Thursday, 13 October 2011

(9.30 am)

THE CHAIRMAN: Good morning. Ms Dunlop, gentlemen, thank you very much for the help you gave me yesterday in considering the steps that might be taken from now on.

As I said yesterday, really very little is carved in letters of stone in an Inquiry like this but I think that it would be helpful to everybody if I were to set out now what I see as the way forward and what I would envisage being the framework, subject to any applications that are made hereafter.

In saying "subject to applications", I should make it clear that I think from now on, informality is simply not acceptable. I have tried to make the point before. But if anyone wants to deviate from the anticipated course of events, I think it would be necessary now to have a formal written application, supported, as is appropriate, intimated to everyone else, so that everyone can see and consider just exactly what the implications might be of change. But for the time being, what I envisage happening is this.

Each participant will produce, by the end of January 2012, a statement of the issues thought to arise on the evidence and to require a decision by me in writing the final report. I don't want a story of

absolutely everything; it's to focus on the issues that it's thought I will have to decide.

I would like those issues to be arranged by reference to the topics that have been used in marshalling the oral evidence led in the Inquiry, both to date and between now and the closing stages of the oral evidence.

I wish to emphasise that each issue should be supported, as it were, by a general reference to the evidence that's considered to be relevant to the resolution of the issue.

What I have in mind is, for example, that one would say, "Dr Cash, Day 48, between pages 1 and 20". I don't want a detailed analysis, but, because I have done a certain amount of analysis of the evidence myself, if I have a reference to the broad areas, then it will enable me to find out pretty quickly whether we are talking about the same body of evidence or something different. So I would like that to be part of the application.

I will make it clear that it will be acceptable for the statement to be produced in parts by the individual counsel who have taken the lead in the examination of specific issues. I think that applies primarily to Inquiry counsel and to Mr Di Rollo, but I'm not going to

require things to be cobbled together; indeed, I would prefer to have the identification of the person who is making the contribution quite clear because it will help me in responding to it.

The evidence for the purpose -- and this is a point, I think, raised by Mr Di Rollo yesterday -- may include statements of witnesses obtained by the Inquiry team, whether or not the particular witness has been called to give oral evidence. I think everyone knows that relates to the very large volume of material which will instruct the general impressions, for example of the adverse consequences for patients of suffering from one or other of the conditions that are the subject of investigation.

But I should make it clear, as certainly counsel will appreciate but others may not, that evidence that has not been open to be tested may be inherently less satisfactory than evidence that has been led orally and where the witness has been available to be examined by others. Also, it will be understood that what I have in mind are the signed statements of witnesses, because the signed statements again are likely to be inherently more acceptable than drafts or documents that have not been signed by the party.

Also, I will not entertain submissions or arguments that relate to issues that could have been explored with

witnesses who were called and which were not, for whatever reason.

As parties will appreciate, I have heard of or I have seen, comments in other quarters directed against particular people who have been led as witnesses here. I simply will not accept, as part of this process, an attempt to introduce allegations that have not been properly explored before the Inquiry, and I'm likely to be extremely critical of anyone who tries to introduce such a matter.

Thirdly, I will not entertain fresh evidence at this stage at all.

Because of that last stricture in particular, I'll turn to my next chapter. It will be open to any participant -- and for this purpose I include Inquiry counsel -- to launch a statement of representations that any particular issue identified in the statements that have been lodged should not be the subject of further discussion or examination. I really want people to ensure that at the end of the process we know what ought to go forward for detailed discussion and what should not, and there may well, for all I know, be issues that any participant at all seeks to introduce at this stage that, taking a broad view, really should not be taking up the Inquiry's time, and I would like these matters to

be cleared out before one goes any further.

Each representation of that kind will have to be accompanied by an application for a hearing and an estimate of the time required for disposal of the matter, and that application must be intimated to all other parties so that they have an opportunity to take part in any debate that arises out of the point.

I have no idea what might arise but it's clear that there could be issues introduced, or perhaps even the way they are expressed, that provokes an adverse reaction from other participants and there could be a benefit and a bit of discussion before finalising the point to take it forward.

The period for any such representations will expire on 11 February 2012. That, of course, is on the assumption that the 31 January date is adhered to strictly.

Having regard to the general restriction on the introduction of new evidence at this stage, I intend to invite parties now to consider whether they wish to make any applications for the introduction of new evidence in the Inquiry.

Any such application must be made within four weeks of today's date in relation to business that has already been dealt with. I can't put an application limit on

evidence that we have yet to hear altogether. That would not be appropriate, but if it relates to material that has already been led, I wish the application within four weeks. And that, Mr Di Rollo, you can take it, relates in particular to Tamburrini because that's the only case I know where this may arise, but if there are others, the same stricture will apply.

The application must identify the issue that arises and the existing evidence on the matter with the same degree of particularity as I have already mentioned, and it should indicate why it is thought that the evidence that has been heard to date is not sufficient to dispose of the point.

As I say, I have in mind the particular case of Tamburrini and yesterday I made some comments about the broader issues involved in introducing evidence of that kind. That's all I propose to say on it. It's entirely a matter for the participants to decide whether they should make such an application or not. I would only hope that if any such application is made, Mrs Tamburrini and the others involved are fully and properly advised of the potential for adverse implications that can arise from their being led in evidence on a matter of this kind. That's just a reflection of past experience. People can be very

badly hurt by what happens at a hearing of this kind and the risk should be fully understood before any such application is made.

Going on to the next stage, before 31 March 2012 each participant will produce a statement of answers to the questions that have been posed in the statements of issues, revised by any representations, et cetera, that have been made and disposed of in the interval.

The particular statements must provide the participants' answers to their own questions. It's not just an attack on other people's work. I want to know what those who have posed a question propose the answer to that question ought to be.

Apart from that, I'm not requiring any other participant to answer all of the questions that others raise. It will be open to each individual participant to deal with such issues as they think require to be dealt with by me in arriving at final views.

I think that's as far as I need to go on that. I'm not trying to put handcuffs on people at this stage. I don't want work to be done that's not necessary and I hope that that is sufficient basis for parties to exercise a degree of common sense in how they approach this issue.

In the light of the written statements, the

representations and all the other procedure that may well have taken place by this stage, I think it remains an open question whether there will be any need for a further hearing for oral submissions or not. I don't want to foreclose that and I don't want to attempt to determine in advance what the scope of any such oral hearing should be. But I think that what I ought to do is to give an indication of the mechanism that I think would be appropriate for dealing with such matters.

So it will be open to any participant within two weeks after 31 March 2012 to make a written application for an oral hearing for the purpose of making a closing statement on any issue arising on the evidence that has been specified in the statements of issues, et cetera, lodged prior to 31 March 2012.

I'm not going on entertain an application to deal with something totally new. It's to deal with matters that have been properly focused already. I would expect the statement to specify again, in general terms, the evidence relied upon in suggesting that an oral hearing is necessary and I would like a clear statement of the purpose that is thought to be promoted by hearing oral submissions at that stage.

I want to make it absolutely clear that at the moment at least, I have no intention of allowing new

evidence at this stage. Indeed, I would be inclined to resist it and the only reason I don't make an absolute prohibition is that I think in this, as in other matters, one must appreciate that things can happen that may lead to proposals for further procedure and it would be inappropriate to exclude the possibility. I can't, in other words, achieve a mathematical certainty in defining a role that would prevent anything else happening. The possibility of other factors just can't be excluded.

But apart from that, Ms Dunlop and gentlemen, that is an outline of where I think I have reached in the light of the debate yesterday.

Thank you very much. I think, Ms Dunlop can now proceed.

MS DUNLOP: Thank you, sir.

THE CHAIRMAN: It's Professor Lowe, is it?

MS DUNLOP: Yes.

PROFESSOR GORDON LOWE (continued)

Questions by MS DUNLOP

MS DUNLOP: We have Professor Lowe with us again this morning to give evidence to topic C3A. Since we are today moving from our introduction on hepatitis topic into this particular, slightly different topic, perhaps I can just read the terms in which the topic has been

expressed.

The use of blood product concentrates in Scotland in the period between the introduction of NHS heat-treated products in 1984 and the supply of NHS products sufficiently treated to inactivate Hepatitis C, which we know to have been in around the spring of 1987.

So it's really that little period that we are looking at now.

Professor Lowe, you have provided the Inquiry with a statement on this topic and we should have that on our screens. It's [PEN0171471]. You remind us of your own personal position between 1985 and 1987. You were at that point a consultant physician in the university medical unit at Glasgow Royal Infirmary, although you also continued to have academic responsibilities.

You tell us that you shared consultant responsibility for the care of haemophilia patients with Dr Forbes, but you go on to record that Dr Forbes, as haemophilia centre co-director, was in charge of the centre's administration and policy and attended the meetings of UK haemophilia reference centre directors and other haemophilia administrative bodies, until he moved to Dundee in 1987, at which point you succeeded him as haemophilia centre co-director.

You undertook that role jointly with

Dr George MacDonald initially and then from 1990 with Dr Isobel Walker.

You respond to our first question, which concerns the level of awareness among treating haemophilia physicians in this period, that the Scottish NHS product was less effectively treated against non-A non-B Hepatitis than what was available in England.

Your answer, Professor Lowe, is that you remember that from 1986 -- you are not sure when -- Dr Forbes told you that the current Factor VIII concentrate -- that was the Scottish Factor VIII concentrate -- might not be effective against non-A non-B Hepatitis. I think it's perhaps just the way it's worded, Professor Lowe, because you are presumably not suggesting to us that that's the first time you had realised there was a risk?

A. No, by no means. I think the preamble probably should have been that, as I recall, heat treatment was introduced at the end of 1984, really because of HIV.

Q. Yes.

A. Which is very susceptible to heat treatment, as I think the Inquiry knows, and that was the rationale for introducing heat treatment in Scotland. And I think at that time it was realised that while progressively increasing degrees of heat treatment might in the future protect against non-A non-B Hepatitis, there was no

assurance when heat-treated factors were introduced into Scotland, or indeed anywhere else, that that would solve the problem of non-A non-B Hepatitis.

I think what then happened during 1996 [sic - 1986] was that there was increasing evidence from studies of other products, which were heat-treated to a similar extent as the SNBTS product, that indeed cases of non-A non-B Hepatitis were still occurring. And it was the inference then during 1986, and I think the evidence was obviously discussed at the meetings that Dr Forbes and Dr MacDonald attended, meetings of the UKHCDO and the Scottish directors with transfusion colleagues, that certainly one could still not make any guarantees to patients that that degree of SNBTS heat treatment would be effective against non-A non-B Hepatitis.

Why I mention 1986 is that, obviously, it was quite customary for the unit as a whole to sit down regularly and discuss policies. I do recall that Dr Forbes told me at some time during 1986 that, because of the increasing evidence that the current SNBTS products could not be guaranteed to reduce the risk of non-A non-B Hepatitis, his policy, together with Dr MacDonald and Dr Davidson, was to continue the unit's policy that those patients most at risk, which is patients with no previous exposure to clotting factor concentrates, or

very minimal, should continue to be treated with alternative products, for example cryoprecipitate for patients with moderately severe Haemophilia A or von Willebrand's disease. And the rationale for that, as I have said in the statement, is the much smaller donor pool with cryoprecipitate, perhaps 20 donors, compared to the thousands for a factor concentrate.

Q. Professor Lowe, before we go too far into 1986, can we go back to December 1984, because I wanted to begin our examination of this period just by looking at what was said by the reference centre directors in December 1984, and that will enable us, I think, then to move forward further on to the period that you are telling us about.

The reference centre directors did meet in December 1984, I think on the 10th, and we know that Dr Forbes was at that meeting as a representative of Glasgow.

Could we look at document [SGF0012388], please?

This is a guidance document which emanated from that meeting, so this is from December 1984, and we can see that the first page is giving a little bit of background about the current difficulties, and if we scroll down, we can see there is mention of the availability of tests, diagnostic testing, general precautions. Then on to the second page. We can see a heading

"Concentrates", and there is a little resume of the current picture as far as heat treatment is concerned. And we see, in the fourth line of the section dealing with Factor VIII, the statement that it is unlikely that this process -- that's the dry heat treatment -- in fact, what's been referred to as "dry heat treatment at 68 degrees for 24 hours":

"It is unlikely that this process completely inactivates non-A non-B Hepatitis."

Then a little bit of discussion of wet heat. The following paragraph talks about Factor IX and the availability of some commercial products there, and then BPL Factor VIII and Edinburgh. Then, if we go down to the options, we can see that this document lists options in probable decreasing order of safety from AIDS for Haemophilia A:

"1. Heated UK concentrate. Note: still NANB hepatitis risk."

Then:

"Single donor cryo or fresh-frozen plasma.

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

Then:

"Unheated UK concentrate and unheated imported concentrate."

Then there is another note:

"Heated concentrates may still transmit hepatitis. Some of the distinctions, for example, between 3 and 4 are debatable and the long-term effects of using heated plasma proteins in this way are unknown. Even pasteurised albumin is not given as frequently to individuals as will be Factor VIII."

We understand what these concerns are directed at, that there was a worry in this period about neoantigens, for example. So we understand that. Then recommendations that concentrates still needed:

"Use DDAVP in mild Haemophilia A and von Willebrand's disease if possible."

Then on to the next page:

"For Haemophilia A needing blood products, virgin patients, those not previously exposed to concentrate and children, use cryo or heated NHS Factor VIII, if available."

Then:

"Severe and moderate haemophiliacs previously treated with Factor VIII, use heat-treated NHS Factor VIII if available or heat-treated US commercial."

Then similar sorts of recommendations for Haemophilia B, fresh-frozen plasma, and then for virgin patients:

"Fresh-frozen plasma or NHS Factor IX concentrate if essential. Severe and moderate Christmas Disease previously exposed, continue to use NHS Factor IX. In individual patients there may need to be a choice."

And so on. Just to let everyone have a look at that paragraph. (Pause)

Professor Lowe, I'm wondering if you remember Dr Forbes coming back from the meeting or receiving this guidance through the post and sharing its contents with you?

A. Oh, yes, I was -- Dr Forbes, certainly in December 1984, spoke to the whole unit about the introduction of heated SNBTS products and that was what was used. He certainly reviewed the different categories of patients, and as far as I can recall, the unit policy was very much in accordance with these recommendations.

Q. There does seem to be a clearly expressed understanding in this that there continued to be a risk of non-A non-B Hepatitis.

A. Yes.

Q. And I just wondered, particularly, I suppose, given your reference to 1986, what the position had been between December 1984 and 1986. What was the picture in Glasgow? What was the understanding as to what treatment should be given?

A. Well, very much in line with what you see there on the screen. The majority of our patients requiring factor concentrates were severe haemophiliacs. They had been treated for many years with Factor VIII concentrates. That was what they continued to have, and while patients could be told that the heat treatment was thought likely to reduce the risk of HIV, there was no evidence at the time that it would reduce the risk of non-A non-B Hepatitis. Hence, in patients who had not been previously exposed to concentrates, the desirability to try, as I have said, to limit the exposure to non-A non-B Hepatitis by considering the use of alternative products, cryoprecipitate or fresh-frozen plasma, according to individual circumstances.

Q. Yes. You see, if we look, for instance, at that passage at the top of the page under the numbered paragraph 3, it says:

"For virgin patients, those not previously exposed to concentrate and children, use cryo or heated NHS Factor VIII."

That's quite a choice: cryoprecipitate or heated NHS Factor VIII, because we saw from the previous page -- can we just flip back to that, please? -- the mention, under the heading "options", of the continuing risk of non-A non-B Hepatitis in association with heated UK

concentrate.

A. Hm-mm.

Q. And then the second suggested option, single donor cryo, doesn't bear a similar caveat. So I suppose I'm trying to tease out from you what in Glasgow was the preference as between those two: cryoprecipitate or NHS heated Factor VIII?

A. As I recall, the majority of our patients had the heated SNBTS Factor VIII concentrate. There were a small number of patients who had not previously received concentrate and for those, if one was particularly concerned about non-A non-B Hepatitis, then cryoprecipitate or FFP, for patients with Factor IX deficiency, might be preferable.

I recall that Dr Forbes's policy was very much to consider the individual patient. We didn't have many of these patients. An additional complication with von Willebrand's disease is that Factor VIII concentrate may not be effective in preventing bleeding in von Willebrand's disease, and for those patients, cryo was preferable because it contained high amounts of von Willebrand factor.

So I think Dr Forbes's policy was very much to say, "Let's look at these small number of patients on an individual basis, look at their previous history of

bleeding, distinguish between haemophilia and von Willebrand's disease, look at the haemostatic challenge that was forthcoming" -- because many of these moderately affected patients, you are talking about only the occasional tooth extraction every few years or occasional other type of surgery or a traumatic episode, and then to make a judgment on that.

I think the other factor, of course, with HIV was that HIV testing of blood donors came in during 1985, from memory.

Q. Yes.

A. And there may well have been some reluctance to use cryoprecipitates until the blood donors were all tested for HIV because of the potential risks of HIV.

But my recollection is during this whole period of the end of 1984/85, into 86, the directors had to continuously weigh up what was happening and many circumstances. HIV testing of donors and then to consider for the individual patient, in the individual circumstance, what was the safer product. And I recall that Dr Forbes was very active in speaking to these very small number of patients in whom the choice could be made. He had known them man and boy, you know, and was very well acquainted with the patients and their individual problems and would have careful discussion as

to what the choice would be.

Q. Right. Thank you, Professor Lowe.

You have covered a number of different important and interesting issues. During that period, small as it is, 84 to 87, we know that there were some significant changes and the introduction of screening of donated blood in October 1985 is clearly one of those. If the whole exercise is seen as a balancing one, then obviously the knowledge that all donations were being screened for the AIDS virus would alter the balance, and I think we can understand that. You know, it makes blood, and presumably cryoprecipitate, appear safer than it had previously.

I'm still interested in that sentence at the top of the next page about the choice between heated NHS product and cryoprecipitate. We appreciate from what you are telling us that numerically speaking, the vast majority of the patients in Glasgow Royal Infirmary would be on heated NHS Factor VIII, and I think we understand the reasons for that. So what sort of patient would be in the minority and would present the dilemma of choosing between heated NHS Factor VIII and cryo? Can you just explain that a little more for us? What sort of patient are you going to be scratching your head over?

A. The sort of patient I have in mind, and my mind going back 25 years, I have to say, finds it very difficult to think who were these people, how many were there.

Q. Yes, indeed.

A. And because of the very difficult choice -- I mean, I had become a consultant in October.

Q. October 1985, I think you have told us.

A. Thank you.

Having said that, Dr Forbes had years more experience in haemophilia and knew the patients much better than I had. And that kind of patient, I didn't personally struggle much with because that was very much a decision that Dr Forbes wanted to make. So my recollections were very few patients. I struggle to remember individual instances but in general, for patients with moderate severity Haemophilia A, who had never had concentrate before, they might have had just maybe two or three exposures to cryoprecipitate previously, for example every five years for a dental extraction.

My recollection is none of these patients has ever had symptomatic or asymptomatic hepatitis and therefore they could perhaps be assumed, given the diagnostics at the time, to have escaped hepatitis. Then you have the choice between a product which, while heat-treated, the

heat treatment is, you know, insufficient to prevent non-A non-B Hepatitis. We know from UK studies -- well, English studies in 1983 and 1985 -- the reference is, I'm sure, available to the Inquiry -- that prior to the introduction of heat treatment, it was virtually 100 per cent risk that you would get non-A non-B Hepatitis from the serial studies. That was very much in people's mind. So you then have the balance between a patient with moderate severity Haemophilia A, infrequently treated with cryoprecipitate, their previous exposures to cryoprecipitate have prevented the serious bleeding that can occur after a tooth extraction, surgery, whatever, the patients are familiar with the product and you then have to say to them, "Well, you know, there is a choice. You can have a product which, while heat-treated, the concentrate, it's coming from thousands of donors and there is no guarantee that you will not get an episode of non-A non-B Hepatitis, which you don't want." And particularly after the introduction of HIV testing of blood donors, cryoprecipitate, you know, while it could still have a small risk of HIV, had a very good safety compared to concentrate, a reduced risk of getting hepatitis.

So those, I think, would be the kinds of discussions

that would go on. Given that most of these patients you are talking about, elective procedure, the dentist contacts you and says, "I want to extract four wisdom teeth," that would allow plenty of time for consideration between the choice of the two products and obviously discussion with the patient.

If I could just turn from Haemophilia A to von Willebrand's disease, the extra factor I have alluded to already with von Willebrand's disease is that the concentrate might not be effective because it's not replacing the von Willebrand factor, and therefore an additional reason for preferring cryo in that kind of patient who comes up for a tooth extraction is that you are more assured of achieving haemostasis.

Q. You have been alluding to patients with moderate haemophilia. Would it be right to think of patients with mild haemophilia as being, as it were, an even stronger case of individuals who present this dilemma; so somebody with mild haemophilia but who perhaps is having a bleed or is destined for some kind of procedure for which they need some sort of cover.

The first thing that you have said -- and you have said this several times -- is what you would tell the patient. Are we to take it then that in Glasgow, in the Royal Infirmary, in this period, the patients were

involved in the decision-making?

A. Oh, yes.

Q. Right. So you would be frank with the patients about the nature of the risks, both the hepatitis risk and the HIV risk?

A. Yes, I think when I appeared here previously, one of the first questions I was asked was, "Since you joined the haemophilia unit in the 70s, was non-A non-B Hepatitis discussed with patients?" and the answer is yes, it was very much part of the unit's policy to recognise that there was a risk of hepatitis and to share that with the patients.

Q. And --

A. To go back to mild haemophilia, obviously the treatment of choice from about 1980 was desmopressin, and we were very rigorous in assessing all newly diagnosed patients with mild haemophilia; they all routinely had desmopressin infusions. The majority of those would have a predictable response from Factor VIII and you could therefore say to those patients, "You have got mild haemophilia. If have an injury or if you have to have surgery, this is the product we will use, and hopefully that will allow us not to ever use blood products on you." For patients with mild Haemophilia A and for patients with mild severity von Willebrand's

disease. And that, in conjunction with ancillary haemostatic measures, like tranexamic acid, would be the treatment of choice, and I really cannot remember in this period of time, which you are asking about, 1985 to 1987, any patients in the category of mild haemophilia and von Willebrand's disease who had to have a blood product, for example, due to failure of desmopressin and tranexamic acid. So that was very much the policy for that quite large group of patients with mild haemophilia.

Q. You will correct me if I am wrong about this but I think I can imagine that the easiest situation for you to be dealing with at that time would be the patient with mild haemophilia who is having a planned intervention of some sort.

A. Yes.

Q. Because everybody has time to organise the DDAVP or something like that.

Let's ratchet it up slightly and ask about the patient with mild haemophilia but who is having a bleed. What was the thinking in Glasgow about that sort of patient in this era?

A. Most of the time desmopressin was effective. It gives you a transient increase in Factor VIII and von Willebrand factor, which is usually enough to sort

out the problem. In addition, if you look at the biology of Factor VIII and von Willebrand factor, if you have an injury or trauma, that leads to what we call an acute phase response, where the level of certain proteins in the blood increases, including Factor VIII and von Willebrand factor.

In a sense, even if desmopressin's effect is limited to 48 hours, after 48 hours, we, sitting in this room with, say, 100 per cent Factor VIII and von Willebrand factor levels, would have gone up to 200 per cent, and a mild haemophiliac, say, going along about 10 or 20 per cent would have gone up to 30, 40, 50 per cent, which is approaching the levels required to achieve normal haemostasis. So the response to injury, response to surgery, in itself often made the mild haemophiliac almost into a normal range for haemostasis.

So what I'm saying is that, even after a bleed, the combination of desmopressin and the response to injury, which is present in haemophiliacs and vWD patients as well as the normal population, usually allowed one to not have to give blood products.

In the event that somebody had a major bleed or major surgery and this combined treatment would then result in the patient continuing to have major bleeding, a discussion would have to take place with the patient

about the risks of blood product treatment: "You are keen that we stop your bleeding. We are keen to help you, but you will have to recognise that if you are an infrequently treated patient, your first exposure to concentrate has a high risk of giving you non-A non-B Hepatitis, and even if we give you cryoprecipitate, you know, if we have to give you a large dose of cryoprecipitate for several days, that, again, is building up to a risk of non-A non-B Hepatitis, given the prevalence of the virus in the population that we now know."

Q. This is a hypothetical patient and we can create for ourselves certain difficulties with hypothetical patients, but sticking with the concept for the moment, this hypothetical patient is in a difficult situation because they are unwell and they are having explained to them two possible choices, neither of which is completely safe or even particularly attractive, that they could have cryoprecipitate, which might give them the AIDS virus, or they could have NHS heated Factor VIII, which is safer than unheated Factor VIII because of the treatment against the AIDS virus, but which carries still a risk of hepatitis.

As doctors, you must have been giving them some sort of steer. What sort of a steer would it have been?

A. Well, as I say, these patients were infrequent.
Q. Yes.
A. And I cannot remember, as an individual, having to make this decision, like, in the middle of the night. Dr Forbes knew the patients well, had very up-to-date information and I think in that situation he would be seeing the patient --
Q. I'm going to quibble with you, Professor Lowe, because this patient is a mild patient. So an infrequent visitor and not somebody particularly well-known to Dr Forbes. So let's just change that little bit of hypothesis. What sort of a steer do you think would be given to the patient? I appreciate it's very difficult to recall and you are trying to reconstruct something you can't remember ever actually personally having to deal with. With those caveats, do you think there was, in Glasgow Royal Infirmary, a sort of a preferred solution?
A. Well, if it was me in the middle of the night and Dr Forbes is in Hawaii or something, so it's up to me making a decision in such a patient, what I would do in that theoretical case is to say, "We have guidelines at a national level in the UK, we have a choice of products. At the end of the day, you and I, here and now, have to make a decision between cryoprecipitate or

a concentrate." I would go through the risks and hopefully, you know -- it depends on the exigencies of the situation -- and say, "Well, there is HIV and there is non-A non-B Hepatitis," and lay it out with them. My approach as a doctor, as I think I said the last time I sat in this chair, has always been to try and give them my summary, as a doctor, of the best evidence and to then work with them to make a decision. At the end of the day, if the patient says, "It's up to you, doc" --

Q. "What would you do, doctor?" That's what patients say. They say that to lawyers too, they say, "What would you do?"

A. You are absolutely right. And my position has always been, if we reverse positions and I'm the patient lying in that bed with the bleed, what would I choose, just based on my knowledge and if it were me. And you are now going to ask me what I would say --

Q. I think we are actually on the edge of our seats, Professor Lowe.

A. You think you are on the edge of your seat; I'm even more so.

It's interesting. I think -- and you are talking about what period of time?

Q. Let's make it slightly easier and let's take it

post-October 1985?

A. When people are HIV tested?

Q. Yes.

A. I would say to myself, right, I have a bleed which is not stopping. If I have cryoprecipitate for 20 donors who are HIV tested, I would take that.

Q. Right. Thank you.

It feels like a long time since we were looking at your statement, so let's look at it again.

THE CHAIRMAN: Let's not go there just too quickly.

I have to say, I have a certain concern about just how realistic this scenario is. The patient who comes in in dire need of treatment is not going to be the most rational person in some cases, and the notion of getting a lecture on the comparative advantages and disadvantages of forms of therapy perhaps might be rather lacking in reality in some cases.

I'm wondering whether in fact the only question that would be of interest to the patient was, "Doc, what do you want? What would you do for me?" And you see, that would be the positions that would put the doctor at maximum risk. He is then being asked to take the responsibility.

In those circumstances, would you not just accept the responsibility and say, "The best way of dealing

with your case today, now, is X"?

A. Yes.

THE CHAIRMAN: Did you really give a lecture? Think of the amount of time we have spent here trying to get to understand these factors and we may not have reached there yet, Professor Lowe. Did it really happen, you know, as a matter of fact -- let's get down to the realities. Did it really happen that there were these long lectures or was it much more stark?

A. Well, sir, I'm a lecturer and have been since 1978.

THE CHAIRMAN: That's no excuse.

A. I tend to lecture, and sitting here looking at me, you think, "This man is giving us a lecture," but I'm just trying to distil for the Inquiry what I would have done.

No, of course. If it's two in the morning and you are at the patient's bedside, you have to make a decision, you have someone with urgent bleeding and you need to order something in the next ten minutes, I would not sit and give them a two-hour lecture, no, sir. What I would do is try and encapsulate, in the patient's own language and understanding, that there is a choice, and I think it would be bad as a doctor if you didn't tell them there was a choice, and then to say, "There is this and there is that," wait for a bit and then, if they said, "Right, I don't care, you do what

you think best," and then just give them what you would give yourself.

MS DUNLOP: Yes. Thank you, Professor Lowe.

We should return to your statement, [PEN0171471].

As is apparent, we are on the second page. We have covered some of this already, Professor Lowe. The second question concerns just those very matters: treatment policy for patients with haemophilia in that period.

I think your explanation, certainly in paragraph 2.1, is really as you have said, save for the additional information which you have provided this morning about particular hypothetical scenarios.

Would I be right in thinking from the tone of your answer that in this conversation with the patient who is having a bleed and is needing treatment, your default setting is that you are trying to avoid the use of concentrate?

A. Well, I think we were aware in 1985 that unheated concentrate would give you non-A non-B Hepatitis. So all the evidence was, from all round the world, including the UK, that that was happening.

And to my knowledge there were no serial studies in any Scottish patients like were conducted in England, the other one, you could assume that that would apply to

the SNBTS concentrates.

I think also, remember in 1985 that the consensus was, until about that time, that "non-A non-B Hepatitis" was a relatively benign disease, given that after years of treatment, you know, you were not seeing patients with clinically severe liver disease. That perception started to change, I think about 1985, with reports from Dr Hay's group in Sheffield and others, if you were brave enough to do biopsies in numbers of haemophiliacs, you could see more severe changes in the liver histology, and therefore there was an increasing concern that you should do everything you could to prevent that first episode of non-A non-B Hepatitis.

So I think there was awareness that heat treatment was initially not effective, that non-A non-B Hepatitis was more or less inevitable if you got concentrate, and that there was increasing evidence that that could lead over the patient's lifetime to an increased risk of liver disease. So I think haemophilia treaters generally were, you know, very keen to avoid concentrates, to try and use desmopressin and other measure if possible, and then to seriously consider, in this small number of patients with moderate severity haemophilia and vWD, the use of cryoprecipitate. Does that answer your question?

Q. Yes, I think so, thank you.

2.2 goes on to address Factor IX.

THE CHAIRMAN: Before you go to it, one question, another question of fact: you became consultant in 1987 but no doubt you were very -- sorry, director.

A. Director at the end of --

THE CHAIRMAN: No doubt you were very much aware of what was going on before. Did you have any impression of the proportion of patients in each or any of the classes, severe, mild et cetera, who had NANB hepatitis at that stage in your group?

A. In the group of patients attending Glasgow Infirmary, there were certainly a high percentage of patients who had been treated with concentrates over the years, who had occasional or persistent elevation in liver enzymes, as was the case throughout the world.

THE CHAIRMAN: So you were doing the LFTs and all the rest of it, regularly and had that information available.

A. Those were done routinely from, I think, the late 70s, certainly the early 80s, and like every other centre in the world, we found that a high percentage of previously treated patients had intermittently or persistently elevated transaminases.

THE CHAIRMAN: Was it a relevant factor in deciding as between different courses of treatment that there was

information available about the individual patient relating to the probable NANB status?

A. I think the group of patients, the small number of patients, in whom the choices between cryoprecipitate or concentrate for the first time -- I don't think that really applied to that group of patients. As far as I recall, they would have normal liver function tests, and what you were trying essentially to do is to stop that situation going into one where they might well have chronic non-A non-B Hepatitis.

So the patients I'm talking about are the severely affected patients who had had treatment with concentrates in the past.

MS DUNLOP: What about the patient in the middle, the occasional user? You have spoken about people with moderate haemophilia and I suppose they might present too and need treatment. They are not virgin patients because they have had concentrate maybe once ten years ago or something like that. In the circumstances that the chairman is sketching, would you be looking to see what are this person's LFTs?

A. Okay. Again I'm struggling to find an individual patient but say you have two patients with moderately severe haemophilia A and they are coming up for surgery and desmopressin aint going to work and you are choosing

between cryoprecipitate or a first exposure to concentrate. I suppose you could say that if that patient, for whatever reason, had abnormal liver function tests at some time, then that might cause you to say, "Maybe we will just go for concentrate because, however you got it, it's quite likely that you have had non-A non-B Hepatitis before."

But remember that serum transanimases are a notoriously non-specific indicator of hepatitis. Working in Glasgow, alcohol was quite prevalent in our patients, as in the non-haemophiliac population, obesity was becoming a factor and you cannot really assume in the 1980s, before, you know, Hep C testing, what somebody's abnormal liver function tests are due to.

For example, as well as doing haemophilia clinics, I did general medical clinics in the east end of Glasgow and, you know, routine blood tests included abnormal liver function, and every afternoon I would see half a dozen new patients and write to the GP saying, "By the way, the serum transaminases are up; check the drinking."

Q. I think the chairman was perhaps thinking of that sort of patient who is not a virgin, you know, a previously untreated patient, but somebody who has maybe had concentrate ten years ago on one occasion or something,

and I think perhaps in that circumstance it might be that you would want to know how are this patient's LFTs looking?

A. Yes, it's a reasonable question and, yes, if somebody had definitely had abnormal liver function tests and he didn't think it was due to alcohol, a reasonable inference would be that that patient had already been exposed to non-A non-B Hepatitis, whereas the patients with perhaps persistently normal liver function tests might make you say, "That might swing you towards cryoprecipitate because they haven't yet got hepatitis."

So, yes, it would be a factor, and I think, as the guidelines say -- the document you put up at the end of 1984 saying individual patients -- no guideline can ever be for the blind obedience of fools; they are there for the guidance of wise doctors. And within a guideline, yes, of course, you have to consider the individual patient and make an individual assessment.

Q. Yes.

THE CHAIRMAN: Yes. I still have some difficulty seeing how the doctor resolves the problem. It is the occasionally treated person who will, on that hypothesis, have been exposed to risk in the past, but if the position were to be that at the time you only had variable transaminase records -- and they almost certainly would be

variable -- and these were not diagnostic of hepatitis, another possibility might, in the case in question, be obesity when you saw the person. Another one, if they were from the east end of Glasgow and in the cohort you have described, could be alcohol.

You have got one out of three possible causes of the raised transaminase that might indicate prior exposure and therefore infection. How you are going to decide which risk to take becomes a factor. We are not dealing now with Koch's Postulates and mathematical certainty or anything else; we are dealing with balance of probabilities. So how do you deal with it?

A. It's very difficult in an evidence-free zone, in the days before Hepatitis C testing was available. You know, you look at the clinical -- you look at the patient's history. Within moderately severe haemophilia, there are people who bleed more than others. It's a big spectrum. You would start with that. You would then look at the haemostatic challenge that the patient was about to face, like the severity of the surgery. You would enquire about previous bleeding, after dental extractions or whatever. You would enquire about the family history, siblings with similar deficiencies, what has their experience been, because it's not just the level of Factor VIII and Factor IX;

there is individual variability in bleeding.

So, on the one hand, the doctor has to weigh up the likelihood that that patient will suffer, you know, serious bleeding; on the other hand, you have to do your best, with limited evidence, to assess have they had previous exposure to hepatitis.

I suppose, if you think about this more and more, if that person is an alcoholic, they are going to be at greater risk of progression of liver disease if they get hepatitis. So there are factors in the individual that will determine not just their risk of being exposed to the virus but what long-term consequences are there going to be.

So what you are trying to do, as in any other branch of medicine where you are considering a choice of treatments, is weigh up the two factors.

That's a very long-winded answer. But, yes, it's multi-factorial. At the end of the day I think you are down to a gut feeling. You have the patient saying, "You are the doctor, what would you do?" And you have to do your best to assimilate the individual person's risk of bleeding, risk of hepatitis or HIV and then give them your best, honest answer as a doctor, and that usually is what would you want yourself.

Q. Yes. Can we just look at 2.2? As you say, this has

been mentioned before but from April 1985, as far as Factor IX was concerned, there was a decision to use commercial heat-treated product until SNBTS product became available, as it was destined to do in the autumn.

Question 3 was on a slightly different matter, whether any of the hepatitis-safe products supplied in England were made available to Scotland before May 1987, and you told us that you looked at your statistics and appendix 1 and also the use of commercial Factor IX in the table and then FEIBA. But you say you can't see in the table any other use of other Factor VIII products and you can't recall any being used. So in Glasgow, in the Royal Infirmary, you didn't use any product from England?

A. Well, I cannot remember any being used. I think, at the Inquiry's request, I was asked some months ago to clarify, after Dr Forbes's evidence, the types of product that were used during this time period. So I can think of no better place than to go back to the Inquiry's preliminary report, go through the table and, to try and help you, work out, supplementing my memory, as to what kind of products might have been used. I cannot see in that table, as I have said in my statement, any use of the English product 8Y and I

cannot recall any being used. It's maybe that colleagues in England -- well, as far as I recall, England was not self-sufficient in their heat-treated products and something like only one third of patients in England were able to have that and the rest were still using commercial Factor VIII and, as you know, Scotland was ahead of the game compared to other UK countries in terms of self-sufficiency, and indeed with heat treatment of the Scottish product, due to the efforts of colleagues in SNBTS.

While, I suppose, it is possible that the English product, being heat-treated to a higher degree than the Scottish one, might have been an option for the occasional patient with moderate severity Haemophilia A being exposed for the first time to concentrate, I can't recall any being used. It doesn't appear in the Inquiry's table and it may well be that during that period of time, between the English product being thought on some preliminary evidence, as I recall, in 1986 to have a potentially lower risk of non-A non-B Hepatitis, that might have been an option for an individual patient being exposed for the first time.

It could well have been that during that period of time, 1986 to 1987, before the SNBTS fully heat-treated product appeared, we had no such patient having surgery.

Q. Right. Let's just learn a little more about the position in England. Can we look at [DHF0030476], please?

This is a BPL information sheet from July 1985 and it relates to a new Factor VIII concentrate known as 8Y, which is going to replace the intermediate specific activity products with instantly forgettable names:

"General issue will begin from September 1st 1985."

Can we go a little bit down? We can see that the heating protocol for this product is 80 degrees for 72 hours to reduce the risk of infection by viral agents. What's interesting is the statement that:

"Safety and efficacy trials of the 8Y concentrate are already proceeding at several haemophilia centres as of 1 July 1985. Eight patients receiving 14 infusions of three batches of concentrate have shown dose responses in the range 1.1 to 2.9 and a mean half clearance time of ten hours."

These are, I take it, acceptable, these statistics for the dose responses and the mean half clearance time. That sounds acceptable, does it?

A. In terms of getting the expected rise in Factor VIII?

Q. Yes.

A. Yes.

Q. Yes, okay. And then it goes on to say:

"Clinical trials at six haemophilia centres are in progress to gain evidence of reduction or elimination of viral transmission and several patients have safely passed the point at which first evidence of NANBH virus transmission would normally occur with unheated Factor VIII."

So that's one snapshot. There are others from England in 1985. That shows, I suppose, cautious optimism about the new English product. Do you remember hearing about this on the grapevine, people telling you at meetings or in the department?

A. No, as I think I have made clear, I did not start going to meetings of haemophilia directors until I became a haemophilia director at the end of 1987.

Q. Right.

A. So I didn't go to these meetings. Dr Forbes, Dr MacDonald, the co-directors in our centre did, and while they would usually update me and other members of the unit as to what was going on, in July 1985 I think I was still a junior doctor. I became a consultant in October that year and obviously, once I became Dr Forbes's consultant colleague, he would probably spend more time telling me about developments than when I was one of his junior doctors.

But I cannot remember seeing that document

in July 1985, although I was aware that all manufacturers of products with heat treatment or any other virus inactivation procedure would very much want to try and get that rare small number of patients who had previously been not exposed to do serial studies of non-A non-B Hepatitis.

Q. Yes. I mean, this is approaching the holy grail, isn't it? A product that's severely heat-treated, so will inactivate HIV and also, probably, the agent for non-A non-B Hepatitis, and it works.

A. I'm not sure that you could make that interpretation from the document that you are showing me because I think it was about this time that the International Society of Thrombosis and Haemostasis, under Professor Mannucci, was setting up strict guidelines as to how these studies should be --

Q. I take that absolutely, professor. I think I'm just meaning it was good news and would it not have been at least discussed or mentioned or referred to, Dr Forbes saying to you, "Of course, you know that in England they are moving forward with a severely heated product and, you know, we would hope that in Scotland we will arrive at the same result," or something like that? No?

A. I have no memory of that.

Q. Well, then, the next question is academic, because I was

going to suggest that it might have occurred to somebody in the Royal Infirmary to try to get some from England.

A. It might have. I was lower down the food chain. I did not interact regularly with haemophilia centre directors in England. I mean, the first question, where you are saying to me, during this period was there an awareness amongst treating haemophilia physicians, that the Scottish NHS product was in effect inferior to the English product, well, the only haemophilia treaters I spoke to across the country were Dr Forbes, my boss, and Dr MacDonald. I did not go to haemophilia meetings; I did not get the gossip, and I was not involved in the policy-making or the selection of blood products. So I'm not quite sure why I would have been involved in those discussions.

Q. Well, fine, but even then just in retrospect, if we look back on this situation and we imagine these hypothetical patients we have already discussed, the person with mild haemophilia who has a bleed and needs some treatment or the person with moderate haemophilia, likewise needing treatment, perhaps a very low exposure to concentrates in the past, if there had been a small supply of the English product in stock within the Royal Infirmary in Glasgow, it would have been jolly useful for patients like that, wouldn't it?

A. It might well have been but in 1985 I did not have this information. That possibility was never discussed with me.
Q. Or 1986?
A. I have no memory of that product being available to Scotland in 1986. I was never told that.
Q. I suppose you don't know what's available until you ask, but in 1986 -- let's then position this during a period when you are a consultant -- you don't have any memory of anyone proposing that you see if you could maybe get a small supply of the English product?
A. No, none at all.
Q. Right. I think you are telling us it wouldn't have been your job to have the idea; is that right?
A. Yes. I mean, what's the point? You have Dr Forbes as chairman of the UKHCDO. He heads the viral safety committee. He is in receipt of all the information published and unpublished. Who better to make the decision?
Q. Did you ever feel out of the loop?
A. I had plenty to do before I took over as haemophilia centre director. Both Dr Forbes and I were busy general physicians coping with all the acute medical problems that the east end of Glasgow can throw at you. That was the major part of our practice; the

50 per cent of our job that was NHS as distinct from our big teaching and research loads, which are the university ones.

When I became a consultant in October 1985, I sat down with Dr Forbes and he said, "What do you want to do? How are we going to do this?" I said, "Clearly you need help with haemophilia and I'm very happy to help you out with the administration of the haemophilia unit," but it was very clear that Dr Forbes was running it, it was his unit and I was his assistant.

My remit clinically, apart from general medicine, was to try and develop thrombosis and vascular services, which was my main interest. So I was developing a lot of clinical research but also clinical services in, venous thrombosis, in peripheral arteries and in stroke, all orphan areas.

The cardiovascular disease that is Scotland's biggest curse, that is ignored by cardiologists, who deal only with the heart; that was my mission in life, to develop vascular services for the east end of Glasgow, where people were having strokes and thrombotic episodes and dying like flies, and working very closely with the diebeticians and the vascular surgeons to try and improve the medical care of those patients.

I was developing those services and that was my

remit. And while I would discuss with Dr Forbes what I was doing, that was my area of control, administration and organisation.

He was very much the leader nationally, and in the centre, of the haemophilia service. We were colleagues, we collaborated but, you know, he had his business to do with haemophilia and my clinical and administrative interests were the other side of the haemostasis/thrombosis equation. So I don't think it was up to me, as somebody who was much junior to Dr Forbes, Dr MacDonald and Dr Davidson and the Blood Products Laboratory, who were very much leaders in the fields of haemophilia, to interfere with their decisions about policy.

Q. Right. Just lastly, Professor Lowe, I should remind you -- you have probably looked at it again recently -- of your article in the Scottish Medical Journal, that you published on these matters. It's [SNB0015523]. This is from 1987. I don't think it's very obvious to us when in 1987.

A. I looked at this the other day and I think it was published in August.

Q. I'm sorry, in August, did you say?

A. Hm-mm.

Q. Right.

A. I think if you look at the cover of the journal, it's around August that year.

Q. Right, thank you. This is, I think, a more general survey of the position as at that time, with, as it's entitled, "Haemophilia Blood Products and HIV Infection". It came out in the August 1987 edition, roughly when would it have been written?

A. Oh, I think probably a few months before, probably about the spring/early summer.

Q. Right.

A. I think the idea of this is that Dr Forbes, as editor of the Scottish Medical Journal, and HIV and AIDS being a topic suitable, he wanted an edition devoted to that, largely for the education of medical practitioners across Scotland, including general practitioners. So this is one of a number of AIDS-related articles, and he asked if I could review the situation of AIDS in haemophilia with particular reference to the UK and to Scotland.

Q. Right. Just if we could take a bit of a look at it, we can see the abstract at the start. Then can we just complete our scrutiny of the first page, which I think is largely introductory. You point to the difference between cryo and concentrate on the right-hand side:

"One therapeutic or prophylactic infusion of

cryoprecipitate comes from about 20 blood donors. One infusion of lyophilised clotting factor concentrate originates from several thousand blood donors."

In terms of incidence, you record that the majority of concentrate-treated haemophiliacs were noted to have intermittently or continuously elevated serum transaminases after the introduction of clotting concentrates. You say that:

"Recent serial studies have shown that hepatitis is a constant finding after only one exposure to clotting factor concentrate, and that the histological picture on liver biopsy tends to worsen with time from normal or chronic persistent hepatitis to chronic active hepatitis or cirrhosis."

I think actually the reference there -- can we just look at the last page? It's the editorial in the Lancet which refers to some of the papers that we have been looking at about incidence and severity.

Can we go back to the second page, please? You went on to say that:

"On top of this morbidity and mortality from viral hepatitis in haemophiliacs, has come HIV."

There is a bit of a discussion of AIDS, HIV and AIDS. And then if you go down a little bit, please, mention of current state, as far as infection is

concerned; prevalence in Scottish haemophiliacs, we can see on the left. Then, I think, is that -- at the bottom of the page, a little bit further down -- the mention of what we tend to call the Edinburgh cohort, in a passage on immuno-suppression by blood products. Then you say you have shown that concentrate-treated severe haemophiliacs had some altered immune responses. Then another mention of Edinburgh:

"Progression of HIV in Haemophilia", which I don't want to spend any great time on. Can we just move down to the bottom of the page. Then "Preventive Measures Against New HIV Infection."

You refer to the first preventative measure to the selection of donors and then secondly to the heat treatment of clotting factor concentrates since 1985. Then if we go over on to the next page, we can see that the third suggested measure is to use lower risk treatments than clotting factor concentrates where possible:

"This policy should also reduce the risk of viral hepatitis, which is not prevented by heat treatment of concentrates. Lower risk treatments include cryoprecipitate ..."

Et cetera.

Professor Lowe, the heavy marking that we can see

here appears to have been applied in PFC in fact, and there is a note that goes with this copy of the article, expressing a view that the passage in the paragraph that we can see on the left-hand side is dangerous, and I think doing the best we can to reconstruct the train of thought, the idea being that advocating any use of unheated products, including cryoprecipitate, was exposing people to a risk of HIV. I think that's the point of view.

I just wondered, in the light of the discussion we have already had at some length, if you want to respond to that suggestion, that it would be dangerous to advocate the use of these products, I think particularly cryoprecipitate.

A. Well, could I ask you about this statement that it's dangerous? Who did that come from and was it sent to me?

Q. No, it wasn't. It's an internal -- like many documents the Inquiry has come across, it's an internal comment, and I think it's actually referred to in the preliminary report, so you can go away and study it if you want, but I think I'm really just interested in the point that someone obviously strongly disagreed, a fractionator, let's say, or somebody working in the --

A. Somebody making concentrates?

Q. Yes.
A. Yes.
Q. So someone very heavily involved in the heat treatment of concentrates, who is, I suppose, taking an opposite point of view.
A. Well, in that first part of 1987, as I recall, the policy of the co-directors in Glasgow Infirmary was still to consider in occasional patients not previously exposed to concentrates, cryoprecipitate and FFP as an option, as we have already discussed.

I accept that there is a variety of opinion about that. If it's a colleague in SNBTS saying that current heat-treated SNBTS concentrates are safe from viral hepatitis, they do not have an evidence base for that statement, because I clearly remember that the studies of previously untreated patients in Scotland didn't start until 1988. That was after I became a haemophilia centre co-director. And while the report of that study was finally published in 1993, showing, within the limited number of previously untreated patients that a small country of 5 million people can assemble with great efforts by all my haemophilia co-directors, particularly in paediatric centres, the best evidence could be got that, that statement could only be made in 1993. And with regards to your previous

statement about the English product was shown to be safe in 1985, which I do not accept --

Q. I don't think I'm saying it was shown to be safe. I think there were early indications that it might be safe?

A. There was optimism by the manufacturer. Well, there always is.

Could I remind you that it was not until 1993 that the final report of the English previously untreated paper was published at the same time as the Scottish one. So I think it could be argued that if you are looking at scientific evidence, it was 1993 before both north and south of the border there was reasonable proof of freedom from the risk of viral hepatitis.

Q. Yes.

THE CHAIRMAN: I think maybe we should have a break.

MS DUNLOP: I'm actually at the very end of Professor Lowe's evidence. If it would be possible just to complete that.

THE CHAIRMAN: Well, if you can.

MS DUNLOP: Yes.

If I were to suggest that Dr Perry had actually told the haemophilia directors in March 1986 that BPL were issuing a Factor VIII product, heated at 80 degrees for 72 hours, and preliminary data indicated that the

material was non-infective with respect to both viruses, that would, I suppose, be a further instance of slightly better founded optimism, if you like. So we looked at something in 1985; by 1986 the picture is still good.

A. It may well have been, but I'm not party in 1986 to that information. I don't go to these meetings with SNBTS or other directors.

Q. And you wouldn't have been there? Right, okay.

Thank you very much, Professor Lowe.

THE CHAIRMAN: I want to come back to this question of "I wisnae there" after the break, professor, but we will have the break at this stage.

(11.07 am)

(Short break)

(11.39 am)

THE CHAIRMAN: Professor, we are all victims to some extent of our own professional background and sometimes our expectations are influenced by that, even if our experiences aren't typical of others. But you see in front of you examples of the sort of relationship that I would expect among advocates. We have Ms Dunlop and her team. We have Mr Di Rollo and Mr Dawson sitting beside him, and you will see them exchanges information and discussion all the time, to the extent that I think I could say that mutual support in pursuit of whatever

happens to be the immediate interest almost characterise the relationship of counsel. So it's perhaps not unnatural for us to think that other professionals may operate in the same way.

However, what you have tended to communicate to me is a relationship between yourself and Professor Forbes that in relation to a significant part of the work of the hospital, really didn't involve that degree of communication at all. I would expect Mr Di Rollo to keep Mr Dawson fully engaged in what he was thinking, and Ms Dunlop to keep the others in her team fully engaged, and yet the impression that I get from some of your evidence is that Professor Forbes attended all these meetings, heard a great deal of information because we have the minutes, but didn't communicate what was happening to you.

That needs explanation, it seems to me. You may say I'm totally wrong and I have misconstrued it but, you know, my present impression is that there is a problem there and I would like you to help me understand whether there is a solution to it.

A. Well, thank you, sir.

Well, first of all, I should respond by saying that obviously Dr Forbes and I were colleagues for many years. We were friends socially, and I never had any

impression that there was a lack of communication between us.

As I -- what I'm careful to say, I think, before coffee, is that I was not a co-director at the time, I did not go to any of these meetings, but I think I also did say that, following these meetings, Professor Forbes, particularly when I became a consultant from October 1985, would invariably give me a briefing as to what was happening in general, and in particular as to whether there should be any change in the policies, protocols or procedures of the unit. So I would not wish you to infer, sir, that there was a lack of communication.

What -- just when we finished before coffee, Ms Dunlop was asking me about this possibility that 8Y, the English product be used in Scotland, and I think what I said was that I did not remember that as a possibility. I'm not saying that that was not discussed; it's just I cannot recall that.

But I'm wondering, sir, if there was any other respect in which I have given you the impression that we didn't speak to each other.

THE CHAIRMAN: I'm not going to analyse all of your evidence here and now, but I may in due course, Professor, do so. But it may be from what you say that I have got the

wrong end of the stick and, if so, that's unfortunate.

Ms Dunlop, I don't know whether you wish to follow that in any way?

MS DUNLOP: No, I have no other questions, sir.

THE CHAIRMAN: Then we will go on.

Mr Di Rollo?

Questions by MR DI ROLLO

MR DI ROLLO: Yes, thank you, sir.

Professor Lowe, I wonder if I can ask you to look at the preliminary report at paragraph 9.326, please.

When the topic was introduced today -- we are dealing with a slightly different period, I think, but I won't worry about that for present purposes. 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. No doubt those people would come in a number of shapes and sizes and situations, but plainly that is a significant number of people that decision-making, relative to treating with a blood product during this period, would affect. Do you agree with that?

A. Yes.

Q. And both in the East of Scotland and in the West of Scotland -- I don't think there is any figure

there for the rest of Scotland or whether we are to take it that the east goes all the way to the top of the country et cetera, and the West likewise, but whether there was anybody else in Scotland, but even leaving that aside for the moment, plainly it is a significant number of individuals being treated for the first time.

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 -- and that is something which would be of concern to anyone administering -- or should be of concern to anyone administering a blood product during that period.

A. I agree.

Q. And would it be reasonable to say that one should not give a concentrate unless it was unavoidable to do so, given that there was that risk?

A. Yes, in general terms.

Could I just follow up your statement about these patients coming in all shapes and sizes. I think "size" is the relevant word here. I'm not sure about what references 382 and 383 are but, as you are aware, we had a previous Inquiry into hepatitis in Scotland about ten years ago, conducted by the Scottish Office and

published. And I think at that time all haemophilia directors were asked to look back at their patients during the period of time that you mentioned and produce data for that Inquiry as to how many patients at each haemophilia centre were treated for the first time with a blood product, and out of those 13 in the West of Scotland, my memory is that the majority of those would be children attending Yorkhill Hospital, the children's haemophilia centre, because obviously it's as a child that most patients with haemophilia get their first exposure to a blood product.

I looked at that data recently and in our Glasgow Royal Infirmary data, I think we only had about three adult patients during that period of time treated. So out of those 13, I think only about three patients were treated for the first time in our unit at Glasgow Royal Infirmary, which is what you would expect for an adult haemophilia population.

Q. Can I ask you: as far as the Yorkhill ones, it's not unusual for patients from Yorkhill to be referred from other parts of Scotland, of course? Presumably the children may well be referred there, it being a centre, obviously?

A. Yes, so if a child in the West of Scotland, anywhere between Carlisle and Stornoway, was diagnosed for the

first time or haemophilia was queried, they would be referred to our paediatric colleagues at Yorkhill for diagnosis and the initiation of treatment.

Q. I think we are aware, from information that we have, that what you have told us about cryoprecipitate and Yorkhill and the approach that was taken is that it seems to be that cryoprecipitate would be a preferred option because of the concern of non-A non-B Hepatitis during this period?

A. Yes, I think that was what was recommended in the UK national guidelines at the time. But obviously, you would have to ask my ex-colleagues at Yorkhill about that.

Q. Right. But getting back to what I was suggesting to you, the position is that one would not give a concentrate to a previously untreated patient unless it was unavoidable, and I think you agree with that?

A. I agree.

Q. And just in very general terms, obviously, in looking at the situation as it presents to the doctor, the first thing a doctor has to do is to assess the situation and work out what the specific problem is or may be before one goes into any decision about what to do or not to do. Is that fair?

A. Indeed.

Q. And in particular, one would have to determine what the nature of the bleeding disorder was?
A. Yes.
Q. And find out exactly what the patient's deficiency may or may not be?
A. Yes, of course.
Q. And the issue about a concentrate would only arise if one has a situation or has information, which is reliable information, that one has a Factor VIII or a Factor IX deficiency or a von Willebrand's disease problem.
A. That's what one would like.
Q. Yes, well, that's what should happen, isn't it? Is that right?
A. Oh, yes, absolutely.
Q. The issue about whether you use a concentrate would only arise if one decided that there was no alternative but to use a concentrate therefore.
A. Correct.
Q. I think the suggestion has been put to you, and you have indicated that you didn't play any part in the decision-making process, but if English 8Y had been available in this period in Scotland, a small supply had been available, then consideration might have been made that if you had got to the point at which you had no

alternative but to use a factor concentrate, in a previously untreated patient you might decide, "I'll use 8Y because it gives a better level of protection".

A. Yes, that might well be the case but, as I said before coffee, I have no recollection of such a product being in Glasgow Royal Infirmary or used in Glasgow Royal Infirmary.

Q. I don't think we have any information that it was used or was available and I think your position is that you yourself had no involvement in any decision-making process, but if 8Y had been asked for, then it might then have become available and therefore might have been used.

A. It might have been used, yes.

Q. Thank you. I have no further questions.

THE CHAIRMAN: Mr Anderson?

Questions by MR ANDERSON

MR ANDERSON: I'm obliged, thank you.

Professor Lowe, you were discussing with Ms Dunlop the situation where the doctor had a difficult choice to make and you had to weigh up the various factors according to the circumstances of the patient; do you remember that?

A. Yes.

Q. And you used the phrase, I think, "It's very difficult

because it's an evidence-free zone". Would I be right in thinking that one of the factors that one would take into account would be the anticipated treatment, in other words the length of treatment, for example, the number of doses one might require? Would that be correct?

A. Yes, I think it would. For example, if you are thinking about the choice between cryoprecipitate or the first use of concentrate, an important question regarding the bleeding episode is how bad is that bleeding. So, for example, if somebody is exsanguinating or having a major bleed into the brain, you would come to a stage where you are thinking now, how much cryoprecipitate, if you use cryoprecipitate, are you going to have to use; and in either of these situations you might well be in the case of giving, for example, daily cryoprecipitate for two weeks to make quite sure that that bleeding was arrested, in which case, any advantage about limiting the donor pool by use of cryoprecipitate vanishes because you are then exposing that patient to several hundred donors, at which point any advantage over cryoprecipitate for reducing the risk of non-A hepatitis, relative to concentrate, becomes irrelevant.

So that kind of factor, what kind of bleeding is occurring and thinking through not only the first

treatment that you give but how long that is going to be given for, that's one example.

Q. So if it was anticipated that it might require, I don't know, 10 to 20 applications, that would be something one would take into account?

A. One would certainly consider that.

THE CHAIRMAN: And at the same time, of course, we tend to think of cryoprecipitate as if it were a single unit, but the reality might be that each day there would be multiple units used. Up to how many?

A. Sorry, the average adult dose would be about 20 bags. So that's 20 donors. It would vary according to the patient's body weight.

THE CHAIRMAN: Yes, indeed. But it's possible to get a wrong impression if one just thinks of cryoprecipitate as a single-donor product. It hardly ever is.

A. Each bag is a single donor but you need to pool together 20 bags for the average adult. So if you then start multiplying that over several days, weeks, or months, you are approaching a significant donor exposure.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: I'm obliged, sir.

I think in your answer to me, professor, you used the phrase "considering the choice between cryo on the one hand and Factor VIII on the other hand," but in

answer to one of my learned friend, Mr Di Rollo's questions, he put to you the issue of whether you use concentrate only if there are no alternatives. I just want to discuss this with you, if I may, because I have some difficulty in reconciling that proposition with the idea that there are circumstances in which one has a choice, because earlier on I had understood you to say there may be quite difficult decisions to make as to whether to use cryoprecipitate on the one hand and a concentrate on the other hand.

So am I not right in thinking that it's not quite as simple as saying you never use concentrate if you have an alternative? Because there are circumstances, aren't there, where you have a choice -- a difficult choice to make. Is that not right?

A. I think that's right, there is more of an equipoise for a small number of patients between cryoprecipitate and concentrate, as I think I was trying to explain before coffee. You have to weigh up the lower donor pool of cryoprecipitate against the larger number of donor exposures using a concentrate but, as I have just been saying, that will then depend on the number of treatments that you have to give and what you may consider exposing that patient to over a period of time.

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

THE CHAIRMAN: While we are talking about choice, there is one thing I ought to introduce, just to make sure that it's here in the context of your evidence.

If one of the products in line for selection, as it were, were DDAVP, does it maintain its effectiveness if it has to be repeated in the course of a procedure, or does it fall off, or what?

A. Thank you, sir. It has a short-term effect. And usually after about 48 to 72 hours, if you are giving a daily or twice daily injection, you observe a phenomenon called tachyphylaxis, which is a reduced response, and this is because you are trying to stimulate release of the patient's own endogenous Factor VIII, von Willebrand factor complex. It starts with the von Willebrand factor that comes from vesicles in the endothelial cells. They only have a finite storage capacity. So you can flog the patient's endothelial cells with DDAVP, desmopressin, and there is individual variation, but usually, after four doses of desmopressin, you don't get any more bang for your bucks. So you have to bear in mind that limited situation.

THE CHAIRMAN: So there is a factor particular to DDAVP that might limit it as a product of choice in particular circumstances?

A. Exactly.

THE CHAIRMAN: Is it also a factor that it might lead to fluid build-up, especially in children?

A. Yes, indeed, and we were one of the first centres to report that, just after Professor Mannucci in Italy published in the Lancet the use of desmopressin in the late 1970s. We tried in on a patient with moderate severity Haemophilia A in Glasgow to cover a tooth extraction, and given the recommended doses, which had been worked out by the experience of about 50 or 60 patients in Italy, during which they had found no evidence of water intoxication, fluid retention. Our patient developed severe hyponatremia, the serum sodium went down from 135-ish to about 110, and the patient developed headaches, and that was the first clinical evidence we published in a letter to the Lancet, that, as you might predict from the physiology and pharmacology of the situation, there are some patients who are more susceptible, due to genetic factors or whatever, to water retention than others.

So we recommended that water intoxication should be always considered routinely and that particularly if prolonged infusions were being given over perhaps more than a day, one should monitor the serum sodium and closely observe the patient.

Shortly after that, over the next five years, several paediatric centres around the world reported seizures in children, and children are more susceptible to water intoxication than adults. So it is there in the literature as one of the cautions to desmopressin that, particularly in children, it may be toxic and that should be carefully considered, fluid restriction, monitoring of serum sodium, et cetera.

It's not the only adverse effect of desmopressin. There are some patients who are intolerant to the vasoactive effects, so that during the infusion, even if you try to prolong that over 60 minutes, some patients flush, they have a fall in blood pressure and feel so uncomfortable that they say, "I don't want that medication". And there are some patients in whom it is ineffective, some who have the immediate intolerance, some who have the delayed intolerance of water intoxication. And also you are elevating the levels of Factor VIII and von Willebrand factor and occasionally you get thrombogenesis, so if you put the Factor VIII or von Willebrand factor levels up too much, you can get venous thrombosis or arterial thrombosis, which is clearly undesirable.

So I think the point I'm making is that desmopressin is not the panacea. It had a very useful place -- let's

not underestimate it -- during the 1980s, in sparing many patients with haemophilia and von Willebrand's disease around the world from getting virus infections. So it has its place, but it's not the panacea. And you have to assess every patient individually across the whole spectrum of haemostatic agents, not only in this period of time that we are talking about, concentrates versus cryoprecipitate or fresh-frozen plasma, but at the desmopressin end, we always tried to make sure, as in all haemophilia centres, I'm sure, that any patient in whom you are considering desmopressin, had to have a trial dose for efficacy and safety, and then you could individualise the treatment.

THE CHAIRMAN: Mr Anderson, I don't know whether you want to follow that. I was merely trying to extend the question of choice a little bit further.

MR ANDERSON: No, thank. I think it's helpful.

THE CHAIRMAN: Mr Johnston, do you have any questions?

MR JOHNSTON: No, I don't, sir.

THE CHAIRMAN: Ms Dunlop?

Further questions by MS DUNLOP

MS DUNLOP: Could I ask one more question about desmopressin, please?

Professor Lowe, I think we have had the impression that DDAVP is useful for the planned intervention, and

I think we can understand that, but that its role in relation to the patient who needs treatment for a bleed is limited to very minor bleeds, but I'm inferring from what you are saying that it may also have a role in more significant bleeds. Is that wrong?

A. It's a question of degree.

Q. Yes, perhaps if you can -- I don't know, think of some examples and I suppose take into account what the starting level of the patient's Factor VIII might be.

So perhaps if you can talk us through, say, the nose bleed, to take one example, and then up to a more significant bleed but also differentiating between the person who has mild haemophilia and the person who has more severe haemophilia.

A. Well, to take that last point first, it's only ever been useful as a treatment for mild haemophilia and mild von Willebrand's disease, which is, if you force me into a number, 10 per cent or 10IU per DL.

On that basis, if you give the average patient, with either of those conditions and a level of 10 per cent Factor VIII, or von Willebrand factor in the case of von Willebrand's disease, a standard dose of desmopressin, that will elevate it two to fourfold. So you are going to get up to 20 to 40 per cent of normal.

That, experience has shown, is usually effective for

preventing bleeding following dental extractions or other minor types of surgery, particularly if you accompany it, in the case of dental extractions, with tranexamic acid, which acts by stopping the clot being broken down once they have made it.

It has been used for treatment of established bleeding, of which the most common example is somebody who has had a dental extraction and then comes back a few days later with secondary haemorrhage, bleeding again. And you can try desmopressin in that situation.

Obviously, the longer it has been since that first few doses of desmopressin, the more likely it is that the patient's endothelial cells will have synthesised more von Willebrand factor and it will work again.

The problem is that if you get up to between 20 and 40 per cent, say, in a 10 per cent patient, is that enough for bleeding which has already started, as compared to trying to prevent bleeding before the extraction. And in general it's less effective but it may still be worth a try.

So thinking back as to what we have done when I was a practising doctor, in that situation, if somebody had come back a few days after a desmopressin-treated tooth extraction or other minor surgery and was bleeding again, yes, we would give it a try but we would say to

the patient, "Let's try this and let's try all the measures, but at the end of the day, if the bleeding is continuing and if it's going to seriously affect your health, we may have no alternative but to go to clotting factor". And before recombinant Factor VIII came in, that would have to be a blood product.

Q. What about not the patient who has had a planned intervention and who comes back with more established bleeding, but the patient who presents for the first time with a joint bleed, say. Can it have any role there? Is it worth a try there?

A. If such a 10 per cent patient came in rapidly after a knock and you had a very early joint bleed or muscle bleed, again you could give it a try but I would not be optimistic. I think that patient is much more likely to require clotting factor treatment.

Q. Right. Thank you very much, professor.

THE CHAIRMAN: Mr Di Rollo, there has been quite a lot of discussion of DDAVP. Is there anything in that context that would excite you into asking a further question?

MR DI ROLLO: I don't think so. I'm grateful for that opportunity.

THE CHAIRMAN: Professor, thank you very much.

MS DUNLOP: Our next witness, sir, is Professor Ludlam.

PROFESSOR CHRISTOPHER LUDLAM (continued)

Questions by MS DUNLOP

THE CHAIRMAN: Good afternoon, Professor Ludlam.

MS DUNLOP: Thank you, sir.

Good afternoon Professor Ludlam.

A. Good afternoon, Ms Dunlop.

Q. We are examining, as you know, our topic C3A. We have a statement from you on that topic and I should ask for it to appear on the screen. It's [PEN0171790]. We will also be going to an appendix, which you have prepared to be read along with this statement, and it's probably just as well to open that up now too because we may need to flick between them. It's [PEN0171798].

To start then with the statement, you have given us a preamble and you say that:

"Consideration of therapeutic policy in our chosen period with respect to non-A non-B Hepatitis cannot be considered in isolation from the risk of other viral infections, especially HIV."

We understand the consideration that you advance to justify your statement. 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?

A. That, I think, is fair, yes.

Q. Right. You have, of course, also already pointed out, I think in the context of our earlier topic about viral inactivation in the early 1980s, that of course, the whole genesis of the viral inactivation projects was hepatitis, or that was the underlying risk that these projects were devised to meet and that it was only really as a result of the advent of AIDS that the target perhaps moved slightly.

Question 1 we posed in relation to this period between 1985 and 1987, and we asked you if there was an awareness among treating haemophilia physicians in Scotland that the Scottish product was less effectively treated against non-A non-B Hepatitis. And your answer is that:

"When the first heat-treated product, NY 68 degrees, two hours, was introduced in December 1984, it was widely acknowledged that it was very likely to transmit non-A non-B Hepatitis."

You refer to your summary, which I think I would like to go to without further ado. Can we go to the other document, [PEN0171798].

You take us back to 10 December 1984, at the meeting of reference centre directors, and I thought it would be useful if we just looked with you at some documentation about that. Could we go to something we have already

looked at this morning, [SGF0012388].

Just to refresh your memory. I'm sure you have looked at this again recently, can we just go down to the same part actually, the foot of page 2 or on to page 2.

We have the "Options" and then the "Recommendations". That's really the section that I'm asking you to have in mind, and actually you have reproduced this for us in your appendix so you have reproduced it down to -- can we go over the page, please? -- the statement that begins:

"In individual patients, there may need to be a choice."

Which we can see there. And you have included up to and including the words, "until all supplies are heated". So approximately halfway through that paragraph there.

Of course, that comment that:

"Directors may wish to continue to use unheated NHS material until all the supplies are heated.

That really applied more to England and Wales at the time this document was written in December 1984, didn't it, because in Scotland all Factor VIII was being heat-treated?

A. Yes, this refers to Haemophilia B as well.

Q. Well, yes.
A. And there was the question of Factor IX concentrate and whether to use heated or unheated NHS concentrate.
Q. Yes. Just to look at some documents that relate to the meeting itself, rather than this, which is a guidance document emanating from the reference centre directors a few days later, can we look firstly at [DHF0030898], please? Can we go to the end of this, please?

We can see that this is from somebody within DHSS who, as the author says, was invited to the meeting. So that's just to give you the context of this document. Can we go back then to the first page? Do you see that? Paragraph 2:

"As you know, I was invited to the above meeting held at CBLA headquarters and arranged to discuss the implications of AIDS for haemophilia patients."

It's recorded that this guidance letter is coming, and that's the document we have just looked at.

Then the following main issues were discussed: testing patients, dealing with patients, and then on to the next page, please:

"Use of heat-treated Factor VIII. After prolonged discussion, it was agreed that children should be treated with cryoprecipitate or, if necessary, with heat-treated Factor VIII."

You and I have discussed this meeting before, Professor Ludlam, and you have told us that there really was a lot of discussion and debate, and I think that --

A. That is correct.

Q. -- this observer has noticed that, but I was interested because this does seem to be a slightly different emphasis:

"It was agreed that children should be treated with cryoprecipitate or, if necessary, with heat-treated Factor VIII."

Of course, I'm sure anyone would understand that there would have to be a case by case assessment and that individual doctors would have discretion to assess the circumstances of an individual patient, but I just wondered if you recall that slight preference for cryoprecipitate in children.

A. Well, the following sentence says:

"New haemophiliac patients shall be treated with heat-treated Factor VIII."

Q. Yes.

A. And children --

Q. Are often new haemophilia patients?

A. -- are often new diagnoses. So this isn't quite, sort of, consistent. It -- what it doesn't deal with, I think, is the severity of the haemophilia. Can I just

read it a bit further on?

Q. Yes, certainly. (Pause)

A. Yes, it opens up the debate and difficulties about whether to use unheat-treated NHS product, versus heat-treated commercial.

Q. Yes. And that, as you say, is a debate that would be taking place in Scotland in relation to Factor IX.

A. Yes.

Q. Yes. But I suppose one could read the second sentence as referring to patients presenting for the first time but not in childhood.

A. It could be, yes, certainly. It's a patient not previously diagnosed, found to have haemophilia and how should they be treated, and with concentrate.

Q. Yes. Well, let's look at what I think are a more official set of minutes, [SNF0013850].

I think, notwithstanding its entitlement as "notes", it is really the minutes and we can see that you were there and also Dr Forbes.

I really just want to go to page 4 but perhaps if we move slowly through the first three pages, just so everyone can see what was on the agenda. Screening we can see. Then page 2, still tests. Page 3. Dr Tedder is explaining his virologist's viewpoint, and then on to page 4, please. Advice to patients and donors. Then

further down:

"Factor VIII concentrates.

"It was agreed that heat-treated products should be given to all patients, if freely available, to include those found to be antibody-positive. Antibody-negative patients. It was agreed that from now on treatment must be with heat-treated material."

No doubt subject to considerations of supply.

Then on to the next page, please, we can see various contributions. If we can just scroll a little bit further down, thank you, before we move on to advice and testing of staff.

Can we then go on to the last page of this document, please? It was just that bit that we can see at the bottom of the screen. Item 6:

"Advisory statement. At this point Dr Lane suggested that for the remainder of the meeting, the haemophilia directors be allowed to have a private meeting with only themselves present. This was accepted."

So the fractionators left. Is that right?

A. I presume so, yes.

Q. Yes. Do you remember this, that the format of the gathering was that there was this discussion involving everybody and then people from the transfusion services

left. I'm not sure whether our mystery person from the Department of Health stayed or went but you had a private meeting, the reference centre directors had a private meeting, and what, thrashed the issues around?

A. I think that's what happened. I think it was quite late in the afternoon by the time the main meeting had come to an end.

Q. Right. And the actual production of that advisory document, was that really pulled together by Professor Bloom?

A. Yes.

Q. Yes. Okay. Can we go back then to [PEN0171798], please? On to the second page.

You tell us that the guidance set out in this important document was adopted for treating patients in Scotland.

The next page, please.

There is a reference in your paragraph 3 to what happened in December:

"Patients were invited to return their unheated stock and were given in exchange the heat-treated stock."

I would like to come back to that, if we can loosely, and I think slightly inaccurately call it, "product recall". So we'll come back to product recall

later.

In paragraph 4 you are emphasising that during 1985 to 1987, the principal concern of those concerned with haemophilia therapy was to prevent further HIV transmission. You say that:

"Non-A non-B Hepatitis virus is seen as a much less severe infection than HIV."

Actually, pretty much everything one can think of is a much less severe infection than HIV, certainly as it appeared at that time.

A. At that time, yes.

Q. Yes. And there also, you say, was an understanding that it was much harder to eliminate hepatitis viruses from concentrates. I wanted to suggest to you that there was actually quite a lot of uncertainty about non-A non-B Hepatitis at that time, perhaps not so much in relation to incidence but in relation to severity. The incidence seems to have been widely understood to be very, very high in those treated with factor concentrates. That would be correct, wouldn't it?

A. Unheated concentrates, yes.

Q. Unheated concentrates, yes. And certainly we have looked in previous sessions at the work of Dr Craske in UKHCDO in looking at the problem of hepatitis-associated with concentrates, and we know that material started to

come through. We have looked at an article published in 1983, for example, showing a very high incidence of hepatitis in people given concentrates for the first time, whether NHS or commercial.

As far as severity, however, the picture seems to have been a little less clear, and I wanted to, in preparing for today, try to look at articles that might have caught your eye. Jumping forward in time here to [LIT0013859], please. We noticed it because it emanated from Edinburgh, but if we look at the second page, we can see that this is a letter that you and colleagues sent.

Can we just look at the second page to see the authors? Thank you. Here we are.

This is you sending a letter to the Lancet and it was published on 2 September 1989. But what's interesting about it is that it seems to show an expectation on your part that really all your patients might be HCV-positive had you started testing them around this time. Is that correct?

A. The vast majority who had received pooled concentrates or a great deal of cryoprecipitate.

Q. Yes. So can we just remind ourselves of the first part of the letter. Can we go back, please, to the previous page?

What was happening was that pretty quickly after some sort of test had become available for HCV antibodies, you were looking at your patient group to see what the prevalence was. Is that right?

A. That's correct, yes.

Q. And you looked at this particular number of 48 patients, who had received non-heat-treated products before 1985, 41 of them were seropositive. Then you make that comment in relation to that 85 per cent figure, ie 41 out of 48. If we read over on to the next page:

"We do not know why all such patients are not anti-HCV-positive."

You say:

"All would be expected to be infected."

We have speculated, Professor Ludlam, that there might have been something to do with the kits, that the sensitivity of the first generation testing kits was not as good as some later kits, or an explanation of that sort. But at any rate, it shows firstly a very high prevalence and secondly an expectation on your part that that would be so.

A. Yes, I think that's correct. And there always seems to be the possibility there are, in fact, a few patients exposed to unheat-treated concentrate who do not develop Hepatitis C infection. And the reason for that I don't

understand. It may relate to their tissue type or something rather individual in that, I think, in that person.

Q. Yes. We understand that there are obviously genetic differences between individuals, which may govern their response to infection.

Just to look at, as I said, articles that I thought maybe would have caught your eye at the time, can we look firstly at [LIT0010335]?

We know that there is a companion work, which was entitled "Progressive Liver Disease in Haemophilia: an Overstated Problem", and that it emanated from Manchester and had been published a couple of years before this one, but do you remember noticing this article at the time? Would this be something where you would think, "I need to read that"?

A. Oh, yes, this was an important article.

Q. Right. I expect at the time you knew Dr Hay?

A. Indeed, yes.

Q. I don't think we necessarily need to go through it in any detail but the general thrust of the article is really betrayed by its title, that the problem may be more serious than some people had appreciated. Is that right?

A. I think it was the progressive nature of the problem

that perhaps hadn't been appreciated adequately, prior to this paper.

Q. Yes. So they are saying -- and we just get this from the summary -- that:

"Serial liver biopsies had shown progression from chronic persistent hepatitis to chronic active hepatitis and cirrhosis within six years, suggesting that chronic persistent hepatitis in haemophiliacs is not as benign as hitherto supposed. Symptoms and abnormal physical signs were uncommon in these patients; in other words, it may be an insidious onset."

A. Absolutely.

Q. Yes:

"It is anticipated that liver disease in haemophiliacs will become an increasing clinical problem in future."

Just to let you have a brief look, perhaps, at the rest of it. They are reporting their observations. Patients and methods. They have been screening their patients since 1977. I'm sure you have told us this before, Professor Ludlam, but perhaps you can remind us: is that sort of screening something that formed part of your regular review of your patients?

A. Very much so. Every few months they would have their liver function tests measured, going back before my time

into the 1970s. And it's full of results of liver function tests.

Q. Then they have done a percutaneous liver biopsy in 34 patients, and actually I think this is an article with a table, or maybe I'm misremembering. Can we move through it onto the next page? Yes, there is a table of results at the bottom there, then the discussion:

"Progressive liver disease is a potentially serious problem in haemophilia. Of 79 haemophilic patients, selected solely on the basis of previous exposure to blood products, 17 had evidence of progressive liver disease ... serial liver biopsies showed progression of chronic persistent hepatitis to chronic active hepatitis and cirrhosis within a period of two to six years."

And the reference to explanations for this. The widespread introduction of the treatment in the mid-1970s. Then on to the next page, please, some of the histology is reproduced. And then the concluding paragraph is worth looking at too. They are predicting that deaths attributable to liver disease in haemophilia will become more common.

The next article I wanted to look at, the next publication, is [LIT0010505]. I'm sorry, I should have recorded, that's 29 June 1985, that article.

So just to locate it time-wise. The next one is

from Blood, August 1985, and we can see that if we go on to the second page of this, please. Even though you were a haematologist, Professor Ludlam, I don't want to take for granted that you consulted Blood. Did you see this regularly?

A. Yes, this is one of the journals that we try and read regularly.

Q. And will have done at the time?

A. Yes.

Q. One of your staples?

A. Yes.

Q. Right. We recognise the name of Dr Aledort. This is referred to in other publications, this one. Do you remember noticing this one at the time?

A. Yes.

Q. Right. And you will have read it too?

A. A long time ago, yes.

Q. Yes, and no doubt looked at it again recently?

A. Perhaps a year or so ago.

Q. Right. And in the context of the sorts of studies that were being done, we can see this is quite a large study, so it's talking about 155 haemophiliacs. Clinical information, they say, on the frequency of complications from biopsies in 115 haemophiliac patients provided a unique opportunity to assess the safety of liver

biopsy. Then they say that the incidence of cirrhosis at 15 per cent and chronic active hepatitis at 17 per cent was lower than previously reported. The frequency of severe liver disease in patients receiving large pooled concentrates was no greater than in patients treated principally with cryoprecipitate or plasma. They point out also the risks of liver biopsy in this setting, which I think we can understand.

THE CHAIRMAN: Professor, what about the team? Dr Aledort on this occasion seems to have quite a number of supporters, as it were. What about their status? Do you know any of these people?

A. Yes, my recollection of this paper is that they had collected up these biopsies, or the slides from the biopsies, from many haemophilia centres in the States. This wasn't a study, I think, done at one haemophilia centre.

MS DUNLOP: Yes, it says in the slightly smaller type, if we go down to the left-hand side, sir. There is a description of methodology, which explains that they had a small group who were designing the study, and then they say -- actually it went beyond the United States.

A. Yes, it was a multi-centre study and the authors at the top. Dr Aledort was the director in charge of a major haemophilia centre at Columbia in New York.

Peter Levine ran a very go-ahead haemophilia centre, very concerned with blood safety, in Worcester, just outside Boston, about 60 miles west of Boston. Margaret Hilgartner, I think was a paediatric haematologist, looking after children in New York.

PROFESSOR JAMES: I can do most of the rest.

MS DUNLOP: We should understand the team to be a mixture of haemophilia clinicians and hepatologists --

PROFESSOR JAMES: From Bianchi onwards. Bianchi, Desmet, Scheuer and Popper were all pathologists, actually, respectively from Switzerland, Belgium, London and New York, and Berk was a hepatologist from New York.

MS DUNLOP: Thank you.

THE CHAIRMAN: I think I could also get an answer to my question about their standing from Professor James.

PROFESSOR JAMES: Yes, they had the highest standing in the world at that time, the liver doctors.

A. And the same applied to the haemophilia doctors.

MS DUNLOP: I'm sure of that.

Similar sorts of descriptions of materials and methods, patient classification, and the patients were divided into different groups, depending on their treatment history. Perhaps interesting to note that there were some who had received a lifetime exposure of more than 100,000 units of concentrate. Then some

details of how the analysis was conducted by the pathologists.

On to the next page. The results. We are told what the breakdown was as between Haemophilia A and Haemophilia B. And then that little table, table 1, we see the text just above that:

"64 per cent of all cases had trivial, mild or moderate hepatitic lesions and only 7 per cent had severe lesions. 15 per cent had cirrhosis and 14 per cent had other lesions."

Their -- "verdict" is perhaps the best word. I don't want to say "spin" or "gloss", but if we look at the discussion, which we find on page 370 of the article, so two pages further on, they are highlighting the fact that their finding of 15 per cent having cirrhosis was less than previous reports. Actually, one of the references there is to a previous Sheffield paper. So in tone this is not an alarmist piece; it's saying that their finding is less than some other people's findings. But they do go on to say on the next page that -- and this is reading the first full paragraph:

"The lack of severity of the histopathologic findings in the current materials may not be entirely reassuring. Some recent evidence suggests insidious

progression of non-A non-B Hepatitis to cirrhosis, although other studies suggest the possibility of reversion toward normal hepatic architecture."

Then they go on to deal, towards the end, with their separate findings on the risks of liver biopsy in patients with haemophilia.

I'm saying "separate" but, of course, it's not an entirely discrete consideration because I think we can understand that if a clinician wants to try to assess the condition of the patient's liver, he or she is going to want to do a biopsy and for patients with haemophilia that raises particular problems. So not surprising that they are also devoting part of their study to that particular topic.

A. Very important that they do so, yes.

Q. Yes. The other publication -- it's actually a letter -- I wondered if you might have noticed at the time is from the Lancet of February 8th 1986. The reference for it is [LIT0010341] but on the next page. We can see there a letter from a Dr Schimpf. Another well-known name?

A. A very well-known name. A very distinguished haemophilia treater.

Q. Yes. Liver disease in haemophilia. And he -- yes? He is a he?

A. He is a he, yes.

Q. He is aligning him with Hay and others, the Sheffield authors. He says:

"Like Hay et al, we think that progressive liver disease is an understated problem."

And he is offering his own figures from his centre. They found progressive liver disease in 29 per cent of their patients, 16 per cent having chronic active hepatitis and 13 per cent having cirrhosis. "He multi-centre study by Aledort et al, to which he contributed biopsy material, came to a similar conclusion about the frequency of cirrhosis."

So perhaps interesting just to maybe gently contrast the tone. I don't know if this is my imagination as a layperson but if the tone of the Aledort piece is that the frequency of serious liver disease is not as high as others are saying, whereas this, taking very similar sorts of figures, is saying that it is an understated problem, it seems to be giving perhaps a slightly different sort of spin or gloss to very similar data. Is that reasonable or am I off line?

A. No, I think it's reasonable and I think the crucial thing is whether it is progressive.

Q. Right.

A. Because one might say 13 per cent cirrhosis is one thing and might be seen as not a severe problem, but if the

liver disease is progressive, so you go back five years later and, instead of it being 13 per cent, it's 25 per cent, then it's serious.

Q. Yes.

A. But there was, as you know, a debate from mid/late 70s onwards as to how progressive, how severe, liver disease was but I think around about this period was when it became clear that it was potentially serious and potentially progressive.

Q. I'm obliged, Professor Ludlam, because you are really, I think, focusing for us something that I certainly hadn't completely appreciated and that is the need to take on board the use of the word "progressive". That is the title of the Sheffield paper, "Progressive Liver Disease in Haemophilia". So it's not just liver disease in haemophilia, it's progressive liver disease that people are worrying about?

A. That's as I see it, yes.

Q. Yes. Do you remember noticing this letter?

A. I'm sure I saw it.

Q. Yes. Can we go back then, please, to where we were, which is in the appendix, [PEN0171798]. We were on the third page of that, so at 1800. I did put to Professor Thomas, when he was here earlier this week talking about this problem, the proposition that in an

era where the data was a bit uncertain much depends on the question one posed. So if the question had been, "Are we dealing with a very serious problem," it might have been difficult to give it a very meaningful answer, but if the question had been, "Is this something we don't have to worry about," the answer to that would be that one couldn't be reassured; it was something to be concerned about. Is that reasonable?

A. Sorry, is this in relation to the two-hour heat treatment?

Q. No, no, liver disease in haemophilia, progressive liver disease in haemophilia. It might have been difficult to get an absolute sense of the magnitude of the problem. But, equally, at the other end of the spectrum, as it were, one wouldn't be saying, "This is something that needn't concern me."

A. Oh, yes, I agree.

Q. Right.

A. I'm sorry.

Q. No, it's my fault.

You make the point in paragraph 5 that there were studies from 1985 onwards which were showing both continued transmission of HIV and continued transmission of non-A non-B Hepatitis by heat-treated or otherwise treated concentrates. I think we know that to be true

and I don't think we need to go to those documents in relation to HIV. We know there was a problem with Armour heat-treated concentrate, and the second of those references is an article we have looked at many times already by Kasper in the transfusion periodical, I think in 1993.

Then you say in paragraph 6 that:

"When the first heat-treated product was introduced in Scotland, it was uncertain whether it would transmit HIV and to what extent, if any, there was a reduced risk of non-A non-B Hepatitis."

Then you talk about evidence about there having been contaminated pools but fortunately no development of HIV in the recipients of some of those pools which were looked at retrospectively, and I think that reference is to an article in Vox Sanguinis. Is that right?

A. Yes.

Q. For anyone who wants to look at it, it's [LIT0010664] but I'm not proposing to go to it.

In section 7 you talk about the need to try to assess the efficacy of heat treatment. I think we understand that that could be done with HIV using the virus itself because, obviously, once the virus had been found, one could do experiments to see if it was inactivated by a particular heat treatment protocol. It

was very much more difficult for non-A non-B Hepatitis and I think we can understand this because we are talking about a time before the virus has been identified.

You say that there was an internationally agreed protocol for that sort of work, so those sort of experiments were governed by a protocol, and then you go on to identify further difficulties in trying to assess the hepatitis-related safety of heat-treated concentrates.

You say it was difficult to know which previously treated patients were not already infected:

"The ideal patient group was, therefore, those who had never received a transfusion of blood or a blood product and required treatment with one. It is considered possible also to include patients who had only been minimally exposed."

You say:

"As between these two groups, the former patients only rarely present and the latter were a rather heterogeneous group of individuals."

We understand that it was not a straightforward matter to assess the safety of a product. Can we then go on to paragraph 8, please, on the next page? You talk about early 1985 at BPL and you say that:

"The initial batches of 8Y were available for use in patients but it was not until October 1985 that 8Y at 80 degrees for 72 hours was in full production."

And you say that:

"That product only represented about one third of Factor VIII concentrate used in England. The other two thirds were of commercial origin."

But, of course, professor, in the discussion we are having we should bear in mind that the particular group of patients on whom you were, I think, trying to focus is the previously untreated or minimally treated patients. So it's not the patients who have had years of concentrate therapy already who are your main concern. Is that right?

A. Yes, and for assessing new concentrates you needed to have patients who had not previously been transfused.

Q. Yes.

A. But in this paragraph 8 perhaps what I don't say is that BPL went on manufacturing, as I understand it, non-heat-treated NHS Factor VIII up until the spring for distribution in England. In parallel they were doing this development work on 8Y, so they could give some test infusions and check that it was reasonable to give to people.

Q. Right. In any assessment, however, of how well

a country did in meeting different needs over this period, it's perhaps less relevant to look at how much of the total requirement for concentrate was met by NHS product, in that, when you are trying to protect patients from hepatitis, the patients you are trying to protect are those who you think won't already have been exposed. So they are a much smaller group. Presumably, the efforts of clinicians are particularly focused on trying to protect those who have not already been exposed?

A. But during this period the principal objective was to avoid HIV transmission in early 1985.

Q. Yes. Can we go back to your statement, where the position in England is dealt with in slightly more detail, please? So that's going back to [PEN0171790] at paragraph 2. This deals a little bit with what I'm calling "product recall". Then paragraph 3. You say:

"The viral safety of this BPL product ..."

I think it's 8Y. We can call it that:

"... introduced in England in September 1985, was unknown at that time."

That may be strictly correct, professor, but was there not a kind of expectation that it would be safer in relation to blood-borne viruses than products treated with a lesser heating protocol?

A. I think that was a reasonable expectation but the history of heat-treating Factor VIII concentrates to try and destroy non-A non-B Hepatitis was not good, even heating up to 68 degrees. Clearly, going a little higher might destroy the virus or viruses but there was no certainty at all that 80 degrees would be effective and there was a lot of international scepticism about dry heat treatment at all at any temperature as being effective. If I recall correctly, the FDA was very sceptical about dry heat treatment, even at 80 degrees.

Q. Yes. You do go on to cover that. You talk about the response of the FDA. But I suppose, as the first building block in trying to recreate the atmosphere of the time, I was suggesting that, as soon as you heard about this, whenever you did, this product in England, you might be thinking, "Oh, that might be safe against hepatitis as well as against HIV."

A. Safer.

Q. Safer?

A. Safer, rather than safe.

Q. Now, just to look at that question of state of knowledge, can we look firstly please at [SNB0075664]? We can see that this is a meeting that took place at PFC on 17 March 1986 and some very familiar names are there representing SNBTS: Dr Perry, Dr Foster,

Dr Cuthbertson, and I think we also have heard of Dr Prowse and Dr Dawes and Dr Urbaniak, and I think Mr McQuillan as well, and then some the names from BPL: Dr Lane, Dr Snape, Dr Smith.

Can we just look through this at the topics that were being discussed: This, kind of, state of play, plasmapheresis. Then on, please, to the next page. Dr Cuthbertson is talking about his recent model virus studies. Then on to the next page, please. Do you see paragraph 5:

"Dr Smith outlined clinical trial results of the 8Y F8 product so far. While results cannot be considered conclusive at this stage, he indicated that no cases of virus infection have occurred attributable to 8Y material after 12 months' experience of 8Y in virgin haemophiliacs."

So, in response to your suggestion that it wasn't until mid-1986 that evidence started to be reported to suggest that it might be a hepatitis-reduced concentrate, it looks as though there was a bit of evidence before that.

A. It doesn't say how many patients, and we know that from this study not all the patients were not previously treated patients and also that the frequency of liver function testing met international standards; in other

words, once a fortnight testing.

Q. All right, perhaps we could agree that it is evidence and the question of the weight it should bear might depend on some of the factors that you have mentioned?

A. Yes.

Q. All right, okay.

I wonder, sir, it's 1 o'clock. Perhaps we can pursue this after lunch.

THE CHAIRMAN: Yes. Not immediately.

Professor, would you look back just for a moment at [LIT0010335], please? I didn't want to disturb Ms Dunlop's flow of thought but I do want you to think about this. I think it's on the next page, the passage that I'm interested in. Could you go to the next page, please, and we will see? No. It's the passage that refers to observation of raised ALT in the 1970s. Yes, 80s:

"The prevalence of abnormal liver function tests in haemophiliacs increase rapidly with the widespread introduction of Factor VIII and IX concentrates in the mid 1970s."

Professor, what I'm interested in is whether there were recorded increased levels of ALT and AST, or whatever, before that in two areas: One, your area, Southeast of Scotland, and the other, the Oxford area,

because in respect of each Dr Cash, in the one case, and Dr Biggs, on the other, reported the use of Cohn Fraction I throughout the 1960s. I think one might expect Cohn Fraction I to be, if anything, less pure than the Factor VIII that came in the mid 1970s. Could you think, please, whether there is anything that you can help me with in the way of information to understand whether there was a problem known at that time?

A. Not immediately.

THE CHAIRMAN: So we can rise now.

(1.02 pm)

(The short adjournment)

(2.00 pm)

MS DUNLOP: Professor Ludlam, just before we stopped for lunch, I was beginning to probe the extent of awareness in Scotland in 85/86, about the developments in England, and we did look at the minutes of a meeting in March 1986 on the topic. I think it would be helpful just to look at what you have said in both your statement and your appendix.

Now, firstly, the statement, which is [PEN0171790]. Looking at paragraphs 3 and 4, which are on the next page, just to let everybody read what you are saying there. (Pause)

We have you saying that:

"The viral safety, with respect to the transmission of non-A non-B Hepatitis, of the BPL severely heated product, was unknown."

You point to the fact that it only met the needs of about one third of the total use of Factor VIII in England and go on to say that during the period December 1984 to June 1986, there was no clotting factor concentrate available in Scotland or anywhere else in the UK which was reported and accepted to be hepatitis-safe. It was necessary to assume that all concentrates could transmit the causative agent, or agents, for non-A non-B Hepatitis. And after June 86 it was assumed 8Y was less likely to transmit non-A non-B viruses.

Then if we go to the appendix, [PEN0171798], at 1802, I think in particular we are looking at paragraph 9, so if we could go a little bit further down, we can see some more details surrounding your suggestion that it was really June 1986 that was a turning point in the realisation that this product might be safer.

I just wanted to look at one or two sources of information over this period. Could we look, please, at [DHF0017386]? That's a meeting of the Central Blood Laboratories Authority, central committee for research

and development in blood transfusion. It's obviously a body relating to England and Wales, taking place on 9 July 1985, and there is a reference to product in development in this.

Can we go on to the page after the next page?

If we go down the page, please:

"The immediate safety and efficacy of the 8Y concentrate have been demonstrated by clinical trial. Eight patients at three haemophilia centres receiving 14 infusions of three batches of concentrate have shown dose responses ..."

Certain figures, which Professor Lowe told us, meant that the product was acceptable in doing what you would want it to do from a therapeutic perspective. Then evidence for a reduction or elimination of viral transmission is being sought:

" ... after infusions in haemophiliacs who have been treated with concentrate, either for the first time or after a long interval, and who are thought to be susceptible to infection with Hepatitis B, NANBH and HTLV-III. This trial is at a critical stage but several patients have already safely passed the point at which the first evidence of NANBH transmission would have been expected."

A document, which I think really goes with the

minutes of that meeting, is [DHF0030476]. We looked at it with Professor Lowe. This is really, I think, a product information sheet from July 1985, issued by BPL and dated 24 July 1985. It's going to haemophilia directors in England and Wales. It's the same information: it has information about the heating, about the product and its performance and then a little bit further down about the clinical trials.

So there were already some optimistic indicators in the summer of 1985. I don't suggest for a minute that you were at the CBLA meeting -- I'm sure you weren't -- but you must have been hearing news from England, were you not?

A. I knew the studies were going on and I know that it is incredibly difficult to find true, previously untransfused patients and that these studies are very difficult to do because of that and because you have to get fortnightly samples and that often these turn out to be small children, and it's difficult for all sorts of reasons to get samples from small children.

I don't think -- I hadn't seen this last sheet that has disappeared from the screen. It was distributed to haemophilia directors in England and Wales. So I didn't receive that.

Q. I accept that, professor, but I think we have been

painting for ourselves a picture of the haemophilia doctors in Britain all being in close touch with one another, being professional colleagues who did share information, and it just struck me that perhaps this would have been mentioned to you at a meeting or in some conversation you might have had with a haemophilia director in England. Did nobody say to you in 1985 that the initial information coming through about 8Y was looking good?

A. I'm sorry, it's 25 years ago. These things evolve on the grapevine, if you like, informally. You sit next to someone at a meeting or you have a cup of coffee with them and they say, "I have had a patient who hasn't had an ALT rise after they got 8Y. It's beginning to look a bit promising." But exactly when I had these conversations, I'm sorry, I can't remember.

There was a general feeling. I put it at 1986 -- yes, 1986. And I suppose there was a certain amount of scepticism as I was hinting before lunch, about dry heat treatment and its efficacy. There had been so many disappointments with commercial dry heat-treated concentrate apparently killing non-A non-B viruses when tested in chimpanzees, but then we know, as you know, that it still transmitted.

Q. Yes.

A. So there was a lot of scepticism about, as I say, how effective dry heat treatments would be, however hot. This difficulty was really exemplified by the discussions that SNBTS were having, as to whether to go for a pasteurised product, wet heating, in a liquid state or whether or not to go for dry heating, and it was a bit of a knife-edge decision which way to go.

So some of us would want quite a lot of convincing that dry heat treatment really was going to be effective against this or these viruses.

Q. I certainly take your point, Professor Ludlam, that it must be near impossible to remember a conversation you might have had over a cup of coffee at a meeting with an English haemophilia director in 1985.

If we move into Scotland, however, we can see that Dr Perry mentioned these developments in a report he wrote in January 1986. Can we look, please, at [SNB0015469]?

Dr Perry is preparing this report for what I think you call the "joint meetings". I think we call them the "joint meetings" now as well, the haemophilia directors and SNBTS directors' joint meetings. This seems to be one that's coming up in March 1986, and the report has actually been written in January 1986 and he is talking about supply and demand, but he does go on to mention

developments in England, I think in section 3, if we can go forward to that, please:

"Heat treatment of coagulation factor concentrates."

A little summary of what has happened in Scotland and then that paragraph that you can see towards the bottom of the screen about awarenesses of what's going on at BPL.

Curiously, professor, you don't seem to have been at the joint meeting in March 1986. I think you are at every other one we have ever looked at but I don't think you were at that one. What would be the procedure? Would you have received the background papers even if you weren't going to be able to be there?

A. My recollection is I had sent my apologies some time in advance. I think the date of the meeting had been changed and I was disappointed that I wasn't going to be able to attend the revised time. So I wrote expressing my disappointment and I may not have received the papers because I wasn't going to be there.

Q. I see. It's information to the same effect really as the information we have been looking at in 1985 from English sources, except this is coming from Dr Perry and being disseminated to those attending the joint meeting. Just to look at the minutes of the joint meeting, it is, I think, 5 March 1986, [SNB0015448].

A. Would this not be commented -- Dr Perry not be commenting in this way as a justification for --

Q. For the Scottish plan.

A. -- for the Z8 being treated at 80 degrees?

Q. That's how it reads, yes. It reads as a piece of information that has been given in the course of description of plans in Scotland.

A. Yes.

Q. Yes, but nonetheless, it's a statement in its own right. It's a statement of the current position and there we see the list of attendees. Are you shown in the apologies? Can we go down, please? Yes, there we are. So, as you said, you have sent your apologies.

I don't think there is any mention in the minutes of the meeting of this information from England. In fact there is not much point in asking you about a meeting you didn't attend. So the statement seems to have been contained in the background papers, and I think you are telling us you are not sure whether you had the background papers or not. I think you are suggesting you didn't?

A. I may well not have.

Q. Yes. Can we go back then, please, to its appendix document, [PEN0171798]. We were looking at paragraph 9, which is on 1802.

You actually identified some other sources of information, which I think had actually encouraged you to think in terms of it being in June 1986, that you began to be aware of the apparent success of the English product. You say that some preliminary evidence emerged at a World Federation of Haemophilia conference in Milan in June 1986. Did you attend that?

A. No, I took this from the preliminary report.

Q. I see.

A. And I couldn't actually see in my electronic version of the preliminary report, the report referred to of the -- Jim Smith's paper -- it wasn't Jim Smith, it was -- I'm sorry -- someone else, who I think presented it --

Q. We are not going to be confusing each other, professor, because what I have been looking at is Dr Jim Smith's paper.

A. In Milan?

Q. Yes. Can we look at that? That's [SNB0075955].

I think in our preliminary report we quote this as being the source of information about proceedings in Milan?

A. Yes, you do. I just couldn't --

Q. You couldn't access it?

A. I couldn't access it on my electronic version.

Q. Right. I think we suggest that what must have happened,

and we are obviously just speculating but nonetheless, Dr Smith had prepared these notes of the different presentations at the conference and had shared them with colleagues in Scotland, who had perhaps not been there.

It does seem to me, having gone through this -- and I don't want to take up time doing so now -- that there isn't actually any paper referred to in Dr Smith's synopsis which covered the topic of progress in England. So perhaps a little bit of a conundrum. I was trying get at what you were meaning when you say in your statement that:

"Preliminary evidence emerged in June 1986 at a World Federation of Haemophilia conference in Milan."

That's why I was looking for a mention of it in this report of the conference, and I couldn't find it mentioned there.

A. I should have given my reference as the Inquiry's preliminary report, and when I clicked on the link, I got this description of everyone else's studies but not what the 8Y study was, so I was at a bit of a loss --

Q. Touche, Professor Ludlam. I think we understand the point you make; we will perhaps research that a little bit further.

The other reference you give is to a paper presented

to UKHCDO in September 1986, and the reference for that -- actually, sorry, before we leave this, could we just look at page 7 of this document? I didn't want to leave this document without pointing out that there is a reference in it to the Sheffield work. So since we are talking about liver disease, progressive liver disease in patients with haemophilia, I thought it was interesting to see that that was the agenda in Milan and we can see that there on page 7. It's the second entry.

Described here, whatever the paper was, it was somebody repeating the view of the Sheffield workers that biopsies were revealing an alarming level of progressive liver disease in haemophiliacs related probably to NANBH.

I'm sorry, I just wanted to note that before we left Milan. The reference to Dr Smith's paper is [SNF0011123]. Yes, I think this is the interim report you had in mind. Is that right?

A. That is correct, yes.

Q. Yes. We can see that this report lists those providing data and then it's shown that the data has been summarised on 30 September 1986 by Dr Jim Smith.

Then can we go over, please, to the text?

The introduction tells us what has led to the study, that there has been a protocol circulated and that

certain selection criteria have been applied to the patients. The frequency of testing is explained, products tested and then results.

I'll just let you read to the end of the results section. (Pause)

Can we just look at the little bit on the next page, please?

So, professor, you have mentioned this in your written answer, and this looks to have been more definitive information about the English product. Is that right?

A. I'm not sure that this is the report that was presented at UKHCDO meeting.

Q. All right.

A. This is dated 30 September.

Q. Yes.

A. And I think the UKHCDO meeting was a few days before that. I suspect this is a revision and it may well be the first draft of the paper that was eventually published in, I think, the Lancet, in 1988, to which I think there was additional patients -- we haven't got to the bit that says how many patients there are in this study. There were 32 in the 1988 --

Q. Right. Perhaps the next page has a table. There are two tables.

Can we go on to the next page? Thank you.

About 15 patients maybe? 16. Yes, 16 patients. So fewer patients than were eventually written up.

Then the final --

A. I mean, there are problems with this data. Patient 8Y5 had previously had cryoprecipitate, had an ALT level of 107. That is raised. I don't know whether it's two and a half times the upper limit of normal. The upper limit of normal might have been 40. So this is, I think, probably above two and a half times. It's -- one of the problems with this study is that there weren't strict fortnightly samples and there were sometimes long gaps after a high level with no other sample to corroborate it.

This is a patient who has been treated with cryo in the past. It could have been from the cryoprecipitate, it could have been from the 8Y. Another patient, 8Y/10, a few lines further down -- I'm sorry, I don't know what -- an AST of 66 -- I can't remember what the normal range for an AST is.

PROFESSOR JAMES: The same.

A. The same. So up to 40, so that's raised. Pre-exposure suggests another patient who is probably infected, either with Hep C from the cryoprecipitate, 35 packs, or has some other cause for liver disease.

MS DUNLOP: Right.
A. Then at the bottom there is a 9A patient with an ALT level of 102, without previous exposure, apparently, to a blood product. So one wonders why that patient has got a raised ALT.
THE CHAIRMAN: He is only five. It can't have been alcohol.
A. One presumes it wasn't.
THE CHAIRMAN: Certainly not self-administered.
A. There are all sorts of other causes apart from alcohol, particularly in children with febrile illnesses. This is interesting data, it is reassuring, but as Dr Kernoff said at the meeting at which this was presented, the minutes record, he says it was "soft" data. And even the 1988 paper was soft data, all 32 patients of it. That's why they started on a very thorough, proper study to conform to the 1987 guidelines.
MS DUNLOP: It looks as though possibly some patients were being included in the study who, in retrospect, had confounding factors attaching to them, or may have had.
A. Or non-A non-B Hepatitis was being transmitted by 9A.
Q. Well, I take your point, professor, that it's not perfect data -- or it's soft data, to use Dr Kernoff's words -- but I think we have also been told that it can be very difficult to recruit patients for a study such as this. So sometimes maybe the criteria were slightly

relaxed with consequent diminution in the usefulness of the some of the results.

A. That for the first study, yes.

Sorry, could I just say that this was in an atmosphere where there was a lot of scepticism about dry heat treatment. So I think it was very important the results were looked at very critically, and if dry heat treatment was going to be an effective way of destroying the virus, then it had to be proven very clearly, not just for the UK but internationally, for haemophilia care throughout the world.

Q. Can we go back then, to the appendix document, please? We were on page 5 of [PEN0171798].

You and I between us have been trying to paint a picture of information available and reactions to it in 1985 and 1986. You go on to tell us in paragraph 10 that:

"Immediately it was reported that 8Y may be a 'hepatitis' reduced concentrate, [you] requested, in July 1986, that a small stock should be available which could be used for treatment of virus naive patients in Scotland."

I think it would be helpful if we looked in a little more detail at what happened in Scotland in the summer of 1986, surrounding that acquisition of 8Y. Can we

look then, please, at [SNB0075869]? This is a letter from Dr Boulton to Dr Cash dated 1986, and you are mentioned in it. It concerns trials of Factor VIII products and clearly Dr Boulton is thinking of trials in Scotland; that's why he has been discussing matters with you.

The second paragraph is interesting. Dr Boulton tells Dr Cash:

"Apparently a few weeks ago he [that's you] was asking Brian McClelland if 8Y could be made available in the event of a 'virgin' haemophiliac being present. He tells me that he would be happy to treat such patients with a product prepared by the SNBTS that has been subjected to an 'equivalent' heat treatment regime."

Do you remember having a first conversation with Dr McClelland about this, about maybe trying to get some 8Y?

A. I think this is when there was the first discussion and I'm not so sure that -- it may not have been someone in blood transfusion who had passed on the latest information about 8Y that had been presented at that central blood transfusion safety meeting back in March, that you showed me.

Q. Yes, well, I suppose someone who had seen Dr Perry's report perhaps, that went to the joint meeting in March,

maybe. We are just speculating but it would make sense if it was something of that nature?

A. I think probably I had discussed with Dr McClelland the issue of the then current SNBTS product causing non-A non-B Hepatitis in patients, and it had come up in conversation that, you know, maybe 8Y was a better product from that point of view.

Q. Right. Even the information in September 1986, you are telling us, was soft. So information here that you have in your mind must be pretty soft, but you are still interested in getting some.

A. Yes.

Q. Because?

A. Because the evidence from the 8Y studies was that it appeared to be less likely to transmit non-A non-B Hepatitis, whereas it was highly likely that all bottles of SNBTS, then available concentrate, 68 degrees for 24 hours, was likely to transmit hepatitis. So it's a matter of degree.

Q. Yes. So it would be an improvement on what you currently had?

A. Yes, it might not be hepatitis-free but it might be less.

Q. Can we look at another letter, please? I think it's the same date, [SNB0075871].

This is Dr Boulton to Dr Perry. It is indeed 27 June 1986 and again, the letter features you. It mentions two patients, a virgin patient with Christmas Disease who received heat-treated Factor IX towards the end of 1985, who was continuing to show no elevation of ALT levels or other evidence of non-A non-B Hepatitis; and that Factor IX would be 80 degrees, 72 hours --

A. That's correct.

Q. -- heat-treated?

A. Right, from August -- available from August 1985.

Q. Right. So interesting for Dr Perry to know that.

A. Yes.

Q. And then in the second paragraph, that:

"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. However, the patient is apparently quite well clinically."

Professor Ludlam, one of the things which has struck us about the letter is the use of the unusual word.

It's perhaps not in everyone's lexicon. Were you ruthful?

A. I was a bit sad that we didn't have 8Y to give to the patient.

Q. Right. So you are not disagreeing with Dr Boulton's characterising of your feelings on the matter?

A. No.

Q. Right. Can we look next, please, at [SNB0075909]? This is Dr Perry writing to Dr Boulton and thanking Dr Boulton for passing on your comments about Factor VIII, and Dr Perry is, obviously, focusing on the developments in Scotland and what he is anticipating might happen:

"Scotland is poised to introduce yet another Factor VIII product, which will be heat-treated at 80 degrees for 72 hours and should therefore be comparable to 8Y and better than anything available commercially."

And Dr Perry is anticipating that:

"As soon as this becomes available, virgin patients will be able to gain access to this product before stocks of the existing product are exhausted."

The next letter we need to look at is the next in number, [SNB0075910]. This is still on the same topic, that is what is to be expected in Scotland over the next

few months.

THE CHAIRMAN: Have we got the right letter?

MS DUNLOP: Yes, it's Dr Boulton back to Dr Perry and it's enclosing notes of a telephone conversation, which we do also have but it's handwritten, and in our preliminary report we have reproduced it in typewritten form.

So I was going to look at that because it's easier to read, and that's [LIT0012718] at page 82. There it is. In the hard copy it's page 506. Can we just look at that table, please?

So Dr Boulton wrote to Dr Perry with manuscript data thought to reflect a telephone conversation between them on future production, and we can see that Dr Boulton has sketched the whole thing out, you know, what is to be looked forward to by way of new production in Scotland.

Interestingly for our purposes, on the bottom right-hand corner of the table is a statement that from about September 1987, the PFC version of 8Y will be produced:

"Hence half-life and recovery studies + NANB et cetera on 'virgin' haemophiliacs are required."

Then a line along the bottom:

"In the meantime, any Edinburgh virgin haemophiliacs requiring therapy could be given BPL 8Y."

So the idea is definitely circulating at this time

of trying to obtain a stock of 8Y for a particular category of patients, if we can put it like that for the moment.

A. But it was also the plan that there would be an 80-degree, 72-hour product starting to be produced in September 1986.

Q. Yes.

A. So not waiting until the box in the bottom right-hand corner --

Q. Yes, indeed, I take your point that there is a difference between when there might be some available for certain patients and when it is the product available generally?

A. No, I think the bottom right-hand box is a phase 4 product. That is a new formulation of Factor VIII, what they described, I think, as "phase 4" in the original diagram.

Q. Right.

A. The phase 3, the one that starts in September, I think was Z8.

Q. Right.

A. Okay? I think the one on the bottom right-hand corner was going to be a higher purity, new product, completely different.

Q. Right. Let's look at the handwritten version,

[SNB0075911].

A. At the bottom of this screen -- oh, sorry.

Q. There we are. It doesn't actually mention a phase 4 but that's your recollection --

A. On the previous screen, just below the diagram, there was some text that mentioned a phase 4.

Q. Right.

A. If I can go back to that.

Q. Okay. Can we go next to [SNB0075913], please? There we are.

This is Dr Perry to Dr Boulton on 7 July 1986. The heading is "Factor VIII trials", and Dr Perry appears to be thanking Dr Boulton for the handwritten table. He goes on to make a couple of comments about the phase 4 product, as you pointed out. The manufacturer can't resist adding that the product is more than equivalent to 8Y; it's much better. But in the second paragraph, Dr Perry turns his attention to the needs of the moment. He says:

"While there will be no PFC product virucidally comparable to 8Y until September 1986, after that time it would be my intention to supply the phase III product to 'virgins' since we hope to demonstrate by that time that it is virucidally equivalent thus removing the need to go South. However, in the immediate future

(July-September 1986), we could probably get supplies of 8Y for special cases. It would of course be preferable if these were obtained and supplied through PFC."

Just seeing what happened about that, the next letter is [SNB0075914]. This is Dr Boulton again. He is writing Dr Perry on 7 July 1986, and now the focus is actually on the interval before some Scottish product is available.

Dr Ludlam has written to Dr McClelland asking if it will be possible to obtain some of the BPL products. This is for use if a previously untreated haemophilic presented for replacement therapy. Difficult to estimate his potential use accurately.

I should say we have looked for this letter but I don't think we have it, but we get the general gist of it from this one, as it were. We have looked for that letter, I should say, to make it clear.

Dr Boulton has some reservations about the sorts of quantities which could be requested and perhaps granted from BPL. There is a bit of debate about that.

Dr Boulton is wondering if Dr Perry can get perhaps 50 vials. And his thinking on that is that:

"50 vials would at least enable us to cover the initial injection for such a case, and if the need were to arise to call up more from Oxford over the course of

24 hours or so."

And [SNB0075980], please, which is now the involvement of BPL to Dr Perry on 24 July 1986. The BPL response has been that they are willing to supply 8Y but they would like also to get some information about any data that you obtain by using it.

A. That's correct, yes.

Q. Which seems a reasonable enough request, doesn't it?

A. Yes.

Q. Yes. There is some flexibility here. This is Mr Pettet from BPL. He is saying that he has put aside some 8Y for immediate dispatch to PFC and he has done so because there might be some patients who don't strictly meet the criteria for trial.

Then [SNB0075982]. Dr Perry reports back to Dr Boulton, 24 July 1986. BPL are happy to supply 50 vials, and they ask in return only some information on what happens when it's used.

Then [SNB0075984]. Dr Perry back to Dr Smith at PFL, accepting the offer.

[SNB0075986]. Dr Perry to Mr Pettet, 28 July 1986, firming up the arrangements and that the supply is conditional on users participating in the clinical trial. Although we have noted that Mr Pettet wasn't insisting on that, he was saying you might need it for

patients who don't, strictly speaking, satisfy the trial criteria.

So the 50 vials are coming as a contingency stock of non-infective material in the unlikely event that a virgin haemophiliac presents for treatment in the near future.

[SNB0075990], please. 1 August. Dr Smith to Dr Perry:

"I am sending attached 50 vials of 8Y, in case you wish to protect category 1 patients before your Z8 is ready."

Category 1 patients? Is that some sort of English designation? You don't recognise the term?

A. I don't recognise the term but I would guess it's patients who have never previously been transfused with blood or blood products.

Q. Right. [SNB0076022].

THE CHAIRMAN: I was just looking at the last paragraph, suggesting that the discussions had lit some very long fuses. Were you expecting some sort of explosion in the future? It's just a comment.

MS DUNLOP: Right. [SNB0076022] I think we were at. Yes, thank you.

That's Dr Perry asking Dr Boulton to let him know the batch of Factor VIII involved in the transmission of

NANB hepatitis to Dr Ludlam's virgin patient:

"While this outcome of treatment is not surprising, we need to know the batch number and dose to keep our surveillance cross-referencing records complete."

[SNB0076024]. Dr Perry to Dr Boulton on 5 August 1986, saying that:

"The 8Y has now arrived from BPL and I have sent 20 vials to your centre. There is more here if you need it. I enclose the BPL trial protocol and pro forma for clinical data, since it has been supplied on the strict understanding that data will be collected if the product is used."

Just to finish this sequence, [SNB0076048]. This is Dr Perry bringing Dr Boulton up to date on 7 August 1986 to say that:

"PFC have now successfully manufactured two batches of a heat-treated Factor VIII, treated at 80 degrees for 72 hours, and they are looking to make it available for clinical trial at the end of August/beginning of September."

So a new Scottish product more severely heated is definitely on the way, and I don't want to go too far into that because that's our next topic, but we have looked at that little chain of correspondence from the summer of 1986, which resulted in the obtaining of 50

vials of BPL 8Y. PFC obtained it and they sent you 20 -- well, not you but they sent to Dr Boulton, 20 for storage in the Edinburgh transfusion centre.

Can we then please go back to the appendix document, [PEN0171798]. And at paragraph 10 there is your summary of the request for the 8Y and the grant of that request.

Professor Ludlam, we have looked at a lot of material and it certainly seems, particularly from the early letter in that sequence, 27 June 1986, as though you had first mooted the possibility of getting some 8Y some weeks before the date of that letter, which is 27 June 1986. You said you thought that might have been that you had heard something perhaps from Dr Perry's report or one of your colleagues in Scotland about the 8Y product.

The circumstances in which a patient had been treated with Scottish heated concentrate and appeared to have developed symptoms of non-A non-B Hepatitis, did that, as it were, resurrect that thought in your mind? You might have had it a little before, that it would be an idea to obtain some 8Y for patients who had not previously been exposed and then that very thing happened: someone was given treatment and developed symptoms of non-A non-B Hepatitis. Did that sharpen your focus on trying to obtain some 8Y?

A. To be honest, I'm not certain which way round it occurred. I think it was in my discussions with the blood transfusion colleagues after it had happened, that the real potential, possible extra safety of 8Y was being highlighted in my mind.

There was the view around that England was desperate for every bottle of 8Y it could get. It had been very deprived of heat-treated concentrates, NHS heat-treated concentrates, for the first two thirds of 1985, when there was all the anxiety about HIV transmission, and there wasn't a BPL product that was heat-treated, unlike we had in Scotland. They had unheat-treated commercial concentrate and so there was a big -- I'm not sure it's the right word -- yearning to have a heat-treated NHS concentrate in England.

They were feeling this was really very important, and I got the impression that every bottle of it was being treasured and valued and I wasn't at all certain, even if I had wanted some, I would have been able to get some, and I think that's why we went through the Bob Perry formal SNBTS channels, because that was likely to carry greater leverage than if I had written as a single clinician to BPL.

So I'm sorry, I can't remember exactly how the sequence of thoughts went. But certainly this sad

episode of a patient susceptible to non-A non-B had acquired non-A non-B who had highlighted the issue.

Q. If it had been you personally looking after the patient concerned, and if you had had a stock of 8Y already there, would you have used it?

A. In June 198 --

Q. I think we are actually talking about May 1986?

A. May 1986?

Q. Yes.

A. If I had had 8Y available in the fridge and I had personally been assessing someone who I thought should be treated with a clotting factor containing Factor VIII, then I think I would have been very tempted to use it.

Q. Yes. It sounds as though your purpose in the summer of 1986, in trying to get some 8Y, was for just such a patient?

A. Yes.

Q. Can we then look at paragraphs 11 to 13, and I think we can take this quite shortly.

You have mentioned the uncertainty which was present in 1986 about the efficacy of dry heat treatment. You have mentioned the FDA. Although they seem to have had something of a change of heart.

A. Two years later.

Q. Yes. Then you have gone on to talk about Z8 and as I have already said, we are not quite there yet, so I am afraid that will have to wait for your next appearance.

Can we then go back, please, to the statement? That document is [PEN0171790].

We were at the second page and in paragraph 5 you are again talking about Z8 and in paragraph 6 you draw a contrast with the position in England. I suppose, if we are comparing Scotland and England at this time -- and that's an exercise in which we do fairly often indulge -- we have one country with enough heat-treated product but not quite severely heated enough, and the other country with product which is severely heated enough but not enough of it.

A. For some of the time.

Q. For some of the time.

Much of the next section of your statement has already been covered. You talked here about the aim of preventing HIV transmission, which we understand. You mention the circular of 14 December 1984 by Professor Bloom. Paragraph 8, I think we can move over. Then on to 9, which is entitled "Risks/Benefits of Cryoprecipitate".

You tell us, professor, that:

"Once the lifetime patient exposure to

cryoprecipitate reached approximately 100 donors, about five infusions in an adult, the risk of non-A non-B Hepatitis approached 100 per cent."

That is taking a 1 per cent incidence, is it?

A. It is, and perhaps I'm a little pessimistic. Perhaps we could make it 200 donors, but whether it's 100 or 200, you get there very quickly.

Q. Yes, I think we can perhaps cut matters short because that was going to be the next bit.

We have looked, and we don't need to do so now, at a paper by Minor and others, which gives an incidence of 0.4 per cent. We have also looked at Professor Thomas's map of the world, where we can see a different incidence as between North America and the United Kingdom. North America is green and the United Kingdom is blue, denoting that the incidence in North America is at least double what it is in the United Kingdom, although that map is 1999.

You go on, slightly lower down, to talk about the relative risks that, certainly in the period until October 1985, donors were not tested for HIV, HTLV-III antibodies, as I suppose it would then have been called. So there is that problem, and then we also understood about the window period, which even the introduction of screening in October 1985 did not meet.

You go on to say:

"During the period 1984 to 1987, if only a single or very occasional treatment with a blood product was required, it could be argued that cryoprecipitate was safer with respect to non-A non-B Hepatitis, than heat-treated NHS concentrate. The disadvantage of cryoprecipitate, however, was that it was not heat-treated and therefore could transmit HIV."

We have already looked at Professor Lowe's article with Professor Lowe and I thought perhaps I would ask you just to look at it too. It's [SNB0015523]. I expect you have seen this before too, Professor Ludlam?

A. Yes.

Q. We know that Professor Lowe had been asked to submit an article on AIDS and haemophilia for an edition of the Scottish Medical Journal which was devoted to AIDS, and this is his contribution.

The particular passage begins at the bottom of page 2, if we could go to that, please. He is looking at different therapeutic options. He lists various precautions which can be taken to prevent further HIV infection of patients with haemophilia. Firstly the screening of donors. Well, donor selection, I should call it. Then secondly, clotting factor concentrates

have been heat-treated since 1985.

Sorry, to be strictly accurate, the first option is both selection of donors and screening of donations, the second, heat treatment of clotting factors, and then can we go on to the next page, please:

"A third means of reducing the risk of HIV infection is to use lower risk treatments than clotting factor concentrates where possible. This policy should also reduce the risk of viral hepatitis, which is not prevented by heat treatment of concentrates."

I suppose -- and I'm conscious that Professor Lowe is still here -- one might, if one were being pedantic, slightly challenge the wording of the first sentence because, so far as HIV risk is concerned, the fact that all NHS concentrates in Scotland were heat-treated might mean that it wouldn't necessarily be a way of reducing the risk of HIV infection to use other products.

So if one were thinking solely of HIV infection, the use of something like cryoprecipitate, as against a heat-treated clotting factor, might be debatable but certainly, as far as hepatitis is concerned, he is making the point that there are other treatment options, including cryoprecipitate, fresh-frozen plasma, desmopressin, and so on.

Would you agree with the views that he is

expressing?

A. I would just add that cryoprecipitate only reduces the risk of viral hepatitis if you give treatment or a therapeutic dose from a few donors.

Q. Yes.

A. If you give --

Q. If you are up at 200 donors?

A. An average adult dose is from 20 donors. If you give it twice a day, that's 40 donors you have been exposed to in a day. So if you give a course of treatment for five days, you have almost certainly got non-A non-B Hepatitis at the end of that. But if you need to give just a single treatment on one occasion, then the risk of hepatitis will be less.

Q. Yes.

A. But you might give single treatments on different occasions, spread out over several years, and that is still cumulative.

Q. Yes.

A. But for a single treatment occasion cryoprecipitate has a lower risk of transmitting non-A non-B Hepatitis than most of the heat-treated concentrates.

Q. Right.

I'm conscious, sir, that it's quarter past three. I do have a few more questions for Professor Ludlam and

perhaps rather than rushing them, it might be an idea to have a break now?

THE CHAIRMAN: I don't want to be rushed. I think it would be better to have a break.

MS DUNLOP: Yes.

(3.15 pm)

(Short break)

(3.36 am)

MS DUNLOP: Professor Ludlam, just one or two more questions. In your statement, [PEN0171790], at paragraph 10, which is on 1793, you address the question of numbers and there is a relevant passage in the preliminary report. We have actually already looked at this but just to have a quick look at it again. It's pages 328 to 329 in the preliminary report, which is [LIT0012543] at page 79.

It's this little section between 9.323 and 9.326. We can see that in 2000 there was some exploration of different statistics, the number of Hepatitis C positive haemophilia patients for the different centres, and then 9.325, on to the next page, deaths since 1 September 1985.

Then 9.326, 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. Some

figures are given: 18 for the East of Scotland and 13 for the West of Scotland. Do you happen to know, Professor Ludlam, if the East of Scotland goes all the way to the top, as my learned friend puts it. Does that mean Edinburgh, Dundee, Aberdeen or does it mean just your centre?

A. It means to Kirkwall and Shetland.

Q. Right, yes.

THE CHAIRMAN: I think that's certainly what it was intended to mean because 9.324 in brackets does have a definition of the east coast centres.

MS DUNLOP: East coast centres, yes, right.

THE CHAIRMAN: And that is the way it was looked on in fact, is it, professor?

A. Yes.

MS DUNLOP: Right. Can we just go back then to the statement, please, 11, therapeutic options you have set out.

On to the next page, please. This is obviously during this period, December 1984 to May 1987; children with severe or moderate Haemophilia A were treated with cryoprecipitate or heat-treated Factor VIII and we understand the relative risks of the different products.

In making that choice between cryoprecipitate or heat-treated Factor VIII, would that depend on factors

peculiar to the individual patient and the individual situation?

A. It would depend upon the frequency of treatment. There are some moderate haemophiliacs who bleed very infrequently, usually come up to hospital for treatment and one might give them cryoprecipitate. There are other patients with moderate haemophilia who would bleed really quite frequently and we put on to home treatment, and that's often the trigger for putting them on to concentrate.

Q. During this period, if you had been dealing with a small child and the Factor VIII levels had been very low or quite low, so I suppose severe or moderate, would you have wanted to try cryoprecipitate first, because I suppose you don't have an idea at all how frequently this child is going to bleed?

A. You mean the first time they present with a bleed?

Q. Yes.

A. One would probably have treated them with cryoprecipitate. Having said that, there would be some haemophilia centres who would treat them straight away with concentrate for reasons that have been thought about here before, because they are going to get concentrate after a very short while, in terms of years, they are going to get Hepatitis C out of the

cryoprecipitate after they have received a few infusions.

Q. I suppose, though, what might be in the mind of a treating clinician would be that this is, one would hope, a short period until a safer concentrate might become available. So it might be a question really of tiding them over until a better product arrived?

A. I'm sorry, thinking about this particular period, yes, there is a slightly stronger argument for using cryoprecipitate.

Q. Yes. And then when you talk about the risks that attend cryoprecipitate, you mention the potential risk of HIV, as it was an unheated product, but the magnitude of that risk perhaps would be low because it would mean, if cryoprecipitate transmitted HIV, after October 1985 at any rate, when the donations were screened, it could only be because an infected donation had somehow got through, either because the screening test had failed or because the donor had donated in a window period?

A. Yes.

Q. Yes. In this period, the end of 84 to 87, with patients, would you have been taking the patient into the discussions with you? So with children, would you have been discussing it with the parents and with older patients, discussing it with the patients themselves,

all these different possibilities?
A. Yes.
Q. Right. And trying to explain to them in a way that they could follow what the relative risks were?
A. I hope so. That's what we intended to do. Over the period 1984 to, say, 1988, a slightly longer period, cryoprecipitate was used decreasingly often.
Q. Right.
A. Partly because we were able to offer, I think, better home treatment service and get people out of hospital and not having to come up to hospital.
Q. Right. Did you continue to stock it, though.
A. Oh, we stocked it, yes.
Q. Right. Then you set out under the heading at (b), the options for those with mild haemophilia and von Willebrand's disease, and I think we recognise these: to manage without the use of a blood product, and you remind us of the increased trouble that patients can experience if a bleed is left for a while untreated. DDAVP, I think we have talked about a lot already, and we have had the views of Professor Lowe on this too.
Onto the next page: another option, cryoprecipitate occasionally for treatment of Haemophilia A or heat-treated Factor VIII, and then you are saying that after August 1986, 8Y was available for virally naive

patients presenting with a major bleed. When the initial stock was used up, a further supply was obtained from Newcastle. So obviously you did use those 20 vials?

A. We used them, not in a previously untransfused patient but I think in another patient who had allergic reactions to the Scottish product.

Q. Right. What happened to the other 30, do you know? Did you get them in due course?

A. I suspect we used those and when those were used up -- I'm sorry, I don't know, you would need to ask blood transfusion issue departments.

Q. Don't worry.

You have talked also in paragraph 12 about the therapeutic options for Haemophilia B, and we understand that a slightly different picture obtained there. We know that there was the gap between December 1984 and October 1985 for Factor IX?

A. Could I correct this? It is in fact August 1985 --

Q. Right.

A. -- that it became available.

Q. Yes.

A. The middle of August.

Q. Right. And we actually know that in Glasgow in April 1985, they decided to buy heat-treated

commercial Factor IX. You didn't do that?

A. No.

Q. Just on this whole question of the different options for treatment -- and this has obviously been a difficult and anxious exercise, trying to define different therapeutic options and point out the advantages and disadvantages of each and in what patients one might be more suitable and so on -- can I ask you to take a look at the transcript, and I would like to go back to May, when you came to give evidence, in block 2. Transcript TRN0010018.

THE CHAIRMAN: Which day is it, please?

MS DUNLOP: This is 3 May.

THE CHAIRMAN: No, which day? It helps me to find the material if I know the day. 18?

MS DUNLOP: Day 18? Right, thank you.

On Day 18, when you were, I think, giving a much bigger contribution than you had on the previous visit, when you had only talked about statistics. We took some basic information from you. Can we go to the third page, please? I think at this point I'm going through your CV. Anyway, looking at about line 10, there is a question:

"... referrals from other Scottish centres with which you worked closely, and there is a, I think,

elsewhere, in relation to networking of systems, mention of the East of Scotland. Are you in Edinburgh connected to centres in Dundee and Aberdeen? Is that right?

"Answer: Yes, we are the comprehensive care centre for the East of Scotland ... "

We are back to how far up does it go and you tell us it goes to Dundee, Aberdeen and Inverness:

"So Glasgow doesn't have a tertiary function in relation to any of the other centres in Scotland, I suppose, apart from Yorkhill?"

You go on to say that the situation is a bit flexible. Some patients come by plane and it depends a bit where the plane lands, but you say:

" ... in general, for administrative reasons, I have responsibility for trying to provide the service in the East of Scotland ...

"Question: Is that a longstanding arrangement that you have additional, as it were, tertiary responsibilities for the centres further north?

"Answer: Yes, that's a longstanding arrangement."

Then if we look at 62, we can see another reference to this status as reference centre, and I'm quoting from some minutes where unofficially Glasgow and Edinburgh acted as reference centres. This is 1980.

Let me just go a little bit further down. You said

you were keen that Edinburgh and Glasgow were seen as reference centres, you were part of a UK arrangement for overseeing haemophilia treatment. What steps did you take during this period, end of 1984 to 1987, to give guidance to people in Dundee, Aberdeen, Inverness and points beyond?

A. The position of haemophilia centres in Scotland has been a slightly unusual one, as I pointed out in these quotations. Edinburgh and Glasgow were keen to be seen as reference centres, along with similar services in England and Wales, so that we could be a part of the network and keep in touch with what was happening elsewhere in the country.

There was quite a lot of discussion about -- particularly with the Scottish Office, you may recall, about what our position was because in the original health circular, all the haemophilia centres were seen as equal centres, and so there was not quite -- in those days -- and this was before we started having regular meetings -- the centres in Scotland, I think, were seen as part of a UK network.

Q. Yes.

A. More so, I think, than, if you like, a network of centres in Scotland. And it was a way of addressing this situation, amongst a number of other things we

wanted to progress, was setting up what started out as the Factor VIII working party in 1988, and that progressed into a more general working party for the exchange of information and views about how haemophilia services should be managed and what products were available, and so on.

Before that, the centres were much more independent, standalone centres and there was not a great deal of interplay between them. Occasionally I would get a phone call about a difficult patient or something that was causing a difficulty or a problem, but there weren't regular meetings like there are now, where we meet every two or three months.

Q. Right. You did use the word "overseeing" but it seems, from what you are now saying, as though, at least in the mid 1980s, it was more of a reactive role. So if somebody phoned you up for advice, you would be happy to provide it?

A. Yes, I think it evolved from being very separate, individual centres until the mid-1980s and, as a result of the development of all these new products and the need to test them, for one reason, brought us together to collaborate more.

Q. Right. That document, the December 1984 document, which you have told us was really written by Professor Bloom

but which was the product of discussions amongst the reference centre directors, how would that get to Dundee, Aberdeen and Inverness?

A. From Oxford.

Q. Right. So you didn't take any part in issuing guidance or advice proactively to the other centres that, at least nominally, were underneath you. You were a tertiary centre and they are secondary. You didn't take any part in distributing guidance or advice to them?

A. No, the information was not cascaded down through us in Edinburgh to other centres; it came directly from UKHCDO secretariat in Oxford, who sent all these circulars that had been discussed, even the ones that had been addressed to me personally, in fact, had my name typed in because they were carefully done, they all came to each of 100 haemophilia centres in the UK individually.

Q. Okay. So, just to take it one stage further, how would a doctor in a small hospital in, say, Stornoway, get their guidance?

A. They would -- there isn't a haematologist in Stornoway, as far as I know.

Q. No, but there will be people with haemophilia?

A. Yes, absolutely. They, as individuals, once diagnosed, are, I think, usually looked after in Glasgow because

the flights go from Stornoway to Glasgow Airport, although they may get -- may have had some link with Inverness. They got their supplies of Factor VIII, when it was supplied by the Blood Transfusion Service, from Inverness on the bus and then the ferry.

Q. Right. Okay. But Oxford isn't going to send the guidance advice to Stornoway, so how, physically, is the hospital in Stornoway to receive advice on which it may have to draw if it has to deal with a patient with haemophilia?

A. If it has a patient with haemophilia, it would -- the clinician in Stornoway would either use his best judgment or he might get advice from -- by telephone from Inverness or Glasgow.

Q. Right.

THE CHAIRMAN: Professor, did you have any authority over any other haemophilia clinician in Scotland at this time?

A. No.

THE CHAIRMAN: And no one would have been obliged to ask you for instructions or for advice? Is that the position?

A. I think that's correct, yes. If they wished to, they could but I certainly couldn't dictate what went on in any of these other centres.

MS DUNLOP: Indeed. So what then is the point of Oxford

sending the guidance document to all the centres? If everyone is autonomous, what's the point of sending the guidance document around? It's to help, isn't it?

A. It is to help. It's for guidance.

Q. Yes, right.

THE CHAIRMAN: But of course, guidance only managed to break out of the meeting of the haemophilia reference directors if they all agreed, because otherwise they didn't have any authority over each other, did they?

A. I think that's fair. We worked on consensus. There were always people -- there was a range of therapeutic practice and a range of views, and that was played out in the country.

MS DUNLOP: Yes, but we have seen that from time to time -- and this is obviously a good example because it was a very serious situation -- it was possible to publish a consensus document, no doubt recording, as that one does, that individual circumstances will have to be assessed by individual directors, but sketching some broad parameters and perhaps explaining different options that might be available.

A. Yes.

Q. So really, for a centre in a remote part of Scotland, if one can call it that, perhaps a less populous part of Scotland, which is not a haemophilia centre but which is

suddenly confronted with a person with haemophilia who needs treatment, there isn't necessarily any guidance on which they can immediately draw because it's unlikely that anyone has sent it to them, or if they have it will be a sort of initiative of any particular individual, and I think what you are telling us is that the person in the less populous area, the clinician, is going to have to ring someone to get advice. So it's really dependent on their initiative in making contact with somebody.

A. Well, it usually depends upon the clinical circumstances. If a patient gets off the ferry in Stornoway, a known haemophiliac, knows what his treatment is and has an ankle bleed and goes to the hospital and asks if they have got some of that treatment they have in the fridge, then it's fairly straightforward.

Q. Yes.

A. The physician may have experience of treating other patients with haemophilia in Stornoway. I'm sorry, I don't know.

Q. I think I'm just suggesting, professor, that it might happen that a generalist, as all doctors in very remote hospitals have to be, maybe in Stornoway or Kirkwall or Lerwick, it might have been a while since they last saw

a virgin haemophiliac patient and they might need a bit of help.

A. It is likely that they may never have seen a virgin, non-transfused haemophilia patient because there are so very few, as we have been discussing. We see about one a year in --

Q. So it's not a common occurrence for you?

A. It's not a common occurrence for us and it would be uncommon, as a new patient, in somewhere like Stornoway.

Q. So in that situation, although obviously we are purely talking hypothetically, you would think it would be quite likely that such a doctor would want to seek some advice?

A. Probably.

Q. Yes.

THE CHAIRMAN: I'm quite worried. Professor James is pointing out that to get effective advice, one has to imagine, for example, taking a blood test, sending the sample to the mainland to find out the Factor VIII level before he could even begin to ask relevant questions, if he understood what the relevant questions might be.

It is quite worrying, you see, I think that is what is coming over from Ms Dunlop, not just in Scotland but in the west, remember the last time we raised this --

MS DUNLOP: Yes, Devon and Cornwall.

THE CHAIRMAN: Yes, where one has remote communities, quite capable of having haemophilia patients within them, they may not have available locally the resources necessary to ensure effective and prompt care of their patients.

Was there a mechanism? The answer appears so far to be not much, if any, Professor Ludlam.

A. Yes, I'm sorry, I don't know enough about the laboratory expertise in Stornoway, as to whether they can measure Factor VIII levels, for example. But if there was a small child presenting with a bleed that was thought to be haemophilia, well, maybe they would be transferred to Inverness, would be the sort of usual -- or flown to Glasgow.

Q. Right.

THE CHAIRMAN: Nowadays we would expect them, I think, to go in the helicopter just because the risks would be there and one would wish to counter them, but perhaps in the period we are thinking about, it might have been Caledonian MacBrayne, and that would only be if it was running given the weather. Not a happy situation.

A. I think it would have been possible to get a child out of Stornoway, to either Inverness or Glasgow, within 12 hours.

THE CHAIRMAN: Right, and would that be, in your view, a sort of sufficient period in most cases or all cases?

A. I think so. The child would be jolly uncomfortable and distraught with a swollen knee joint probably, but if you haven't got a Factor VIII or Factor IX measuring facility in your laboratory, and they may or may not have, then you can't make the diagnosis.

MS DUNLOP: Yes.

A. Maybe they can measure clotting factors in Stornoway, but even then they may not do them very often, and therefore the reliability of the result might be not as good as it would be in a laboratory that's doing a lot of them.

Q. Yes. I mean, these centres of population, Stornoway, Kirkwall, Lerwick and so on, they do have hospitals, of course they have hospitals but necessarily, the clinicians who staff them have to know about a very broad range of different medical conditions because I suppose they never know what tomorrow might bring. So the chances of them being very up to speed on haemophilia care might be slightly less.

A. All the more so because it is increasingly being centralised into haemophilia centres.

Q. Even in the mid 1980s?

A. Even in the -- well, we heard several months ago, in this forum, about patients coming from outlying hospitals into -- particularly Glasgow, and the same

thing happened in the East of Scotland, into centres that were more used to dealing with the patients and therefore hopefully could offer a better service.

Q. Yes. Professor Ludlam, it's five past four, so I'm only going to ask you about one more thing.

I said we would be coming back to this and it's the whole notion of recall. Dr Perry has drawn to our attention a terminological problem, in that I think he would prefer if we used the term "exchange", and we do know that the first such exchange occurred in December 1984, when unheated product was recalled and replaced with heated product. He has provided information on this topic.

Can we just have [PEN0120866], please?

THE CHAIRMAN: While that's being obtained, your question actually put together the two elements of an exchange that I would have thought were proper, and the first was recall. Is there some significance in the substitution?

MS DUNLOP: To be fair to Dr Perry, who isn't here, he says:

"The term 'product recall', when applied to pharmaceutical and other products, normally describes actions taken in response to the discovery of a known or suspected defective product. In this respect, the actions taken by SNBTS are better described as 'product exchanges'."

THE CHAIRMAN: All right, if it's that sort of worry he has, we might well just accommodate him, but I have to say, it doesn't seem to be the most important thing that I'm going to have to think about. Yes, "product recall", one knows, is used in a particular context.

MS DUNLOP: This document deals with more than recall of stocks but just to look at the third page from here, there is a table, which is quite a useful summary of what happened. We see "superseded products" shown and then "New product", "Product exchange/recall", "Rationale" and "Comments".

Because it's late, just to summarise what seems to have happened, that in December 1984 there was a like for like exchange, or a like for unlike exchange. There was a return of unheated product and a replacement with heated product. When the change was made to product heated for 24 hours, rather than product heated for two hours, there wasn't initially an exchange but there was, in the autumn of 1985, a recall, an exchange, and I think, rather than asking you about the details of this, which are all set out for us, I just wanted to find out from you, as a haemophilia director, how physically you got the product back.

A. In December 1984 I contacted people and asked them to bring back their unused, unheated product.

Q. So someone telephones patients?
A. Yes.
Q. Not you?
A. Not me fortunately --
Q. Someone in your department?
A. Yes, probably our haemophilia sister. And I have actually looked at the records for this month recently.

The new product was first issued on 14 December, so all product issued after 14 December was heat-treated. The two hours, 68 degrees.

There was actually very little product brought back because Factor VIII was so scarce that we only issued home treatment batches of ten bottles at a time, which was about enough for three treatments, and so a patient might use that up in a fortnight.

Q. Right.
A. So by the time we phoned them, they said, "I have only got one injection left and I need that now because I'm bleeding," or, "I might need it before I can come up next week, or whenever, to get the new product," but everyone had new product with them by 28 December. So for a two-week period everyone had been issued with new product.
Q. Right. And was that same sort of approach followed on subsequent occasions, when an exchange was being

arranged, that contact would be made with the patient by somebody in your department and they would be told, asked, to bring their product in and exchange it for the new and better product?

A. Yes.

Q. Is that right?

A. Yes. The line at the bottom about DEFIX, I appreciate -- and I'm slightly hesitant to suggest that Dr Perry's dates are not correct because blood transfusion has got exceedingly good records, but we actually did start to receive heat-treated DEFIX on 9 August.

Q. 9 August. I'm obliged.

A. And that was issued to everybody thereafter.

Q. Right. I should say, sir, that I do intend to go through Dr Perry's statement on this. Dr Perry isn't coming. We have given him a rest for the moment, but he has supplied written information which I will be drawing to your attention on this topic.

It was really only, Professor Ludlam, that since you were more at the sharp end of the recovery of stocks from patients, I wanted to establish from you how that was actually effected.

THE CHAIRMAN: Could I ask you one supplementary question: what about Aberdeen and Inverness? At the stage of

recall, did you have any part to play in recalling products from other centres?

A. Oh, it was an agreed national arrangement.

THE CHAIRMAN: Yes. So far as you were concerned, your department made arrangements to recall the material from the Southeast of Scotland?

A. Yes.

THE CHAIRMAN: Did your department make arrangements to recall material elsewhere?

A. No, but the other haemophilia centres, I'm sure, phoned up their own patients and got the recall or --

THE CHAIRMAN: So it is back again to the question of the administrative oversight and so on. So really you dealt with your own area in this respect?

A. Yes, I think it was driven also by the blood transfusion saying, "Please, we want the product back and here is some of the heat-treated."

MS DUNLOP: I'm obliged, thank you very much, Professor Ludlam.

THE CHAIRMAN: Right.

Professor Ludlam, there are two outstanding matters as far as I'm concerned: one, the issue that I raised before lunch, and I don't want you to provide an answer to that now. You may want to look at it. But just to remind you that the information I have so far is that

the blood product unit at the Royal Infirmary began producing Cohn Fraction I material in 1951, and Dr Cash and Dr Spencely produced data in an article that showed the actual use of product from 1961 onwards, so that one can see the pattern that first of all it was fresh-frozen plasma and antihaemophilic globulin, or antihaemophilic factor, with cryoprecipitate coming in quite a bit later.

So the picture one has, looking at that, is that there was a significant supply of concentrate of that sort of primitive variety over 15 years or so before the mid-1970s, when PFC Factor VIII came in. I have at least one death, where this is a practical issue because of the onset of cirrhosis relative to possible dates of infection, and so I would be very pleased if you could find anything that would bear on the issue of whether there were indications of Hepatitis C, as it came to be, before, bearing in mind that we know that all the records of the time essentially related to Hepatitis B and the prevalence of NANB hepatitis was only discovered later.

So it's not a clean and easy topic but it did seem to me that it was material to try to find out whether, in fact, by the time one came to look at PFC Factor VIII, there is a history that one cannot ignore,

that may have been generating Hepatitis C over some considerable period of time.

Does that make the issue clear enough for you to look at?

A. Yes, I think the original observations about hepatitis go back to Rosemary Biggs in the 1960s.

THE CHAIRMAN: I don't want you to speculate or whatever. I know you are coming back again. If you come back some time and can help me on that, or even give me a note about it, I would be pleased.

The other thing I wanted to ask about, and it is something I have asked other haemophilia clinicians, is this: and it's whether there is some sort of dislocation between the theoretical position of giving lots of advice to people and giving them choices, and the reality that one might think had to happen from time to time, that we take the child in Stornoway for example, waiting 12 hours to get to a competent haemophilia clinician. The child has the knee swelling, as you have described, is distraught, as you described. The parent, one would expect, would be responding similarly.

In reality, what happened when one confronted that situation? Was there a great long explanation or was the reality something different?

A. It is very difficult because all these situations are

very different and people's memory of what happened in the distress -- both the distress in the patient, the parent -- the physician trying to deal with a difficult situation may have said all sorts of things that obviously the parents are in no state to hear, and yet maybe they have to be said. And there comes a time when, in a sense, one has to use one's best medical judgment.

THE CHAIRMAN: You see --

A. That's what I'm employed to do.

THE CHAIRMAN: My natural sort of suspicion, as a prospective patient, I suppose, and certainly as a parent and grandparent, would be to think that the response of the parent of a young child, especially, confronted with this condition, would be to say, "Doctor, do what you think is right and get on with it," and that might be the end of it. Is that not so?

A. I think it's awfully difficult for these parents. You know, they had a perfectly well child until 12 hours ago and their world has turned upside down, and they are just as you describe, "Please do what you consider best". So one does, but along the way I try and explain the difficulty the child is in and what the problem is, what the consequences are of not doing anything, what's available, what are the side effects of it, and then you

get on with the treatment of the patients. The parents think that that's what should happen. But it's in a very distraught environment for everybody.

THE CHAIRMAN: Including the clinician.

A. That's what I mean, yes, everybody.

THE CHAIRMAN: And so really, if one thinks about the risks of error in recollecting observed events anyway, whether it's what's heard or what's seen, and the problems of the memory working on what has happened and confabulation, as one of your colleagues put it, the creation of a situation out of a mixture of memory and an impression of what should have happened, it must be extremely difficult to be confident as to what was actually said to any individual patient or any individual set of parents.

A. Well, I think -- I can only talk about my practice and perhaps other people that I see working with me. Confronted with a particular situation, like a new patient, well, it's my responsibility to point out the benefits and the drawbacks of the treatment. So that's sort of part of my automatic -- one of the automatic, things, if you like, I do. So it doesn't have to be thought out carefully each time.

THE CHAIRMAN: So if one has a child with a complex compound fracture of the thigh having fallen on a hill in Skye,

I can't imagine people spending very long talking about theory. The child would be in theatre, anaesthetised, and there would be attempts being made to reduce the fracture very, very quickly. Is that not so?

A. Absolutely, but if that child is being given a medicine that has potentially serious side effects, let's think about -- well, there used to be an anaesthetic agent that gave rise to hepatitis. I'm sorry, I forget how serious the hepatitis was but it was certainly sort of around. You might expect possibly, if it was a bad form of hepatitis, if it gave permanent hepatitis, you might expect the anaesthetist to mention it before the anaesthetic.

THE CHAIRMAN: If the anaesthetist did, I'm not sure I would expect the parent of that child to remember anything about it.

A. I agree, that is -- you have put your finger on the difficulty.

THE CHAIRMAN: Anyway, those are the two things I wanted to ask you at this stage. It's 20 past four.

A. I'm sorry, we do give patients leaflets, you know. It's a bit post hoc but there are things that people can take away, maybe after they have had their first infusion, but, you know, the Haemophilia Society is very active in producing a lot of very good leaflets, for example,

because there is much more to haemophilia than the first injection of Factor VIII.

THE CHAIRMAN: Yes. I won't make any comment on my cynical response to leaflets as a way of helping people understand. It might not be appropriate, but anyway, I think we should stop and allow you to go for the moment, Professor Ludlam.

Is it tomorrow Professor Ludlam is coming back?

MS DUNLOP: Just to explain, sir, what the story is about tomorrow. We have Dr Colvin coming, he might not be here sharp for half past nine but actually I think that, I hope, will work quite well because obviously others have to have the opportunity ask some questions of Professor Ludlam. Professor Ludlam has very kindly made himself available tomorrow anyway. So that, I think, takes care of that.

The only other point to make is that there is a procedural matter which I think counsel need to discuss in front of you, sir, first thing in the morning. So perhaps we can do that before Professor Ludlam again takes the stand.

THE CHAIRMAN: Do you want to start early?

MS DUNLOP: No, I think there will be plenty of time. 9.30 will be perfectly adequate.

THE CHAIRMAN: Mr Anderson is showing obvious distress at

the thought of being here at 9 o'clock.

Very well, tomorrow morning then.

(4.24 pm)

(The Inquiry adjourned until 9.30 am the following day)

I N D E X