Friday, 4 November 2011

(9.30 am)

PROFESSOR VAN AKEN (continued)

Questions by MR MACKENZIE

THE CHAIRMAN: Yes, Mr Mackenzie?

MR MACKENZIE: Thank you, sir.

Good morning, Professor. We have asked you to come and give evidence on topic C3 and you have prepared a statement which we will bring up on the screen, please. It's PEN0171597.

We can see in bold type the central question we asked you to consider was:

"Could or should SNBTS/PFC have introduced Factor VIII concentrate which was sufficiently treated to inactivate non-A non-B Hepatitis, prior to May 1987, in particular against the background that BPL was able to make such a concentrate available from October 1985?"

We can see that in preparing this statement, professor, you were provided with a number of documents, including the preliminary report of the Inquiry, a lengthy SNBTS briefing paper on the development of heat treatment of coagulation factors, also, I think, another lengthy SNBTS paper, "Events concerning the safety of blood products", and also a document the Inquiry team produced, a C3 chronology, and also we sent

you a number of written statements from Dr Smith, Dr Foster, Dr Perry, Dr McIntosh and I think, professor, we also asked you to read Dr Foster's evidence he provided last week, I think it was. Have you had a chance to read Dr Foster's evidence?

A. Yes, I have.

Q. Thank you. You then, in the following pages of your statement, set out the factual position, which I won't take you through because we have gone over that in some detail at the hearings, but I think in short, professor, is there anything in your factual narration you wish to change or are you happy it is reasonably accurate?

A. The only intention I had in writing it down is to show that I have followed the whole sequence of events over those years to see if there was at some point a delay or a discussion about which direction we should go. But as a stance now, I wouldn't like to make any changes and I accept that this factual report is not for discussion so much.

Q. It has perhaps been superseded to some extent by the evidence we have heard at the hearings. Thank you.

I think I can then take you straight to page 1601 of your report. And the subheading "International Developments Regarding Inactivation of Non-A Non-B Hepatitis During 1985 to 1987". You start by saying:

"The evidence that HIV is inactivated by dry heating at 60 to 68°C ..."

Can I pause and ask, when did that evidence become available?

A. Sorry?

Q. You start by referring to the evidence --

A. Oh, yes.

Q. -- that HIV is inactivated by dry heating at 60 to 68°C. Can I just ask, when did that evidence become available?

A. That was after a publication by Dr MacDonald from the CDC showing that using HIV -- purified HIV, which was spiking experiments, that you could heat it and that virus would completely be inactivated. That was in the October 1984, I think, but that is in my previous communication.

Q. Yes. I think we have heard evidence that certainly I think Dr Foster and Dr Smith went to a conference at Groningen in November 1984, when I think there was a representative from CDC who again discussed this evidence. Were you at the Groningen conference, do you remember?

A. I must say that I probably didn't but -- and that's why I was a bit surprised that that was presented here as evidence for the first time, that they were -- became known -- at least became familiar with this type of

heating but very soon afterwards, this publication came out. So that's what I have more in my mind than the Groningen meeting.

Q. Yes. I think we have perhaps discussed Groningen as being the trigger for the UK fractionators becoming aware of this evidence of the inactivation of HIV, but for you the trigger perhaps is not Groningen but the CDC publication in October 1984?

A. Right.

Q. I understand.

You go on to say that:

"That evidence led many manufacturers of plasma products to introduce dry heating. However, it appeared that these heating conditions are not sufficient to inactivate non-A non-B Hepatitis. Hepatitis viruses resist heat inactivation better than HIV does."

You then tell us that:

"In 1985 to 1987, severe dry or wet heated products, heated at 60 to 68°C for 10 to 72 hours, were licensed by the Food and Drug Administration in the USA."

The reference there is to, I think, 7.42 in the preliminary report:

"However, when the positive results of animal testing were not confirmed when higher infectious doses were used, and when a number of clinical studies in

various countries did not substantiate the initial positive animal results, confidence in this method for the inactivation of NANB hepatitis dropped."

You give an example, namely the study by Colombo and others published in the Lancet on 6 July 1985, concerning Hemofil T of 13 haemophilia patients and in 84 per cent of them, non-A non-B Hepatitis developed over a period of 12 months. You go on to explain that:

"Other dry-heated factor concentrates were introduced with heating conditions varying from 60 to 68°C for 24 to 72 hours and furthermore, heating in moist conditions was introduced in the United States but in formal trials of such products, the rate of hepatitis transmission, although being reduced, was not obliterated."

You then go on:

"A different inactivation method using a combination of solvent-detergent that preserved the clotting activity was reported in 1984 and in the following years became used by various manufacturers of plasma products. Combinations of the solvent tri(n-butyl) phosphate and non-ionic detergents such as polysorbate 80 and Triton X-100 at 24°C for a minimum of 4 to 6 hours were shown to inactivate hepatitis viruses. Such mixtures disrupt the lipid membrane of enveloped (hepatitis)

viruses which are then unable to bind and infect cells. No transmission of hepatitis virus (or of HIV) has been observed in any of the clinical trials reported published in 1988 and 1992."

Professor, the reference to "clinical trials reported published in 1988 and 1992", was that a reference to solvent-detergent products?

A. Indeed, yes.

Q. And could you perhaps just help us a little? When was there a move to solvent-detergent as a method of inactivation? When did that occur approximately?

A. Well, it started, as I said here -- the development started in 1984 but it took some time before the technique became known by other centres. So it was in 1986 and 1987 that more knowledge about it existed and gradually it started to begin an interesting technique for more centres.

So, for instance, in Amsterdam we concentrated initially only on dry heating and that was, of course, because we had introduced dry heating at the end of 1984 to inactivate HIV, and since there are a number of products which had to be studied, whether that was sufficient to inactivate HIV, for instance, in cryoprecipitate, in Factor IX, in Factor VIII and in various other products which we developed.

Most of our time was devoted to study how efficient is dry heating, and we used the technique of Baxter, which involves 72 hours at 65 degrees. So we didn't study, as was here in Scotland, so much what happened with non-A non-B. So we were more concentrating on making those plasma products safe as regards to HIV transmission.

Q. I'll come back to ask you a few questions about what was happening in Amsterdam and in Holland but just sticking for now with solvent-detergent, did there come a time when the majority of manufacturers of blood products used the solvent-detergent method to inactivate viruses?

A. That was only much later, when it was clearly shown that this technique was favourable. But you have to understand that the solvent-detergent methodology is quite different from the techniques like dry heating or heating at high temperature, because you introduce a solvent and a detergent which you have to remove afterwards and that is not a situation which was very familiar with the fractionation industry.

So it required also the acceptance of that approach and the introduction of methodology to remove those substances. So that was not a very fast growing process. It took some time and people waited until it was quite convincing that this was a superior technique.

Q. Can you identify a year or a period approximately when the majority of blood product manufacturers used solvent-detergent as a method of inactivating viruses?
A. Well, I think that would be in the late 80s but I cannot give a precise date at which that would have occurred.
Q. Thank you.

Returning, please, to look a little at what happened in Holland in respect of the question of using heat-treating to inactivate viruses and blood products, can you tell us perhaps what, if any, work occurred in Holland in 1982/1983 and the first half of 1984 in respect of considering heat treatment of blood products to inactivate viruses?
A. Before we started to introduce the technique from Hyland -- and we didn't have access at that time to sufficient HIV virus to monitor how efficient the inactivation would be -- we did some small scale experiments to see what it mean in terms of solubility of the product and notably in yield, and also those experiments were quite disappointing because we lost most of the Factor VIII during those heating experiments. So we didn't make very much progress and therefore we looked around to see if there was another methodology which would perhaps help us to solve those two problems in terms of what I said, solubility and

yield.

Q. When that research was being undertaken in Holland, was that with a view to inactivating HIV or was any consideration given to also trying to inactivate the virus or viruses which caused non-A non-B Hepatitis?

A. No, it was concentrated on HIV. And non-A non-B was not so much an issue which we included in those studies.

Q. So just before the information in October 1984 from the CDC, that HIV is inactivated at heating between 60 and 68 degrees -- just before October 1984, what stage had your research reached in Holland?

A. Well, as I said, we were not quite far. We didn't have product. We had only disappointing results. So we needed some other methodology to make any progress and that's after a long discussion with Baxter, we managed to get their patent and to use that for our own product.

Q. Yes. So, after the evidence became available in October 1984, what happened in Holland after that?

A. We started in January/February to introduce a dry-heated Factor VIII concentrate, a cryoprecipitate, and that development took some time before the whole market was served by those products. It took until about June or August of the same year, 1985.

Q. And I think you have explained the reason you were able to introduce dry heating was because you, presumably,

purchased the technology rights from, was it Baxter you said?

A. Yes.

Q. During 1985 -- so you have now in Holland a dry-heated Factor VIII concentrate -- what was the heating protocol? What was the heating temperature of that product?

A. That was, as I said, 65 degrees and we heated for 72 hours.

Q. Thank you. So during 1985, was any consideration given in Holland to trying to achieve greater heating of Factor VIII concentrate and was any consideration given in 1985 to try to inactivate the virus or viruses which caused non-A non-B Hepatitis?

A. The first question, we did not consider a higher temperature. What we considered was to see if we could purify the product to a higher degree because at that time it was intermediate pure and we did some experiments to see if we would purify Factor VIII further, and that was successful. I mean, we had a technique which used glass beads to remove fibrinogen and fibronectin but when we started to use this clinically, it appeared that a number of patients developed Factor VIII inhibitors and so we had to stop that production.

Q. Why in 1985 were you seeking to develop a higher purity Factor VIII concentrate?
A. For the same reasons as what other people were doing. They were just judging that if you had a higher purified product, you would also increase the rate of virus inactivation. So it would be a more efficient virus inactivation method if you had a purer product.
Q. Presumably at some point, professor, you became aware of the 8Y product and that PFL or BPL in England was able to heat their high purity Factor VIII concentrate at 80 degrees. Do you remember becoming aware of that information and what your reaction to it was?
A. That's a difficult question because I don't remember when it was the first time that I heard about 8Y and what sort of information was transmitted to me. I am afraid that I cannot directly answer that. I forgot when it was. It was certainly not in the very early stages.
Q. Yes. Do you have a general impression as to how that news was received in the fractionation community that BPL or PFL had been able to achieve heating at 80 degrees?
A. What I remember is that -- it may be my bias, so that certainly has to be taken into account -- that I didn't hear very much about it. It was not, in my view, an

issue which was giving rise to much discussion in the fractionation centre.

Q. I see. I know you have difficulty pinning down when you first heard that PFL were able to heat at 80 degrees and if you can't answer the following question, please say so, but when you did hear that news, did you have any view as to whether 80 degrees heating was likely to inactivate the virus or viruses which caused non-A non-B Hepatitis?

A. Well, it would seem logical to expect that if you increased the temperature, that you get a higher degree of virus inactivation, but as I said before, our experience with a higher purified product which gave rise to a number of patients with inhibitors, also took us to the counter side of that, and that is if you change the circumstances for inactivation, that it may result also in the development of new antigens thereby creating inhibitors in patients. That is what maybe diverted our attention from the non-A non-B virus inactivation.

Q. I see. Just to finish this point, I suppose in considering whether a product was likely or unlikely to transmit a virus, you would want to see some proof before coming to a view on that?

A. What is the question here?

Q. Yes. I think I had asked you whether you had a recollection whether 80-degree heating was likely to inactivate the virus or viruses which caused non-A non-B Hepatitis, and just following on from that, I suppose the answer is you would need some proof before you could come to a view on that question?
A. Yes.
Q. Which would then bring us back to clinical trial data.
A. Indeed, because I think in 198 -- 198 -- there were only data available from a limited number of patients and so it was quite clear that we were awaiting the outcome of a larger clinical study to show how efficient it was.
Q. I take it there is no question that you were supplied with the clinical trial evidence during 1985. Presumably you simply had to wait and see what was published in due course in the publications?
A. No, I have talked with other people in Amsterdam and nobody knew exactly what was going on.
Q. Yes. So I won't ask you any more on that, professor.
THE CHAIRMAN: I wonder if I could take it up.
MR MACKENZIE: Yes.
THE CHAIRMAN: Professor, I'm interested in the perception within the international community of different workers' positions. At this stage, in the first half of the 1980s, did you and your continental colleagues look

primarily to find out about what was going on to England or to Scotland or what?

A. I think the West was certainly -- what happened in the US was certainly taken very seriously, because, you see, the whole -- of course, as you know, the AIDS epidemic started in the US and so we were expecting that they would be the first to isolate the virus and also to make it available for this type of study.

But at the same time in France, there were also virologists doing very good work. So it was those two sides which, in my recollection, we were predominantly focusing on when it came to new information.

When you asked me about UK and Scotland, I don't recall -- well, of course, I should refer. Here in Edinburgh you had a virological group which was also very active in the international scene. So they were, I think, also making a lot of progress at that time. So I would say these three groups.

THE CHAIRMAN: Well, you see, we have already heard quite a lot of evidence from Professor Weiss and Professor Tedder that in 1983 and early 1984 their contacts for obtaining material to begin to study HIV were Montagnier on the one hand and Gallo on the other.

A. Yes.

THE CHAIRMAN: And indeed, isolates were obtained from both.

And we know, for example, that there was collaboration that involved Montagnier using the cell line that was developed here, rather than the Gallo cell line, and therefore avoiding all sorts of trouble with the H9, isn't it, aspects of it?

So in a sense it wouldn't be a surprise to discover that the wider continental expertise also focused on France and America, but I really have to try and get a feel from evidence for that and, yes, we know that work was being done by virologists here in Scotland but it doesn't necessarily follow that the world would take particular notice of it.

So a sort of objective view as to what was going on at that time would be very helpful.

A. Yes, well, again -- you pose a very interesting question, which brings me back to -- well, almost 30 years back now, and in my mind, what happens in France, in Montagnier's laboratory and in Gallo's laboratory and the discussions between these two groups, who was where and which virus was in fact responsible for AIDS, still dominated my mind, yes? Because -- well, the nomenclature was different and the methodologies which these people used were different. So it was, at that stage, quite complicated to know who is right and which line is probably the most profitable

one.

As usual -- no, that's not correct. You should skip that. There is a sort of bias to believe Americans earlier than French people in certain scientific circles. It's absolutely wrong, but at that stage we may be biased for having a sort of more trust in what was happening in the US than in France. We were wrong. I think that the Montagnier group did a fabulous job and in the end they were in fact the real inventors of the HIV virus.

So I hope that helps a bit what you wanted to know.

THE CHAIRMAN: It does because I think, realistically, one has to face the possibility that perception and reality may not actually coincide in this sort of area.

A. Absolutely.

THE CHAIRMAN: And if the perception at the time were that the American scientists were the leaders in the field, I might not be surprised if experts generally responded to that and looked primarily to American sources.

A. Yes. I have to add one other aspect. That is that in the beginning of the 1980s -- it would be notably when the threat of virus transmission by blood products, by HIV, became known, at least the first indices was there, it surprised me that when I visited the US -- and during that time I was there quite frequently -- that a number

of what I would call prominent people in the transfusion area did not believe that AIDS would become a problem for the transfusion society. So it took again -- whereas we were already quite convinced, they were still doubting about it and very sceptical about it.

So you would expect that, because of the other developments in the US, they would gradually become in advance of us but, no, that was not the situation.

THE CHAIRMAN: Yes, thank you very much.

I think that we have followed the different responses of different professional groups to emerging knowledge with more than a little interest.

A. Yes.

THE CHAIRMAN: It's very, very difficult to recreate, isn't it, the atmosphere at the time?

A. Indeed, and I'm sorry, again, my mind is also of course restricted to certain developments, certain events, which happened and I may have forgotten some important things.

THE CHAIRMAN: Yes, thank you, Mr Mackenzie.

MR MACKENZIE: Thank you, sir.

Professor, if I may perhaps develop that line a little but from a different angle. I think that line of questioning perhaps looked at the things from a virology point of view and in particular HIV, but if

I can look at things from a different standpoint, please. In the 1980s, as a fractionator, as someone who was involved in the manufacture of blood products, who was seen to lead the field in respect of the manufacture of blood products, where would one look perhaps with particular interest for developments? Is it a case that the US commercial companies were seen to lead the field or the US public health manufacturers, or were the European commercial manufacturers or European public health manufacturers also leaders? Do you see what I'm asking there?

A. In my opinion, I think it was the commercial sector. The commercial sector was very, very much aware of the risks and they spent a lot of money in doing studies and had safe products earlier on the market than the not for profit sector, so to say.

Q. So in the 1980s, if one had to manufacture blood products and one was interested in viral inactivation techniques, where would one look for the latest information or developments?

A. Well, a lot of that information was not openly available. You had to go to congresses and meetings to discuss with people but, of course, as is usual, the commercial sector was not very open on some of the details of the methodologies because it was all

protected by patents or it was in the process of being patented, so therefore you had to guess what sort of ways they were going; which is of course in contrast to what the not commercial sector was doing, the not for profit sector, which was quite open usually when it comes to publications and also presentations and meetings.

Q. Yes. So in the 1980s, the non-profit blood product manufacturers in Europe -- we can understand the difficulties they would have had in trying to get information from the commercial companies for understandable reasons -- would perhaps discuss and share ideas among themselves?

A. Yes, but, of course, there were also representatives from commercial companies present because these meetings are open, they are not closed. So if you pay your registration fee, you can come.

Q. And in the 1980s, not for profit manufacturers, presumably, were trying to develop new blood products, including viral inactivation techniques?

A. Yes.

Q. And can you remember, in Europe in the 1980s, was there any view among the not for profit manufacturers who was particularly well regarded in respects of development of new products and techniques, including viral

inactivation techniques?

A. You see, the not for profit sector during that time was quite different from what it is now. Then they were usually small facilities which were mostly dealing with albumin and immunoglobulins, and some of them were dealing with Factor VIII, but a lot of them were not interested in Factor VIII or Factor IX because they left that to the industry and they had not the capital and the possibilities to invest in research and in doing the clinical studies. So they kept it mostly to albumin and immunoglobulins, and there were only a limited group of fractionators which, like the pharmaceutical industry, were dealing with coagulation factors.

Q. Can you remember which countries were producing their own coagulation factors?

A. Okay. In Europe that was Finland, so Helsinki. To a certain degree people in Denmark, but that was a very small scale; Amsterdam, Brussels, Belgium, Paris, Lyon. Switzerland, Switzerland was very active. You see, in Germany the situation was quite unclear because there you had about ten fractionating centres but only I think in Munich and in Frankfurt they were fractionating for Factor VIII.

Q. And of course in England and in Scotland --

A. Sorry, sorry, I should have started there. Of course,

in England and Scotland.

Q. And can you remember in the 1980s how the fractionators in Holland viewed the work going on in England and in Scotland and the fractionators there? What standing or reputation did the British fractionators have; can you remember?

A. At least for Holland, I can say there was one blood bank director in Groningen, which organised this meeting you were talking about, and he had quite a frequent contact with Professor Cash. So he knew, I think, quite well what was going on in Edinburgh. We had also our contacts with Edinburgh and also with BPL but not in a very regular or systematic way, it was just by chance or because certain developments or certain meetings led to further discussions.

Q. Yes. I'm not sure that directly answers the question but it may be it's not a question you can answer. The question really, in short, was what reputation did the Scottish and English fractionators have in the eyes of the Dutch at that time. Is that a question you can answer or ...?

A. I think they were considered at the same level as what we were doing. So there was no difference in quality or in reputation; it was just the same.

Q. I understand. Returning now, please, professor, to your

statement, if I may, and the question towards the bottom, back to the central question we had asked, which was:

"Could/should SNBTS have introduced Factor VIII concentrate which was sufficiently treated to inactivate non-A non-B Hepatitis prior to may 1987?"

I suppose there are really two ways of looking at this, professor. One is to say, having regard to what was known at the time, should something different have happened and then perhaps the other way of looking at it is, with the benefit of hindsight, so knowing all we know today, should anything different have happened.

I think I'll keep the benefit of hindsight question to the very end. So here we will perhaps try and stick to knowing what was known at the time. Should something different have happened, and in particular should Factor VIII concentrate, which was sufficiently treated to inactivate non-A non-B Hepatitis, have been introduced prior to May 1987, and in your answer you say:

"In December 1985, SNBTS/PFC decided that an intermediate purity Factor VIII concentrate that could be treated at 80°C should be developed. Before that moment, in fact starting in 1981, SNBTS investigated pasteurisation of Factor VIII concentrate with the

objective to inactivate the agent(s) responsible for the transmission of NANBH. The initial pasteurisation project, the zinc heat treatment process, was stopped at the end of 1984, at which point priority was given to the high purity pasteurisation project with Professor Johnson of New York University."

You go on to set out what happened at the end of 1984 with the introduction of dry heat treatment, with the aim of inactivating HIV, and that between October 1984 and January 1985, the manufacture of Factor VIII at PFC was largely suspended and then the reference to the evidence from the literature. Then you say:

"Meanwhile, there was evidence from the literature that dry heating at 68°C was insufficient to prevent transmission of non-A non-B Hepatitis. There were also concerns about the degree of dry heating required to inactivate HIV."

Do you remember becoming concerned at the time, professor, so in 1985 and perhaps towards the end of 1985, that the dry heating regime you were using, for example in the Dutch product, may not inactivate HIV?

A. No. That was only after a publication by Fred Prince from the New York Blood Centre that we heard about that and we had no evidence ourselves that there was such

a concern. So I looked again at this paper of Dr Prince and I must say that he himself is also quite -- well, to a certain degree, uncertain about what the significance of his findings is because he mentions also that there are other data which are quite the opposite. So I'm not sure how to use that. The developments in Amsterdam were not affected by that publication.

Q. Yes. Am I right in thinking the first you became aware of that paper at the time was when it was published?

A. Yes.

Q. I think that was some time in 1986?

A. Yes, indeed.

Q. We have heard evidence that in Scotland there was a pre-publication version of the paper available in the second half of 1985. And then returning to your statement you say that:

"In early 1986, SNBTS started research to increase the degree of dry heating using Factor VIII concentrate of a higher purity than its existing Factor VIII product, but less pure than 8Y, and discussed with PFL heat treatment at 80°C for 72 hours. PFC's severe dry-heated product, Z8, was available for clinical trials in December 1986 and was introduced into clinical use from April/May 1987."

Now, you then go on to say:

"In retrospect, it may be asked if PFC should have changed its policy at an earlier stage, ie before December 1985."

You say:

"In my opinion, which is shared by Dr Smith, PFC had good arguments to pursue the wet heating of Factor VIII concentrate as it was doing. Before December 1985 it was uncertain if the BPL product would be safer than the SNBTS/PFC product."

When you say, professor, that in your opinion "PFC had good arguments to pursue the wet heating of Factor VIII concentrate", can you explain that a little bit please? What were those arguments that you think were good?

A. What I understood from the various reports is that Dr Foster was somewhat concerned about the stability of the product. He described that not all the batches which BPL or PFC made were in fact suitable for distribution and/or usage. So that would indicate that high temperature would in fact lead to a less stable product. Therefore would not be so good to be used clinically.

The second argument which he has is the limited capacity because it was known that BPL was only able to serve 25 per cent of the patients with this product. So

there was clearly a logistical problem which needed to be solved, and I can very well imagine that if I would be in the position of Dr Foster, I would also be concerned about that because that's something which you don't want, certainly not in Scotland.

Certainly, at that time -- because that was later -- there were some concerns about the pharmacokinetics of the product, so the shorter half-life which was indicated, but that later on was shown not to be an issue. What was an issue was also the neoantigen formation, as I indicated earlier. At this high temperature you can introduce molecular changes and therefore introduce antibodies directly to this modified Factor VIII, and finally -- and I think that is an argument which I can very well see -- is that it wasn't certain what degree of virus inactivation was in fact obtained and achieved by this superheating, because BPL didn't have apparently the facilities, the possibilities to use model viruses and see what the effect was of the heating on those model viruses.

Q. I think those are largely reasons why Dr Foster may not, at that stage say in early 1985, have wished to adopt this severe dry heating process, arguments perhaps against that, which call it into question. But how about looking at that a different way?

We know that Dr Foster's preference in the beginning of 1985 was to continue to try to develop a high purity Factor VIII concentrate, which ideally could be pasteurised but if there were difficulties there, at least keeping the options open of severe dry heating or possibly later solvent-detergent. But do you think Dr Foster had good reasons in the beginning of 1985 to seek to continue to try and develop a high purity Factor VIII concentrate, which ideally could be pasteurised?

A. Well, if you take first the high purity, the answer is yes. I think everybody was aware that the intermediate Factor VIII products, which were used at that time, had some limitations in terms of the potential side effects which would occur in patients, but also of course, the commercial competition would of course, sooner or later, lead to a higher degree of purity and therefore you want to compete with those products, and that you can only do by, just like the industry does, increasing the purity. But that is purely a commercial marketing point of view.

From the more scientific point of view, you have to be aware that the dry heating is a process which involves the vials, the individual vials of Factor VIII which it is stored in, and those vials may introduce variation from batch to batch when it comes to heating

because the moisture content of the various products in each of these individual vials may not be the same. Therefore, you get not a uniform product. When you introduce wet heating, then you have one dollop(?), and that's what is heated.

So the chances that you have a uniform product are much better than when you have this dry-heated treatment on these vials. So I agree that there are indeed arguments to propose that maybe wet heating would be better than just the dry heating.

Q. And I think we also heard evidence that a high purity product would result in a smaller volume, which would have been less viscous and that, as a general principle, a smaller volume product, which was less viscous, was easier to manufacture at all steps really in this process. But also that a smaller volume product would be easier to heat and in particular easier to pasteurise. Do you have any views on these statements?

A. No, not particularly, no. No. It's possible but I wouldn't know, no.

Q. Okay. Returning to your statement, please, professor. The next question you look at is the communication between BPL/PFL and PFC, and whether that was sufficient to allow PFC to keep track of the development of 8Y.

I think we have heard quite a lot more evidence

about that during the hearings but from the evidence you looked at, you say:

"First of all, it should be emphasised that close professional and scientific collaboration between BPL and SNBTS was repeatedly and strongly advocated by Dr Cash. From the various witness statements it is obvious that between 1983 and 1986, several exchange visits took place from PFC and PFL. Dr Perry and Dr Foster regularly discussed and exchanged information with Dr Smith."

Also, a reference to the patent application. This will be a matter for the chairman in due course but in your opinion, professor, you consider that there does not appear to have been a lack of shared information which might have impeded the progress of developing heat-treated Factor VIII by PFC. You then go on to look at the next step of events, ie:

"Once SNBTS/PFC had decided to start the development of an intermediate purity Factor VIII concentrate that could be treated at 80 degrees, it took until August 1986 before the first production scale trial batch of Z8 began ... During this period, the project had to be taken from a laboratory scale to pilot scale, and subsequently to large production scale. This involved the development of new purification of

Factor VIII and its concentration, the formulation of the product, the heat treatment and the proper freeze-drying conditions. Although several of these methods were well-known at PFC, it is time-consuming to determine the proper conditions for each of them to create optimal Factor VIII yield and solubility ..."

A reference also to:

"... standard operating procedures for quality control and product release requiring to be developed."

You say:

"In my opinion, it is quite an achievement to successfully complete all this within one year (in fact between June and December 1986)."

To pause there, professor, I think our understanding of the evidence is that between approximately January and May 1986, work was undertaken in the laboratory to develop Z8, and June 1986 was the first pilot scale production?

A. Yes.

Q. So when you say June and December 1986, is that reference to the first pilot scale production until the product being available for issue?

A. Indeed.

Q. I understand. And you say:

"The experience of BPL shows that it may take

considerable time (almost 4 years) before there is sufficient stock of 8Y to meet the demand of all patients."

You conclude by staying:

"In my opinion, it is very unlikely that SNBTS/PFC could have introduced Factor VIII concentrate that was sufficiently treated to inactivate NANB hepatitis before 1987."

Now, professor, I have one or two further questions with a view really to trying to explore all of the main issues from every possible angle.

Going back, please, to the beginning of 1985, I think the PFC position is that dry heating of their interim purity product was essentially a temporary response, following the news at Groningen, and in the longer term the plan was to continue research and development into producing a high purity Factor VIII that ideally could be pasteurised.

As at the beginning of 1985, do you consider that that was a reasonable or unreasonable plan?

A. I consider that very reasonable.

Q. Again, just the main reasons for that?

A. Well, we all know that on the one hand you need to have a product which is immediately available so that you can continue to serve your patients, but you also need to

think ahead to what are the real wishes from the market, and at this time, as I said earlier, it is a higher purity product. But you cannot obtain that immediately, so you have an intermediate product which you can use in the time before you have that higher purity product, and you have to take care that the intermediate product is also as safe as possible.

So you cannot do them both -- at least not bring them on to the market at the same time. You have some developments on the one hand and you have a sort of routine production, which you have to do troubleshooting at, to see what are the problems there.

So this is not like the commercial sector, where they have many people who can devote all their time to do this. You have to take into account the size of the operation to see what are the opportunities and the possibilities.

Q. Yes. Professor, I think we asked you to look at this document, if we could bring it up on the screen, please. It's SNB0074867. This is a document by Dr Foster in February 1985, a progress report for Factor VIII study group. We have looked at this before and in short it sets out Dr Foster's preference for continuing to seek to develop a high purity product. I think you have had a chance to look at this document, professor?

A. Yes, indeed.

Q. Could I ask, please: if Dr Foster in February 1985 had sent you this document and said, "Professor van Aken, I have produced this document, I'm a little unsure whether we should be continuing down the path of seeking to develop a high purity product. What do you think? Do you think what I say in the document is reasonable or do you think I should ditch that and seek to develop severe dry heat-treated Factor VIII concentrate?" What would your response have been then?

A. I think I would have told him that it is, of course, quite ambitious to work at that stage with your capacity on a new purification technique. On the other hand there was quite some effort done before, so it was not starting from zero. There was already a lot of work done and therefore you could take profit from the experience which was already collected and continue on that line.

So I think that would be my argument to motivate him to continue on that line. Why not go for the superheating, so to say, for the BPL method? You have to start from scratch. You have to start from a technique which you have to learn from somebody else, and to transmit it to your own environment. That has a number of risks because what may be successful in

Oxford is not necessarily successful here. There are so many details in the methodology which you have to take into account.

Just for an example, freeze-drying, as is clear from the document. The freeze-drying in Oxford is probably not the same here. Thanks to all the experiments which were done here, we now know the importance of some of the parts of the freeze-drying process, how it can affect the quality and the yield of the product. That, I think, is a risk if you transmit it from one laboratory to another. So you cannot just assume that what has been done there results in a production facility, a production method here, within a couple of months. It can easily continue much longer and it can be very difficult to find out what are the differences, where exactly do the people hear something different from there.

You balance that with the other way, where you have already experience and have already invested into a higher purification method. I could very well see that you have the tendency to continue with what you know already and what you are good at, rather than to go for a technique which has some uncertainties.

Q. Thank you. That perhaps links into the next question, which is this: we know that in December 1985 PFC did

decide to change direction in their research in that they decided to introduce a severe dry-heated product. At that stage, in December 1985 or early 1986, do you think it was reasonable for them to seek to develop their own process, building on their work to date, or do you think it would have been better for them to have followed the 8Y process or at least key parts of it?

A. The difference with the January and December is that during that year, of course, there was far more information about the 8Y process. So that uncertainty must also have been in the head of Dr Foster when he decided not to go for the 8Y method in early 1985. Yes?

In December 1985 there was more experience, and although it was not yet certain how it would work out clinically, that's phased out, because there were only a limited number of patients treated with the 8Y product and the real study, the real clinical trial is still to be done. So again there was some uncertainty there. But at least it looked as if 80 degrees was not bad in terms that it would be unsafe and that it would present problems which could be avoided otherwise.

So I think that to go for a higher temperature, there were arguments for that. Also, the uncertainty from Dr Prince, which was also playing a role, whether that dry heating at 75 degrees was sufficient, may have

played a role.

Q. Okay. So one can understand why one would seek to achieve that outcome, 80 degrees heating. The question really is: how does one achieve that outcome and from PFC's perspective, was it reasonable for them to try and achieve that outcome by seeking to develop their own Z8 process, building on their existing work do date or would it have been better for them to achieve that outcome by following the 8Y process or at least certain parts of it?

A. Well, as I said earlier, the same arguments which are used for the previous question are still applicable to this situation here. So if you had arguments that the purification method wouldn't work, then it was different. Then it would have been no choice because then you would have said, "Okay, we will stop with the purification attempts. We now go straight forward to the 8Y method because otherwise we have no product."

Q. Yes. In the question I asked, I made a reference to the key parts of the 8Y process. Would it have been possible in late 1985/early 1986 to identify what were the key parts of the 8Y process which meant that the product could be heated at 80 degrees?

A. Well, if you go through the methodology of the 8Y, which is published in Vox Sanguinis, I can see that the key

parts are first of all the extraction, the cryoprecipitate extraction, which requires a certain pH, which is critical, because otherwise you have low yield, then the heparin precipitation, which is crucial because you have to precipitate fibrinogen and fibronectin, which, up until that moment, nobody else was, I think -- (inaudible) where it was attempted.

But there was some doubts about how that would work and then you have the precipitation of Factor VIII by glycine and sodium chloride buffer. That is also used in other methodologies, so that is not new. And then, of course, you have to remove all the salts which you have by Sephadex chromatography. That is not something which is so standardised that you can assume that if what has been achieved there can immediately transmit to here.

Then, as I said, finally you come to the freeze-drying again, which is an essential part of -- at least appeared to be the essential part.

Q. In saying that, professor, I think you really listed all of the main steps in the process. Does it really come down to this: that in late 1985, if one wanted to use the 8Y process as a means of achieving a 80-degree outcome, it was really all or nothing? One would have to have adopted all of these main steps, rather than

saying, "We will just take the first step or the last step"?

A. No, no, that doesn't work. You cannot say, "I'll just take this step and the rest I will continue", as you used to do so. You have to do it all or not to do. That is usually the experience, that you cannot, without getting into all sorts of surprises, just say, "Well, I'll use this element and this element, and the rest I'll leave as it is".

Q. Thank you. Again, sticking with 8Y, are you able to help us, professor, with why it was possible to heat 8Y at 80°C? Was it because it was a high purity product? Was it because of the freeze-drying process? Was it a combination of these two factors or were there other factors at play we don't know about?

A. I will have to look against all the evidence and all the papers which you have sent me. I think the most likely is that it's a combination of freeze-drying and -- what did you say? Purity?

Q. The high purity?

A. Yes, the high purity, sorry, yes.

Q. Why do you say that?

A. Well, the high purity because the high purity, of course, from the theoretical point, is a major factor but other people have also gone through to a higher

purity and I have never heard that they were able to heat it to the same degree. And secondly, because what I heard from the freeze-drying methodology makes me believe that there are elements there which should also be taken into account.

Q. We know that 8Y and Z8 were heated at 80 degrees. Did any other commercial or not for profit manufacturer adopt the 80-degree dry heating protocol for Factor VIII, and if not, why not?

A. Well, at least you have some of the documentation, the paper from Kasper et al, 1983, where you get an overview of all the products which were on the market, and if you go through that, you will not see that there is any other commercial company at least who has used 80 degrees. That doesn't exclude that there are perhaps other institutions which have used it but I have not heard about it.

Q. Are you aware whether commercial manufacturers tried to --

A. No.

Q. The 80-degree protocol?

A. No. But again, I think you have to take into account that there was a concern that this superheating would perhaps introduce new antigens and that was in the mind of a lot of people when they were discussing the level

of the temperature.

Q. Professor, one final question, please. This is with the luxury of hindsight, so sitting now knowing all that we know, do you think PFC could have done anything differently to achieve a Hepatitis C safe Factor VIII product earlier?

A. I don't think so. I think all the reports show that there was a group of people there which was very well aware of what was going on, who considered every possibility and even attempted some solutions. So it always requires some luck to have a product, a new innovation, which makes really progress, yes? But if I take the environment in which they were working into account and the size of the operation, I don't think that you can assume that there is one element or more elements which, when they would have been taken into account earlier, would have given them not a profit in terms of coming forward with a product earlier.

I think when I have read this, I was very much convinced that this was really top quality what was done and it could not have been done earlier.

Q. Sir, I have no further questions for the professor.

THE CHAIRMAN: Professor, when did you have a Factor VIII product that was safe from transmission of NANB hepatitis?

A. As I said, we heated for 72 hours at 65 degrees and we thought that this was safe, but the final proof would be that we had later on done some spiking experiments with Hepatitis C to see if that was sufficiently heated. We did not do that. Why didn't we? In between in fact, the Hepatitis C test was introduced, so all our donors were screened for Hepatitis C and therefore the viral load of plasma already would have gone down. So it was not logical to assume that there would still be much virus around.

So in fact I was saying that we didn't do that experiment, but that would have been the proof to see if it was safe. We didn't do that. So I cannot answer the question.

THE CHAIRMAN: What about Factor IX? Is it in the same position?

A. No, Factor IX is always easier than Factor VIII because it was more stable and in fact you don't have the yield problem to such an extent as you have with Factor VIII.

THE CHAIRMAN: Yes, I think we have heard that, because of the relative quantities, one can always select within the material.

A. Yes.

THE CHAIRMAN: Yes.

PROFESSOR JAMES: Could I just add to this? You must have

some idea as to whether your product that you effectively bought in from Baxter between, let's say, 1986 and 1989 actually in retrospect was safe or whether there were cases of what was subsequently known to be Hep C, which arose.

A. First of all, may I correct, we didn't license the product, we licensed the technology. So we made Factor VIII from our own plasma source in our laboratory.

PROFESSOR JAMES: Right.

A. That is the first thing.

The second thing is that we had in Holland quite a good surveillance among haemophilia patients for Hepatitis B and NANB. We did not hear ever about an incidence of non-A non-B after we introduced the 65 degrees at 72 hours product.

But it's indirect proof that it was safe but I would have liked to show you here that we did some spiking experiments to see what degree of virus inactivation we had achieved.

PROFESSOR JAMES: I'm sorry, when did you start to produce that product?

A. That was, as I said, in January 1985, when we started, and we were able to serve everyone who asked for the product in June 1985.

PROFESSOR JAMES: So one final question is: do you think in retrospect that if Scotland or, for that matter, the UK had followed the path of Holland and negotiated with, for example, Baxter, the similar technology that you had, that possibly this product could have been introduced significantly more quickly into Scotland and/or the UK, and much of what we have been devoting our time to and you too from your careful reading, would have been irrelevant?

A. I have always been -- this is the most difficult question that you have asked me during all these sessions here.

Well, of course, that could be a conclusion but again, if we take it back to the time where all these things were happening, notably when it comes to Hepatitis C, it took some time before you could do the real model virus and spiking experiments which were needed.

So in retrospect -- and that comes back to the question -- in retrospect, it would perhaps be yes, a way, but given the circumstances which were applicable to this, I don't think at that time you would be able to convince everybody about that.

PROFESSOR JAMES: Thank you. So it's wise after the event?

A. It's wise after the event.

PROFESSOR JAMES: Thank you.
THE CHAIRMAN: Could I ask something on the development of it? You bought the technology from Baxter. Did that prescribe the engineering sequences necessary to produce the product or did you have to interpret it and produce your own?
A. No, our people went to Baxter to see how they were doing it and we got a protocol and people from Baxter came to us at the initial stage to see if there were problems.
THE CHAIRMAN: So in selling the technology, Baxter were also prepared, in effect, to oversee the procuring and installation of the necessary --
A. In the initial phase, yes. So that was only for the first few months.
THE CHAIRMAN: Mr Mackenzie, do you have anything to follow on?
MR MACKENZIE: Yes, sir, I should perhaps.
Professor, the product you have discussed in Holland, heated at 68 degrees for 72 hours, was that an intermediate purity product?
A. Yes.
Q. And it was dry-heated?
A. Yes.
Q. In 1985 and 1986, did you have any evidence or expectation that that product did not transmit the agent

or agents responsible for non-A non-B Hepatitis?

A. Well, we hoped that it would be sufficient but we had no further proof or evidence or whatever to support that.

Q. So was it more in hope than expectation?

A. Yes.

Q. And the primary purpose in producing that product was to inactivate HIV for which there was evidence?

A. Yes.

Q. Thank you. I'm sorry, it's my mistake, professor. I said the product was 68 degrees for 72 hours, it was of course 65 degrees for 72 hours.

A. Yes.

Q. Thank you.

THE CHAIRMAN: Mr Di Rollo?

Questions by MR DI ROLLO

MR DI ROLLO: Can I just ask one matter in relation to your statement? Your statement is PEN0171597 and the page of the statement that I would like to go to is page 4 of PEN0171597.

A. I missed that.

Q. The page of your statement is PEN0171600.

A. Do we get that on the screen?

Q. I hope so.

Just before coming to that, I think it's fairly clear from what you have told us that you are satisfied,

from the material that you have seen, that there was a considerable amount of cooperation and exchange of information between BPL and PFC in the relevant period? You are nodding to that one.

What you have said in your statement is that:

"An interim review of the clinical trial with 8Y in March 1986 showed that it was likely that the product was free of NANBH, Hepatitis B and HTLV-III. The final report of this trial became available in October 1988."

Is that right?

A. Yes, that report referred to 14 patients which were treated at that time.

Q. I think it would appear then that, as far as you are concerned, with the material that was available in March 1986, PFC would appreciate that there was, or did appear to be, a substantial increased margin of safety in the product of 8Y insofar as NANBH was concerned?

A. That I have not read, I must admit. I don't know where you are now referring to because in the publication of 8Y in Vox Sanguinis, this is not mentioned.

Q. If I could just go to SNB0075664. Have you seen this document before?

A. This is the statement document which you showed earlier, I think?

Q. No, I don't think you were shown it by my learned friend this morning.

A. No, no. Then it must be said I haven't seen it.

Q. You haven't seen this document. If we just carry on over the page, please. If you go to paragraph 5 there, it says:

"Dr Smith outlined clinical trial results of 8Y Factor VIII 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."

That's what he is reported as saying at that meeting.

A. This is what I think is consistent with what I have read in the scientific register.

Q. Right.

A. What you said earlier, that there were more effects, sorts of extra effect of virus inactivation.

Q. No, I wasn't suggesting an extra effect. I think I perhaps put that to you badly. I'm just suggesting that what you are saying in your report tends to suggest that as at March 1986, it happened there was at least a likelihood that the product was free of NANBH?

A. Yes, that was based on this type of remark which I think

I also found in another piece of paper, but that's based on that.

Q. Fine, thank you.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: I have no questions, thank you.

THE CHAIRMAN: Mr Johnston?

MR JOHNSTON: I have no questions either.

THE CHAIRMAN: Professor, it occurred to me as the discussion has been going on to ask something that may be totally wrong, but there is a great deal of mythology in Scotland relating to the production of whisky, that the shape of the vessel used for distillation affects the outcome. Is there anything in this, that the precise configuration of pipework, tubes, connections and all the rest of it has a bearing on what one gets out at the end of a chemical process?

A. Yes, certainly. The shear rate of certain processes, for example, during centrifugation and during tubing from the centrifuge to the vessel -- during that shearing you can see that certain changes can occur and notably, when foam is developing, it can lead to denaturation of a molecule. So that's just two examples of what I have heard that affects the outcome in fact.

THE CHAIRMAN: So the outcome is very sensitive to the physical characteristics of the equipment.

A. Yes.
THE CHAIRMAN: And to the operation of the equipment?
A. Yes, yes.
THE CHAIRMAN: I think that's quite difficult for a non-specialist to understand. I suppose rate of flow would come into it if we are thinking of the physical dimensions of tubing and so on. Is there any key to understanding this or is it simply something you can tell us happens in fact?
A. Well, I was thinking about if there are other examples which you might find interesting. In fact, you see, it starts already with the collection of plasma, yes? I don't know whether you are familiar with how plasmapheresis, for instance, takes place.
THE CHAIRMAN: Yes, we have actually seen it.
A. So you have seen the centrifuge, you have seen the bowl, you have seen what it takes. And you have also seen the normal collection with the tubing.
THE CHAIRMAN: Yes.
A. Then they must have told you that there is a difference in the recovery of Factor VIII of one sort of plasma versus the other one, that the ones which are coming from plasmapheresis have a higher yield than when you use what we call "recovered plasma". But in the background of that difference is, in fact -- of course

there is a time effect but there is also an effect which is due to the fact that if you use normal blood, which is donated, and you use that as your source material, the bags which are used for that are just, immediately after collection, if it is done at least properly, are put on ice and they, during transportation, start to move. So all these factors add to a loss of Factor VIII, which indicates that there is something going on there, which is the movement in the material but also the contact with the environment, in this case the polyethylene plastic bag, which interfere with it.

We know that the blood, even though it is anti-coagulated, when it comes into contact with a foreign surface, a cascade of events may occur leading to clotting, yes? Now, of course, in the process of citrate, which takes away all the calcium, that process is retarded. But again, also here in Scotland, they have tried it find out how it is possible, by the addition of calcium, to affect the yields of it.

So there is a scientific explanation possible how shear stress, contact with a surface, the dimensions of the environment, can indeed all have an influence on what the final product and what the final yield is. It is not just one aspect. It is a whole physical process which I think plays a role there. But you must be

a physicist to ask this so you probably know better than I what could be --

THE CHAIRMAN: Not at all. I daren't go and ask my colleagues out at Riccarton or they would give me a totally different answer, no doubt. You have mentioned more than once "shear".

A. Yes.

THE CHAIRMAN: And I think most of us have heard of shear stresses in relation to civil engineering, construction and such like. What is the meaning of "shear" in this context?

A. The meaning of "shear" is that -- well, of course, if you look in the human body at shear stress, it means that you have blood vessels of different dimensions, which, when it comes to bifurcation, you get a swirling effect there. That means that the velocity of the blood cells in that blood stream is different at various parts. So near the wall it's different from the middle, and that can cause, in certain circumstances when there is a damaged vessel wall, that there is clotting going to happen and the platelets attach to it, and that is affected by the shear stress.

THE CHAIRMAN: Okay.

A. There's quite a lot of literature about that.

THE CHAIRMAN: I don't think I need to go into it for my

benefit; just to have a definition here, is helpful.

Now, Mr Di Rollo, do you want to ask any questions arising from my intervention?

MR DI ROLLO: No thank you.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: No thank you.

THE CHAIRMAN: Mr Mackenzie? Thank you very much, you have been very helpful. And I'm sure we will all benefit from contemplating what you have said.

A. It was a pleasure, thank you very much.

MR MACKENZIE: There are no further witnesses on C3, but I wonder whether it would be convenient to spend five minutes in the usual way listing the statements from those witnesses who haven't attended. It shouldn't take more than five minutes, if that would be convenient.

THE CHAIRMAN: I'm sure if it's five minutes, the stenographer will be able to tolerate that.

MR MACKENZIE: I'm grateful.

THE CHAIRMAN: Professor, make yourself comfortable or whatever.

MR MACKENZIE: Could we please have the inventory for this topic, PEN0172484? This document is now in court book. I have to say, sir, this was compiled by Mr Evans and I certainly found it extremely helpful. It lists all the reference numbers for the statements and also

the witnesses' references. Can we go to page 3 of the inventory, please? I hope you have a copy of this, sir, I should say.

THE CHAIRMAN: I don't recognise it as something I have in hard form but I am sure it will be very helpful.

Oh, I do have it in hard form.

MR MACKENZIE: I'm grateful. We can see on page 3, "Other statements", and in short, sir, all of the statements I will now list deal with the question of collaboration between Scotland and England.

Dr McClelland's statement was PEN0170003 -- we don't have to go to any of these documents -- and also an additional response, PEN0170001.

Dr Scott of the SHHD's statement is PEN0171017.

Over the page, please, in the inventory, Mr Hamill of the SHHD, PEN0170007.

Then Dr McIntyre, again SHHD, PEN0170019.

Again, Dr Forrester of the SHHD, PEN0170005.

Mr Morison of the SHHD, PEN0170014.

Over the page of the inventory, please, Mr Davies of the SHHD, PEN0171020.

There are some other ancillary documents, sir. In particular, under 10b Dr Boulton has a very brief statement, PEN0171825. We asked him a question about the issue of Z8 and I think, unsurprisingly, Dr Boulton

said he couldn't remember but suggested we check the issuing records, which we have done.

THE CHAIRMAN: Which don't actually take you to the downstream end of the exercise, which would have been very interesting to be able to follow.

MR MACKENZIE: The one outstanding matter in this topic, sir, is Dr Cuthbertson had undertaken to check the PFC records again and to try and clarify where and when the phase 1 trial was carried out and in particular whether it included GRI and Northern Ireland. So fingers crossed there.

THE CHAIRMAN: So we still wait for an answer from Dr Cuthbertson?

MR MACKENZIE: Yes. That's the one outstanding matter, sir.

THE CHAIRMAN: Yes.

MR MACKENZIE: Some other ancillary documents, sir, to complete this, if I may. We don't have to bother with 11, but under 12 document PEN0171662 is a copy of our request to the SNBTS for the provision of documents on this topic, together with the reply.

Two final ancillary documents we found in the Inquiry database on the question of clinical trials. Could we, please, bring up document SNB0076312. One could see this is a letter dated 23 December 1986 from Dr Perry to Dr Boulton on the question of the clinical

trial of Z8:

"I wrote to Dr Mitchell advising him that we wished to bypass the formal distribution network for this trial. Bob Crawford has responded (see enclosed) and I see no reason not to drop John Davidson a note of that material which will be issued to Charles Forbes when the time comes."

If we can compare that, sir, with the letter we had looked at, which is SNB0076298, this was the earlier letter of 12 December 1986 from Dr Crawford to Dr Perry and, well, if one looks at this letter in isolation, one may think that Z8 had been sent to Glasgow. I think, when one looks at the later letter of 23 December, it appears that Z8 hadn't been sent. But I think we will leave these matters with Dr Cuthbertson and see what he can tell us in due course.

THE CHAIRMAN: Yes. It doesn't really provide an answer to the intriguing background questions as to what on earth had been going on that led to this situation. But perhaps you don't have an answer to that.

MR MACKENZIE: We have looked in our database for the letter of 9 December referred to here and we can't find that. It may remain a mystery.

Finally, sir, could I just bring up SGH0031745? We will see in a second this is a letter from Dr Mayne

of Northern Ireland to Dr Forrester of 7 July 1987. It really deals with the question of the accuracy of the minute of the meeting of the SNBTS and haemophilia directors. I'm not sure one can take much from this letter other than that I think the general tenor is that Dr Mayne supports Dr Ludlam in wishing compensation before trial. But I'm not sure how much one can take from this letter in isolation, but it's there for what it's worth.

THE CHAIRMAN: I think my impression was that a number of haemophilia clinicians came on board, as it were, over a period of months and expressed their support for Dr Ludlam on this matter. But this doesn't really help us to tell whether any material ever did go to Northern Ireland for trial.

MR MACKENZIE: It doesn't, sir.

THE CHAIRMAN: It doesn't. Are we any further forward on that or are we still dependent on Dr Cuthbertson?

MR MACKENZIE: We are dependent on Dr Cuthbertson, at least in the first instance.

With that, sir, and subject to that one outstanding matter, that completes the evidence on this topic.

THE CHAIRMAN: We can rise now.

MR MACKENZIE: Dr McClelland is due at 10.30.

MR DI ROLLO: Before we rise, we want to observe that, in

relation to Dr McClelland's statement, there is one matter which does arise which I have an interest in.

There is a document, PEN0161152. This is a document we have already seen, sir and if we go to the second page of that, paragraph 14.3 and 14.4, this was a meeting in December of 1985 and there is comment about the progress of Factor 8Y. Dr McClelland doesn't specifically refer to this item in his statement and a request was raised with Dr Ludlam as to whether or not information was passed on to him by Dr McClelland about the progress of Factor 8Y at that time in earlier evidence. That is really to do with the C3A section but there is an overlap between C3 and C3A and I think it's important that I indicate to you, sir, that I would wish to know from Dr McClelland whether or not any information was passed on about the progress of Factor 8Y at this time.

THE CHAIRMAN: Thank you for the notice. I'm sure, if there is any problem about it, it will be drawn to my attention, but unless I'm told there is a difficulty, you just proceed and ask your question.

MR DI ROLLO: Very good.

(11.15 am)

(Short break)

(12.00 pm)

DR BRIAN MCCLELLAND (continued)

THE CHAIRMAN: Almost good afternoon. That's not a criticism of you or the traffic. Don't worry.

Yes, Ms Dunlop?

Questions by MS DUNLOP

MS DUNLOP: Sir, as you are aware, we have Dr McClelland back with us. He has been able to join us to complete his evidence on the B2 and B5 topics. I gather that Mr Dawson has questions for him.

MR DI ROLLO: Yes. Mr Dawson will be dealing with this matter. Can I just say how grateful we are to Dr McClelland for coming back to answer these questions.

THE CHAIRMAN: Mr Dawson, I hope you are properly aligned on a microphone.

Questions by MR DAWSON

MR DAWSON: Good afternoon, Dr McClelland. As you are aware, we have asked you to come back today to answer some more questions on B2 and B5 topics, which, as you know, are part of a series of topics dealing with the HIV section.

So the questions I have for you today relate really to the first half the 1980s, just to put them into some context. Could I start by asking you first of all some questions about the products used in the treatment of haemophiliacs in the Southeast of Scotland over that

period. In your evidence relating to the B2 topic on 6 May, you pointed out that the requirement for the use of concentrates for patients in Edinburgh, did increase quite rapidly after the arrival of then Dr Ludlam in Edinburgh in 1980.

To what extent was the rise in the need for concentrates due to the introduction of prophylactic treatment?

A. I can only answer that from, you know, from recollection because, as I stressed before, I was never directly involved in the care of the haemophilia patients.

But my recollection is that it probably was not primarily related to sort of extension or starting -- or extension of prophylactic treatment but more to the undertaking quite lot of surgery for patients who had probably got quite severe and long-term joint damage, and possibly by today's standards certainly may have merited earlier surgery.

I think Dr Ludlam's predecessor, as I'm sure I and others have said, had a very conservative approach to the care of patients and I think when Dr Ludlam came, having worked in a different clinical setting, he probably felt -- I haven't read his evidence on this so I don't know what he has told the Inquiry, but my sense was that quite a lot of patients underwent surgery,

particularly knee surgery, and that can create very large, as you will know -- a requirement for a very large amount of Factor VIII replacement.

Q. Would it be fair to say that the prophylactic therapy programme was a factor however, but along with the other factors --

A. I honestly don't know.

Q. You have mentioned there the culture that was in place before Dr Ludlam arrived, I think under Howard Davies?

A. Correct.

Q. We have heard evidence from yourself and others that during the period before 1980 there was, I think, almost exclusive reliance on cryoprecipitate in the treatment of haemophiliacs in the Edinburgh or southeast region?

THE CHAIRMAN: I'm sorry, what period are you talking about, Mr Dawson? Because I have to say, that is not my recollection of the evidence.

MR DAWSON: My recollection of the evidence, sir, was that under Howard Davies, before 1980, the treatment of the patients had been, at least predominantly perhaps, with cryoprecipitate.

THE CHAIRMAN: You might like to look at the Cash and Spencely article tracing the use of product. It's the generalisation that's difficult, Mr Dawson.

MR DAWSON: I understand that. I'm really just trying to

create a bit of context. I do want to ask specifically about a period slightly after that which Dr McClelland hopefully will be able to help us with.

Can I ask you about the position in 1983 and in particular whether or not you discussed with Professor Ludlam, then Dr Ludlam, the possibility of starting his patients on cryoprecipitate treatment at that time.

A. I certainly don't have any recollection of initiating that discussion with him and to be honest, I wouldn't have considered that to be my responsibility. Dr Ludlam was extremely well informed about the potential risks, I think he was aware of the -- you know, the potential for risks in relation to AIDS every bit as soon as I was, and was very much in discussion with professional colleagues in the UK and around the world.

It's very possible that we had discussions about the supply of Factor VIII because in a sense -- of cryoprecipitate -- that was my responsibility. We were set up to make cryoprecipitate and we had plenty of plasma. It was merely a matter of taking plasma that would otherwise have gone for fractionation and making cryoprecipitate from it.

So I don't think there would have been any particular difficulties in our responding to increased

demand but I don't actually have any recollection of discussions about this and obviously I only saw these questions yesterday. I haven't had a chance to look at any documents to see if there is any recorded evidence about such discussions.

Q. Okay, thank you.

You mention there the position as regards awarenesses of the HTLV-III risk from products. That's something I would like to ask you some questions about.

We have heard evidence from you, predominantly in the B1 section, as regards efforts made by you in drafting a leaflet relating to donor exclusion in about 1983 and that's covered quite extensively, I think, in the preliminary report, in particular at paragraph 8.28 and 8.33. I wondered if you could answer this question. Would it be correct to say that you had serious concerns at that time, when you were drafting the leaflet, in 1983, that there was a risk that HTLV-III had entered the donor population in Scotland?

A. I'm trying to recreate that and also I think probably everything I have to say about that was probably said in a previous statement and in the evidence I gave relating to that, because I have already been specifically asked whether I was aware of AIDS cases in Edinburgh at the time of the first draft of the leaflets and I have said

that I'm not at all sure that I was. I'm not sure that anybody was aware of AIDS cases in Edinburgh. And that wasn't really -- that wasn't really what was motivating our efforts to prepare the leaflet and take other measures to minimise the risk of anyone who might have infection coming to donate. What we were fairly, I think, confident about, if that's the right word -- and I think you have touched on this in another of your questions -- was that it was inconceivable really that it would not appear in our community.

So in a sense, I don't think we had any conviction at all. In fact, I think we probably were hoping that it was not -- I'm sure we were hoping that it was not in our donor community at that time. But we had a betting man's certainty that it would be there at some point in the future. So we had to take action as soon as we could.

Q. So you were taking all precautions to prevent that possibility?

A. Absolutely.

Q. Okay, thank you.

Could you try and describe for me what your understanding was in 1983 of the risks for patients who did acquire infection with HTLV-III as regards the understanding of the progression of the disease at that

time?

A. I'm not sure that we would have quite described it that way because I can't actually remember when HTLV-III was first named (inaudible). What we did have access to, if you like, was the epidemiological information which was being built up in the United States, and my recollection was that there was already published or available evidence that showed that this condition, AIDS, was associated with quite a high mortality. It would be very difficult to produce a sort of confidence, in if you like, actuarial predictions about mortality at that early stage, because in many cases one didn't know how long people had been infected for and little was known about the natural history of the disease. But I think we were very clear that this was a very serious condition that was likely to kill you.

Q. There is a document that we came across before in the evidence of Dr Boulton, in the B2-section. Could I just ask you very quickly about that. The document is SNB0014033. Hopefully --

A. Is that the meeting report?

Q. It's a meeting --

A. I have got it here.

Q. It's entitled "Notes of meeting with Immuno at London Airport 24 January."

As we found out from Dr Boulton, January is January 1983. Could I just ask you very briefly about page 4035, which is page 3 of this document?

There is a reference about half way down that page so some information about Acquired Immunodeficiency Syndrome, as you will see in. And in particular, in the penultimate paragraph on that page, up to 10 December 1982, some 800 people had been reported as suffering from the AIDS and there was a 45 per cent mortality. And that 45 per cent mortality figure has been underlined.

Dr Boulton was under the impression that it would be you that had done that underlining. Is that correct?

A. I have absolutely no idea. I don't actually remember this note. I remember the existence of this meeting in London. You know, one person's line is very much like another's. I really can't remember.

Q. Would that be consistent, however, the figure there, 45 per cent mortality, with what your understanding around about the beginning of 1983 of the disease would have been?

A. I think this is exactly the data that I was referring to that was being published by the CDC. I think this was already appearing in the Morbidity and Mortality Weekly Reports. All one could really say was that there was

a growing population of people with this syndrome and quite a lot of them had already died. That was, in a sense, the most accurate statement that one could make at that time.

Q. Do you remember having any discussions about the possible risks of HTLV-III entering the donor system in Scotland with Professor Ludlam at about this time, by which I mean 1983?

A. I don't remember specifically. There was an issue, which again you have touched on, later on, that we clearly did have some discussions about the issue of contacts -- and we can come back to this -- with patients with haemophilia, which is on this specific issue.

Whether Dr Ludlam raised that with me or I raised it with him, I can't remember because I have only seen parts of the correspondence, but I wouldn't have -- I think my view at that time would have been that it was my job to do everything I could to safeguard the blood supply. I'm absolutely certain Dr Ludlam would have known, at least in broad terms, what we were doing because we tried to make it very public. Did I consult him about what we were doing? No, it was my job with my colleagues to get on with that. I'm not sure if I'm understanding the question.

Q. I'm not really referring to consulting him in the sense of seeking his permission, or anything like that, to do anything, because obviously you had your distinct areas of responsibility. What I'm talking about is the extent to which you had discussions with him about your concerns, views, understandings, of the risks at that time.

A. I really can't remember. I think it's almost certain that we would have had, frequent informal conversations about it because we met regularly. We worked in the same corner of the same hospital. But in terms of specific recollections -- it was a subject that was very much -- you know, anybody to do with blood, whether somebody treating patients or somebody trying to provide blood, it was very much in our consciousness at that time.

Q. That's precisely what I'm getting at, Dr McClelland, the idea that these issues would affect both the people at one end of the system and the people at the other.

A. Yes, absolutely.

Q. And therefore, what I'm really getting at is whether or not there was any formal system for the airing of views and sharing of information which existed between the two of you at that time. I think you have already answered that it would be informal. Is that right?

A. I think we didn't need a formal system. That would probably have just got in the way, quite honestly.

Q. Okay. Thank you very much.

If I could move on to a slightly different area, now. This is really the B5 topic, which you will recall also having given evidence on. This is moving to a later time period than the one we have been talking about. Really focusing on the late 1984 period and the time when it emerged that there had been some haemophilia patients who had been infected and had tested positive on antibody testing.

Could I just ask you to have a look, please, at one document, which is PEN0161294? I think this may be a document you have been taken to before in this context, Dr McClelland.

A. Yes.

Q. It's an Evening News article from 21 December 1984 and in particular in the right-hand column there, the context of this is set out in the first paragraph where we see:

"The Scottish Blood Transfusion Service today appealed to four groups of people not to give blood following an AIDS scare. Tests in Edinburgh have shown that 50 haemophiliacs have developed antibodies to the AIDS virus."

That's the context here, and under the heading "Vulnerable" in the right-hand column, there appears to be a quote from you, which says:

"Dr McClelland said the 15 people were discovered as the result of routine testing of those most vulnerable because of their reliance on frequent transfusions."

What I want to ask you about was really whether the use of the phrase "routine testing" to apply to the testing which had been done on these patients is an accurate description of that test?

A. I mean, as Lord Penrose has commented on one of my previous appearances here, we can't always totally rely on the accuracy of press reports.

Q. Of course.

A. So whether I said "routine testing" or not --

Q. I'm not seeking to criticise in any way, I just wanted to know whether if someone had got the impression that that was routine testing, whether that would be accurate?

A. It clearly wasn't routine testing at that time. Because it was still -- not routine testing in the sense that every patient with haemophilia was having that test done. This was something that was very new. I think, if I did use the word "routine" -- and whether I did or not is immaterial -- I certainly at that time, I think,

would have taken the view that it would be a matter of not just good clinical practice but actually a duty of care for someone caring, for patients who were known to have a high exposure to blood and blood products, to do whatever they could to ascertain whether they had become infected.

So in that sense it's not an action that I would have questioned, it was a matter of good professional standards of care to ascertain this and then to be -- you know, to take the appropriate action in terms of both information and care for the patients.

Q. Thank you.

A. And doing that, as you will have heard from many witnesses already, was actually not particularly straightforward in 1984.

Q. Obviously the tests that we were talking about, just to recall some time ago that we went through all of this, that these were the tests, the antibody tests, that were done by Dr Tedder on the patients. Is than right?

A. Yes, to the best of my knowledge, this specific group of patients, who led to the -- you know, who were identified by their biology, the appearance of the virus in the Scottish donor population, those tests were all done in the laboratory of Richard Tedder, then in the Middlesex Hospital.

Q. Could I just ask you: as far as the tests, the antibody tests that were being done at that time, what did a positive antibody test tell you about a patient at that time?

A. I think my interpretation of it was that we would take it that that meant the patient was infected with the virus. Certainly from my perspective, as somebody looking at people as potential donors, I would have had absolutely no doubt that the presence of a technically confirmed evidence of an antibody to HTLV-III would totally debar that person from donation because I would work on the assumption that they (a) had the virus and (b) could transmit it.

I think the second question is implied in what you are saying: what did this tell us about the prognosis, ie did it mean they were going to get AIDS and die? That was a lot less clear and you will be aware that in the literature of the time there was quite a lot of controversy, and there was a belief, I think more in hope perhaps than anything else, that quite a lot of people who had this evidence of infection might actually not develop the full syndrome.

I think history proved that there was only a very small minority of people with the particular sort of genetic make-up who would carry the virus and not become

ill.

Q. Thank you. If we could just move on to a slightly different area at about the same time, this was the meeting which you attended with Dr Perry and Dr Ludlam on 15 November 1984. Could we have up, just to refresh your memory, the document SNF0013624?

This is a letter from you to Dr Cash. You refer to the meeting in the first paragraph there:

"I have had several discussions with Dr Christopher Ludlam following the discovery that some recipients of PFC Factor VIII have developed antibodies to HTLV-III during 1984 which must, at present, be attributed to infusions of PFC products. I spent several hours this morning with Dr Ludlam and Dr Perry, acting director of PFC, reviewing the data and write now to report to you, as national medical director, on our conclusions."

You see over the page there are some conclusions listed. You have obviously given quite a bit of evidence on this meeting already but I just want to clear up a couple of things with you. The first is was the purpose of that meeting which you attended with Dr Ludlam and Dr Perry looking at the records to see if you could pin it down to a single batch?

A. I think that it probably was not quite as specific as

that. I think what we were essentially trying to do was to review the evidence that we had -- the objective was probably to decide which batches -- the strength of evidence that we had and therefore the decisions that probably would have to be taken in terms of which batches might have been implicated, and whether any of these batches were still in stock anywhere and would have to be withdrawn.

I don't think that we started with -- we may have started with a hope or with a sort of belief that it probably was only one batch because, you know, it was a surprise to us, a nasty surprise to us that any of the batches were infected. So I think our starting point would probably not have been to say, "We expect lots of batches to be infected," but I don't think we would have started off saying, "We are working on the assumption that there is only one and we have just got to find it".

I think if you read the documents that I wrote at the time, I don't think that implication is there.

Q. Okay. Thank you.

Professor Ludlam in his evidence suggested that you might have had available to you at that time a spreadsheet containing information about the transfusion histories of the infected patients. Do you recall that at all?

A. I don't think I knew what a spreadsheet was in 1984. I was pre-computer literate in those days, even more so than I am now.

Q. Perhaps if we just call it a document that contained that information?

A. I'm sure we had a piece of paper which would have been compiled, probably jointly, by members of Dr Ludlam's staff involved in treating the patients, and I would think also by my own blood bank staff, because they actually issued the products and kept good records of who got what, and I think certainly Dr Ludlam must have had that information.

I cannot remember all those years ago exactly what paper we had in front of us, but looking at the report from Dr Cash, he clearly must have had information about both the transfusion history of these people, you know, the batches and the quantities that these patients had received, and we must also have had information about the test results on -- in some cases -- more than one blood sample, because we had some information about when was the first positive sample and we were trying to tie that in, as one of the clues to which batches might have been implicated.

Q. Could I just ask you --

A. I can't visualise now the desk with the papers on it,

I'm sorry.

Q. There is something else I want to ask you about the document, but just on that very point you were making there, you are assuming, as I understand it, that you had available, or you are recalling you must have had available to you, information about the timing of the first positive test for these patients but presumably also the timing of the last negative test. Is that correct?

A. Yes.

Q. And that would create a sort of seroconversion window, if you see, a window in which it would appear that that person has seroconverted. Is that right?

A. That was a fairly crucial piece of information because, obviously, these patients would be getting certain products at a certain time and you could really only hope to attribute seroconversion of the infection episode to a particular product if you had the information to say, right, the patient was negative here, got the treatment here and became positive there.

Q. How --

A. It's simple cause and effect stuff.

Q. I'm just wondering how exactly one links the data about the seroconversion window, as I have called it -- that may be inaccurate -- to which batch you think was the

infective batch.

So say, for example, if one has a last negative test in March of a particular year and a first positive test in May, what time period -- obviously one would be looking at products that had been administered before that window, but how far before that window would one be considering products that might be implicated in the infection?

A. I think the actuality of this is that these are retrospective studies. You only have the samples that you have, which were taken at times which were dictated by factors other than the investigation that you are now conducting. And you have probably fairly accurate information about the batches and the dates over which they were administered. So you have to do the best you can with that. And it's very unusual in a retrospective study, to have perfectly timed samples that will allow you to pinpoint exactly what happened. You have to say, "Well, the probabilities are that it was this batch because it was negative here and positive here. And he got this batch some time in between."

I mean, we knew, I think, probably at that stage -- well, even if we didn't know, we would have inferred because it's true of all infections, that between exposure to the infectious agent and the appearance of

a detectable antibody in the patient, there will be a gap, it takes time for the immune system to make the antibody. But we probably -- we certainly didn't know with any accuracy what that gap was.

Q. What time gap were you applying in your thinking at that time? Can you recall?

A. I don't think we were. I don't think it was that sophisticated. We didn't -- that, in a sense, wasn't relevant because what we could do was governed by the archive samples that existed. You couldn't invent new archive samples. So we couldn't control those dates. I'm not remembering this; I'm trying to reconstruct what I think we would have done.

Q. Thank you.

Just returning to the document which I described as a spreadsheet earlier, just one thing I want to clear up with you. Professor Ludlam in his evidence suggested that you might have retained a copy of information that was available to you at that meeting, and he pointed out that he might have had a copy but it was probably lost at the time when his department moved from Lauriston Place to Little France. He suggested you might have a copy, though, and I just wanted to find out whether you did or you didn't?

A. I'm not aware of a copy. I haven't seen a copy of that

in any various delvings into my own archives. So quite a number of years.

Q. Thank you very much.

Could I just move on to something slightly different, although it's still related to the issue of the infection of the patients in Edinburgh at that time.

Could we have up the document SNB0086427, please? I'm hoping that you will recognise this document, Dr McClelland. It's an interim report by Dr Cuthbertson which comes from June 1986 and, as you may recall, at that time certain tests were being done on batches which may have been responsible for the infection of the patients in Edinburgh in particular.

You will see at the bottom of that page, that there is a list of batch numbers and you may recognise the one at the bottom, which was the one, as is indicated there, known as the "implicated batch", which was the one that you had taken the view was most likely to be responsible for the infections.

At the bottom it points out that:

"The batches marked with an asterisk were tested for HTLV-III antibody using a sensitive variant of the Wellcozyme assay, no trace of antibody was found in any of these batches."

What I want to ask you about is obviously the theory

which most people have, and indeed the one that I have just mentioned, about the source of infection of these patients, ie that is was this implicated batch, or at least for most of them it was.

Now, this result here, of an antibody negative in 1986, would appear to be inconsistent with that proposal. What I wanted to ask you was whether you thought that it might be possible that the batch was positive for the virus but in some way negative for the antibody, and the theory that I want to put to you for your comment was whether perhaps in the fractionation process the antibody, which is what this test is looking for, may in some way have been stripped away leaving an infective product which is antibody negative.

Do you have any view on the cogency of that theory?

A. I think you have made two statements, which are quite separate. One is, did I believe -- do I believe now -- that one of these batches could have transmitted infection but yet had an negative test for antibody in 1984, and that is entirely possible and there are lots of possible reasons for that.

Your biochemical theory of how it might have happened, I'm not really competent to comment on that but I think there are numerous possible explanations for, and numerous examples in the literature in relation

to this and other infective agents, where no test, except infusion into a human, will detect the fact that this product is infective.

Absolutely classic examples of this with Hepatitis B, where it will not infect primates, it will not infect any other animal species, but the same product given to humans will produce Hepatitis B because the human is a very, very sensitive host.

In 1984 the tests were not particularly sensitive and the tests that were available were all designed to be used on single blood samples. You know, a product which is quite different in nature to a concentrate of certain proteins prepared as Factor VIII is prepared.

And dilution, you know, is another factor because this might have been present in a very, very low concentration, being one donation in a thousand or 10,000.

Q. You pointed out the reliability of the test as being, obviously, an important factor. You mention the test in 1984. This is actually from 1986. Would that --

A. The same applies.

Q. The same applies?

A. All these tests have become progressively more sensitive and it's something -- we have had to be very careful in interpreting the results of things that have happened at

different periods of time, to take account of the fact that something could have been completely undetectable in year 1. Because of refinements and improvements in the tests, it could be quite detectable in year 10.

Q. Who would be the best person to ask about my biochemical theory?

A. Dr Foster.

Q. Thank you.

Can I just move on to something, again related but to do with a slightly different document.

Could we have up the document PEN0121423, please? This is a document to which you have been taken before. You may remember it. It is a letter from you dated 28 November to Dr Tedder, pointing out that you had now, by that stage, November, identified all the donors who contradicted to the batch of Factor VIII under discussion. I'm assuming that's the implicated batch --

A. Yes.

Q. -- that we have mentioned. There are approximately 4,000. Donation samples are available from approximately half of these at present and the remainder will take some considerable chasing up. And you ask him:

"Can you advise on the possibilities of getting these donors screened?"

You were asked about this piece of correspondence in your original evidence on this topic, and you said that the fact that this was not pursued was something which could be criticised in retrospect. I just wanted to get you to explain why it is that you thought that that decision could be criticised in retrospect.

A. I'm not sure I said it could be criticised. I said I wasn't sure now that it was the right decision, which is slightly different. I'm not sure if you are referring to the transcript or my witness statement.

Q. I think it was the transcript that I had --

A. In the transcript what I actually said was:

"... I have to confess I did not think of going to the United States to get an answer to this question. In retrospect I should have done."

I think that's what I actually said.

Sorry, your question?

Q. I apologise if I have misrepresented what you have said.

A. That's all right.

Q. I really just want to explore why it was that you thought it was something that would have been worth following up on the basis that it wasn't followed?

A. Looking at it by the standards of today, this is something that we would do. We would turn the place upside down to test all the source donations.

It was not the standard of 1984 or 1986, whenever this was. There was another problem actually, because it wasn't at that time routine to -- it wasn't required and it wasn't general practice to retain archive samples for long periods. So one or two of the blood centres in Scotland did retain donor samples for long periods. The others did not.

So while we had archived samples for about 2,000 of the donations for the others, the donors would have had to -- or most or all of the other 2,000 -- the donors would have had to be recalled and retested. And actually the results of that recall and retest, even if we had found a positive, it wouldn't have proved anything because they obviously could have become infected by some route subsequent to that contributing to the original batch. And I think that's probably one of the reasons why Richard Tedder didn't -- he wrote me a brief note, which is in the documents.

Q. I think we looked at that.

A. Saying that, you know, unless we could be confident of getting virtually 100 per cent of samples, he didn't think it was worthwhile. And he didn't have the capacity to do it quite honestly; 4,000 samples would have sunk his laboratory without trace at that time.

Q. Would another way of trying to work out the answer to

the same question be to ascertain whether any of the donors whom you had identified, who contributed to the implicated batch, died of AIDS?

A. I think it would be open to the -- if that information was available, it would certainly be interesting and might be suggestive, but it would not tell you, in the absence of adequate blood samples, when this donor had become infected, so --

Q. It might provide a bit of a clue, though?

A. It might provide a bit of a clue. I think it would have been extremely difficult to do. I don't think -- you also asked could we do it now. I would have to talk to David Goldberg and his colleagues about that just to see whether, with the existing information, databases and so on -- I think if we had a name, if Health Protection Scotland were able to identify a relevant group of individuals who died of AIDS, it is possible that a search could be made in historical blood donor archives, but to be honest, I'm not sure whether it would be a particularly useful exercise.

I haven't had time to think that one through.

Q. Okay, thank you very much.

Moving on just to the next topic, this is again a particular document I wanted to ask about. This is SNB0064686. Again, we are dealing with roughly the

same time period, now into December of 1984, and this is a letter which I don't think we have looked at before, which is a letter from Dr Ludlam to yourself. It says:

"Dear Brian,

"Thank you for your letter of 12 December concerning our recent discussions about the desirability of close family members of haemophiliacs not donating blood. As we agreed in our discussion, it would be better to disseminate this information in the haemophiliac community via existing lines of communication, rather than add these potentially high risk donors to your formal list as published by the SNBTS."

At the meeting with haemophiliacs on the 19 December, at which you were present, this point was made clear to make sure that the wider haemophiliac community is made aware that they should not be blood donors. We are arranging for a circular to be sent to every patient with moderate and severe haemophilia A and B. I hope this will prevent any further donations within the Edinburgh and Glasgow areas. We are planning to send the circular to the other three east coast haemophilia centres, asking them to distribute it amongst their patients."

Am I correct to take it this is one of the consequences of the infection of the Edinburgh patients,

that the policy for donor exclusion was, not formally, but informally changed in this way?

A. I think we will have obviously, in sort of following through the implications of discovering that haemophilia patients in Scotland -- some of them now had HIV -- I would certainly have had a concern, particularly sexual partners, or anyone whose contacts with those patients would put them at risk of contracting infection, that could also have included carers who were making up the Factor VIII products and who themselves would then be at risk of needle stick accidents.

I think we were just trying to lock some doors here and say what can we do to minimise the risk that any of these people who may have a slightly higher risk than average -- to minimise the risk of them giving blood. Dr Ludlam was, I think, quite understandably, not enthusiastic about having these groups of people formally identified among its risk groups, the exclusion groups that were very much standard around -- you know, not just in the UK but in other countries as well.

Actually there was not the epidemiological evidence to justify including them in those groups because none of these people had been recognised as being infected or being a source of infection.

So I think this more informal approach was what,

certainly Dr Ludlam as the consultant caring for those patients, felt was appropriate.

Q. What was meant by "close family members"?

A. I don't know what Dr Ludlam, who wrote the letter, meant by "close family members" but what would have concerned me, as I have already said, is people -- the nature of whose contact with a patient, who was or might be infected, could put that individual at risk of acquiring the infection, and that's blood or sex.

Q. I'm just trying to envisage how this might work if someone who was within the excluded group turned up at a donor session. Can you explain to us how that would have been dealt with?

A. Well, it's very difficult to deal with these things and I think in another bit of my evidence I made the point -- and I I'll make it again -- that I was always very clear that the exclusion of people who could transmit HIV was highly dependent on having a good test. All the other deferral measures are contributory and important but of very much less than 100 per cent efficacy. How would you identify somebody who lived in the same house as a haemophilia patient and would that in fact justify not accepting their donation is a very difficult thing to deal with.

What I can't tell you, because I haven't had time to

look, is whether in guidance that I wrote or Dr Anne Smith wrote for our donor staff, we addressed this issue and how we addressed it. But I can't think that it would have been easy to do anything particularly effective. We would have largely relied on people informing us of that.

Q. Would that be something you would ask them when they turned up, "Are you in this category?"

A. No, not routinely because you would be asking thousand and thousands and thousands of people a question to which 99 per cent of them --

Q. I'm slightly having a bit of trouble with how it is that these people would be identified, because if they would be identified through the lines of communication that have been identified by Professor Ludlam there, ie through the haemophilia community, presumably they wouldn't have turned up to a donor session anyway?

A. Professor Ludlam's intention, and he was absolutely right, was to try, through what is quite a small community with quite good communication networks, to try and, you know, encourage and inform and motivate these people to not volunteer to give blood, and that was obviously the most practical and sensible thing to do so.

Q. But there wouldn't have been proactive steps taken at

the donor session to identify these people?

A. I don't think so.

Q. Right.

A. Because I don't think we could have designed a way of doing it. But, as I said, I would have to go -- as the Inquiry knows, there is an awful lot of detailed information over the period of the implementation of testing and so on. For about two years we were issuing instructions for the staff about how to deal with just this sort of problem. Whether we did take specific action to try and address the problem that you have correctly raised, I honestly can't remember. I would have to go back and dig all through that literature.

I have to say I cannot think now how we would then or now have designed an effective procedure to address this.

Q. Thank you. That concludes the questions I had, sir.

There was one further question, which isn't actually on the B2 or B5 topics. Mr Di Rollo referred to this earlier and I don't think there is any difficulty, as far as the Inquiry counsel are concerned, with this matter being raised. It's just a couple of questions.

Sorry to jump about the topics, Dr McClelland, but I just wanted to ask you one question that had come up in connection with the C3 topic, with which the Inquiry

has been dealing over the last couple of weeks. In particular, could we have up your statement from that section, which is PEN0170003? In particular, I wanted just to refer you to the third paragraph of that, where you say -- you are talking about the CBLA research and development committee, of which you were a member, I think, and it says there:

"I have no firm recollection about sharing information from the committee. It was my usual practice to share any information that I judged important for SNBTS with Dr Cash, and directly, or through him, with the other Scottish transfusion directors, and I can see no reason why I would not have done so following meetings of the CBLA committee. Dr A E Bell of SHHD also attended these meetings and I am sure he would also have communicated information both to Dr Cash and to the SHHD."

Could I just take to you a couple of documents, and there are a couple of passages I just wanted to remind you of. Hopefully, you have seen these documents before, which are basically minutes of that committee. In particular, the first one is document number PEN0161142. We can see from the first page there this is not a meeting that you attended and we can see under "Apologies" that you had sent in your apologies.

This is a meeting which took place on 9 July 1985 of the research and development committee. The particular passage I wanted to refer to you was on page 1144, which is the third page of these minutes, and it's the penultimate paragraph on that page, where it says in July 1985:

"Evidence for 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."

You weren't at that meeting but would it be fair to assume that you would have been sent the minutes after?

A. I'm sure I would have been sent the minutes, yes.

Q. Could I just take to you one other similar passage in a later meeting? This is document PEN0161152. Can we just have that up, please? That's a meeting, as we can see there, of the same research and development committee, and this is a meeting you did attend. We can see your name under the list of attendees. This is a bit later on, 19 December 1985. If we could look over

the page, which is 1153, the particular passage I was interested in is the one under 14.3, where it says:

"Heated treat Factor VIII.

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

So we have a picture from these two documents that information had been given to the members of the committee about the progress of the English 8Y product and in particular the fact that there were encouraging signs about the transmission or non-transmission of non-A non-B Hepatitis.

You have said in your statement that the information which was given to you at this committee was shared with others in SNBTS. What I'm interested in is whether information of this nature about that product would have been shared by you with haemophilia clinicians such as Dr Ludlam.

A. I honestly don't remember but I think Dr Ludlam would have known a great deal more about this than me because, you know, he was very closely involved with the haemophilia community, with Charles Rizza and other

people who were doing these studies, and he, I think, had some patients -- I think he probably had one or two patients of his own enrolled in the trial.

So I might well not have passed this rather brief fragment of information to Professor Ludlam because I would correctly, I think, have assumed that he would be much more familiar with the details of this trial than I was or needed to be.

Q. Thank you very much, sir, I have no further questions.

Thank you very much, Dr McClelland.

A. Thank you.

THE CHAIRMAN: Anything arise out of this, Mr Anderson?

MR ANDERSON: No, sir, I'm obliged.

THE CHAIRMAN: Mr Johnston?

MR JOHNSTON: I have no questions, thank you.

MS DUNLOP: Thank you, sir. I have no further questions for Dr McClelland at the moment.

Dr McClelland has two further appearances, I think, both this month, so we will be seeing him again shortly.

THE CHAIRMAN: Thank you very much.

Is that us for today?

MS DUNLOP: Yes, sir, we have no further business for today and we are not sitting next week, so we will be back again a week on Tuesday.

THE CHAIRMAN: We are not sitting next week?

MS DUNLOP: We will be back again on 15 November, when we will be looking at topic C2 and then moving seamlessly from C2 to C4. That's the next --

THE CHAIRMAN: I won't hold to you seamlessly.

MS DUNLOP: That's the next part of the agenda.

THE CHAIRMAN: But that's the agenda. Thank you very much.

(12.50 pm)

(The Inquiry adjourned until Tuesday, 15 November 2011 at 9.30 am)

I N D E X