laboratory are currently issuing a Factor VIII product which has been heated at 80 degrees for 72 hours, and preliminary clinical data indicates that this material is non-infective with respect to HTLV-III, NANB and Hepatitis B."

This discussion is in the context of what are we planning for Scotland. We have that and then finally, and we won't go to this, but [SNB0075664] is a set of minutes of a joint meeting between the English fractionators and the Scottish fractionators in July 1986, at which similar sorts of statements are made. I just wondered, putting yourself in the position of a haemophilia clinician in Scotland at that time, what would your response have been to these indicators?

A. As you know, question 2 I found rather reminiscent of the question, "When did you stop beating your wife?" It kind of assumes an answer. That's why I found it very difficult to answer because I didn't feel that it was fair --

Q. I'm very happy for you to define and answer your own question?

A. I did indeed answer my own question, rather than the question that had been put to me.

Q. It often happens.

A. I think I really would like to refer to Professor Mannucci's paper, dated October 1st 1988. If I can quote it, he says:

"To date, published clinical studies indicate that viral inactivation by pasteurisation and, to a lesser extent, by vapour heating definitely improve the safety

from hepatitis of Factor VIII concentrates over that of unheated concentrates and concentrates heated in the lyophilised state at temperatures lower than 80 degrees Celsius. Other methods, such as (inaudible) superheating at 80 degrees Celsius and monoclonal antibody techniques might prove to be of equivalent safety but the small number studied and the lack of details allow us at the moment only to say 'presumed innocent'."

So the answer to your question is that we were in the position where we could only do what seemed a good idea at the time. This sort of decision-making was based partly on science and partly on intuition and I think the answer is that at an objective level you couldn't say that one product was better than another, despite this encouraging information. Then I think you really are down to making your own judgment about what is most likely to be true.

This is a slightly different issue to be faced with: When we were faced with the problem of do you give unheated NHS concentrate or heated commercial concentrate in trying to prevent HIV infection, then the science left you nowhere and the intuition also left you nowhere because if you chose the unheated NHS concentrate, you were going to transmit HIV, and if you

used the heated commercial concentrate, you were probably going to transmit HIV.

Extrapolating that to the Hepatitis C issue, I still feel that any decision made to use 8Y or the Scottish equivalent at that point was based on a kind of informed intuition. I certainly would have liked to have said at the time that I was convinced that one product was better than another. I think we were all extremely relieved when it became apparent that 8Y and the Factor IX equivalent in due course actually were safe. It was a piece of -- I was going to say good luck; it wasn't good luck exactly but I think we were all extremely relieved that in retrospect this was the case. But I think there is huge danger of using the retrospectoscope to say that one should have taken the particular view because it later turned out that that was the answer.

Q. Yes.

A. So what would I have done? I don't know. It's worth remembering that it wasn't Scotland that was relying on commercial concentrate, as you pointed out at the beginning of this discussion. Scotland was largely self-sufficient and, although commercial concentrate was being used, it wasn't being used in great quantity. In England we could only get hold of enough 8Y to look

after a pretty small proportion of the patients, so that in a sense, even with the circumstances that we found ourselves in, you could argue that the Scots were still in a slightly better position than the English were, particularly, I agree, after they introduced the Scottish equivalent of 8Y, but even before that the overall picture was relatively favourable.

Q. Right. Let's do it the other way round. When you were in the Royal London, if you had heard at that time that there was a more severely heated product available in Scotland, in relation to which early, if limited, results were optimistic, would you have taken any action in response to that news or would you just have waited to see what was going to happen in England and what further information might emerge?

A. Frankly, I think the latter.

Q. Right. Thank you very much Professor Colvin.

THE CHAIRMAN: Yes. Mr Di Rollo, do you have any questions?

MR DI ROLLO: I would like to ask some questions.

THE CHAIRMAN: I can't possibly wait, I have another commitment and I think that I have stretched my capacity for waiting to the limit.

MS DUNLOP: My feeling at the moment is that we should stick to our timetable because next week we are not sitting and the week after witnesses are all programmed to come.

I think we will need to go away as a team and work out what the best means is of affording an opportunity for others to pose questions to Dr Colvin.

THE CHAIRMAN: I'm terribly sorry, Dr Colvin.

A. Certainly from a personal point of view, I obviously would be happy to answer written questions or if you want me to come to Scotland again, it's not impossible for me to do so.

THE CHAIRMAN: I would imagine it's a great privilege to come north of the border. We will adjourn at that.

(4.23 pm)

(The Inquiry adjourned until Wednesday 26 October 2011 at 9.30 am)

I N D E X