Wednesday, 7 September 2011

(9.30 am)

DR PETER FOSTER (continued)

Questions by MS DUNLOP (continued)

THE CHAIRMAN: Good morning.

MS DUNLOP: Good morning, Dr Foster.

A. Good morning.

Q. I wanted, if I could, please, to go back to your memo of 3 May 1983, at which we were looking yesterday afternoon. That's [SNB0073635]. Dr Foster, I just wanted to ask one or two more questions because I wanted to be clear about what happened around about the time of this memo, and what the response to it was.

But looking at the first page, the second point you make, numbered point number 2 -- this is part of the strategy, the then current strategy was to design a full-scale plant to handle 30 per cent production for 1984 to 1985 at the earliest.

So by "full-scale plant", you are really meaning industrial-sized equipment. Is that what we should understand about that?

A. Yes, that's what I mean by that.

Q. Yes. We did look at this yesterday. You then canvass in your memo the possibility that some change of strategy may be required and if we look on to the second

page, this is the second sentence on the back page:

"While I do not disagree with point 2 above ..."

In other words, you are still in favour of moving to full-scale plant to handle 30 per cent production for 1984 to 1985 at the earliest:

"... it may be possible to introduce an immediate stage still using the pasteurisation cabinets."

Bearing in mind the point the chairman made yesterday about the word "intermediate", I suppose there are two possible senses in which you may have been using the word "intermediate". You may have meant intermediate in terms of size of operation, or you may have meant intermediate in a temporal sense; in other words, something we can do in the time interval before we are introducing the full-scale plant. Which of those senses do you think it was, when you said "an intermediate stage"?

A. I have to admit this was such a long time ago, I have great difficulty actually remembering what I actually did mean.

Q. I quite appreciate that, Dr Foster.

A. It could actually mean that in our normal Factor VIII process, as I mentioned yesterday, we tried to complete the process from starting to thaw the plasma to loading the freeze dryer in one day, and with a procedure like

this, it would take more than one day and the question is how do you hold material, how do you progress it in two days or three days, or whatever? It may have been that I was talking about an intermediate holding point, where you would work for a day and then leave something overnight and then come back and carry on the next day. That's another possibility.

As I sit here, I can't really say exactly what I did mean by that. It could be what you suggested, that this is prior to putting in the routine process I had been thinking of, we could have an intermediary kind of production operation.

That's possible. I really don't know the answer to the question.

Q. Right. Perhaps we should just take from it that there is some kind of sense of something being proposed, which is in advance of the main plan that you have set out on the first page?

A. Yes, I was looking to see how can we advance this as quickly as we possibly can. That was the sense of it.

Q. Right. The next thing that I don't think I fully understand is the background or the context, rather, of your worked example. I called this your "worked example" yesterday. That is the text that follows immediately below where you say:

"That is, consider a 1,000 kilogramme pool of fresh-frozen plasma."

When you were explaining to us at the beginning of your evidence yesterday about the manufacturing process, you told us that the 1,000 kilogramme pool would be the 4,000 donations?

A. Approximately, yes.

Q. So that really matches, as it were, the description you gave yesterday of the process?

A. Yes.

Q. What I think I failed to ask you is: how frequently would that size of pool be commenced? How often did you start off a pool that size?

A. That would have been approximately twice a week.

Q. Right. So this worked example then, if we read on down and we see that the penultimate paragraph in the whole memo amounts to you suggesting that doing what you are now proposing would enable PFC to cope with 2,000 kilogrammes of fresh-frozen plasma per week, does that then mean that what's suggested in the memo would really have amounted to a wholesale move over to pasteurisation, albeit on a more temporary basis?

A. Yes, that is clearly what I was suggesting, yes.

Q. Right. Thank you. I just wanted to be sure that I was following that.

A. And I think, just to look at this second last paragraph, I do say "pending a fully engineered process design."

And that does fit in with your earlier comment about what I meant by "intermediate"; let's do this as a temporary arrangement pending the full engineered process design.

Q. So it might have been a bit Heath Robinson-ish. You wouldn't necessarily have been using all the equipment you would have liked to have had and so on, but you would have been able to carry out pasteurisation following the suggestions in your memo?

A. That's correct, yes.

Q. Now --

A. I should perhaps just comment here that I think the purpose of this memo was perhaps to stimulate a discussion around this with Mr Watt. It is obviously not a fully worked up proposal, but it's just to start people thinking and to start some discussion around these possibilities.

Q. Thank you. We are slightly retracking here but --

THE CHAIRMAN: Just pause on that.

On the other hand, at this stage you, from your point of view, were putting up what you considered to be a feasible programme to move from one approach to processing to another?

A. Yes, I think it would seem to me to be feasible but having said that, I would appreciate that this was a very difficult project and clearly writing a memo was much easier than actually making it work in practice.

THE CHAIRMAN: Yes.

MS DUNLOP: Can we look then, please, at [SNB0073638]? We looked at this yesterday as well. This is 5 May 1983 and it's Mr Watt writing to Dr Cash. I think we understood yesterday from your evidence, and indeed we can see for ourselves, that the approach in this letter is slightly different from the approach in your memo, and indeed the chairman suggested one possible reason why that might be so and we will come to that in a moment. But what we can see from this letter is that Mr Watt is really reporting to Dr Cash the current state of play, so he is saying that there has been an interim pilot scale approach to preparation of a pasteurised product really and that that has been going well, I think, quite well. He says that:

"Studies are progressing well."

Then if we look on to the second page, he is saying to Dr Cash that there is a first pilot lot prepared and there is a long paragraph dealing with that. So at the end of the long paragraph he is saying:

"I believe it is sensible to get some clinical

experience of lot NY761 as part of the overall process introduction."

I take it that when a stage had been reached at PFC of having material that was to be tried out, those trials would have to be organised through Dr Cash as the national medical director. Is that right?

A. That's correct.

Q. Right. So Mr Watt is saying, "While we are ready to roll on that aspect, we have some material to trial," and then if we look on to the third page, there is the reference in the final paragraph about speeding up the programme substantially:

"The expansion of the makeshift process now in use ... expenditure now instead of 1984 to 1985 as well as some additional expenditure which would not advance the longer term production process."

That there is some costing going on and again I think we established yesterday that this seems to marry with what was in your memo, that this looks to be Mr Watt alluding to the suggestion that had come from you about possibly speeding things up at this point, and there would be a little bit of extra expenditure to do that but Mr Watt is telling Dr Cash that this is being considered and that it is also being costed. Is that correct?

A. Yes, I would agree with that.
Q. Right. I think what I want to try to find out is what actually happened then to that proposal. So we have the proposal and Mr Watt passing it on to Professor Cash and saying that it is being costed. Apart from asking Dr Cash to make some arrangements for clinical trials, Mr Watt doesn't actually seem to be asking Dr Cash for anything; it's more of an informative letter, that letter. Is that fair?
A. I think that's probably correct.
Q. Yes.
A. I think what Mr Watt is really encouraging Professor Cash to organise are the clinical trials because it's really crucial at the next stage to know whether or not this material is going to have any value in patients, and I think there were two types of clinical trial discussed, which I'm not quite sure in the timescale when this fits but there was a phase 1 trial and a phase 2 trial, and in the phase 1 trial that was intended to establish that the product will be effective in treating haemophilia. That would have measured the half-life, the recovery and the tolerability of the product. And assuming that that was all acceptable, then there was a notion to go on to a phase 2 trial, which was rather like the Mannucci work

that you discussed yesterday, to establish whether or not the infective agent of non-A non-B had actually been destroyed or not. So all of that clinical planning was also having to be undertaken by Professor Cash.

THE CHAIRMAN: The reply was [SNB0073708].

MS DUNLOP: I'm obliged, sir, I had momentarily lost the reference for that.

Can we just look at that then, please, Professor Cash's reply?

That is Dr Cash writing back to Mr Watt in response to the letter of 5 May and picking up the suggestion about the clinical trials and then saying -- and perhaps this corroborates our sense of there being two different moves afoot:

"On another tack altogether ..."

So there is the immediate practical requirement to organise some clinical trials but there is also this question of whether the whole heat treatment programme is to be accelerated in some way, and he is saying:

"I would regard the last paragraph of your letter to be the most important."

And he is very pleased that there is costing going on. There is then a paragraph which we have studied quite a lot actually and I'm hoping that Professor Cash will be able to give us a bit more information about it

tomorrow but I think as matters currently stand it would be fair to say we find it slightly difficult to follow.

THE CHAIRMAN: Rather dense, I think.

MS DUNLOP: Yes. About the reaction of the deputy chief medical officer to the concept that heat-treated Factor VIII is related to the interests of the Medicines Inspectorate. Can you help us a at all with that, Dr Foster?

A. I'm not sure I have it on the screen here.

MS DUNLOP: It's in the fullest paragraph, so paragraph 4.

A. Okay.

Q. I suppose, if one were speculating, one might suggest that somebody has suggested in the hearing of the deputy chief medical officer that the heat treatment project should be funded in connection with the recommendations of the Medicines Inspectorate?

A. That may well be the interpretation, that in order to find a budget and to justify it, there was possibly a pot of money available with the heading "Medicines Inspectorate" on it, and that was an easier way to find money in the short-term than to come in with a new proposal.

Q. If one was carrying on the speculation one might infer that the deputy chief medical officer hadn't been entirely supportive of that proposition, but I was just

wondering if you had any recollection of dialogue about that at the time?

A. I can -- I just saw that letter, it was copied to me. But I don't remember it.

Q. Right. Thank you. So can we then go back to your statement? That's the document which is [PEN0121438]. Can we go to page 1461, please? This is the beginning of your numbered paragraph 15, which is an answer to our question about the memorandum of 3 May 1983. We discussed yesterday what had been the trigger for the writing of the memo, and you have explained to us that you think it was these articles in the Lancet; or letters, I think they are, actually, rather articles.

Can we then look at the next page, please, 1462?

Just so that I understand this, Dr Foster -- and I'm sorry if this feels very plodding -- but when you tell us, in particular in paragraph (d), that:

"The equipment would take some time to design, construct and install, instead of waiting for this, it occurred to me that processing at pilot scale could be progressed by dispensing the mixture into 1 litre bottles which could then be heat-treated in the spray cabinet that was used to pasteurise albumin."

In that paragraph, you are not actually talking about your proposal in the 3 May memo, you are talking

about your proposal connected to the pilot scale preparation?

A. Yes, you are correct. It would apply to the memo which talked about really full-scale as well as pilot scale.

Q. Yes, right. So when you say in paragraph (e):

"This procedure was introduced ..."

What you are meaning is pilot scale lots were prepared; you are not meaning that what was outlined in the 3 May memo was introduced?

A. That's correct. That's entirely correct, yes.

Q. Good. I think I had misunderstood that until yesterday.

The question is then: what happened to your, let's call it, "full-scale proposal", as outlined in the 3 May memorandum? That is the Heath Robinson-ish proposal. What happened to it?

A. It's very difficult for me to remember, as I mentioned earlier, but my sense is what I said a few minutes ago, that this memorandum was me putting out some ideas for a wider discussion with Mr Watt and their consideration and the heads of department within PFC, and it's conceivable that they said, "Look, this is going to be too difficult." I just don't remember but that's a possibility. But what did happen fairly shortly after this was that I went to Stockholm to attend the two congresses there, where I met Dr Johnson and learned

about his proposals. And at that time, the immediate thing that struck me was that this could actually help us because this was a very difficult process we were trying to develop and I immediately recognised the value of Dr Johnson's work, that this would actually make it much simpler to introduce a pasteurisation process at full-scale. And of course when I came back from Stockholm, I learned that Mr Watt had resigned and was going to leave and to be honest, I can't really remember if we discussed my earlier proposal beyond that.

Q. Yes. I completely appreciate the points you make, Dr Foster. I mean, we are asking you about events 28 years ago and it would be extraordinary if you had a clear recollection of everything that happened, but perhaps an easier question about the 3 May memo is, rather than asking you what did happen, to focus on what didn't happen. There wasn't, as I understand it, in early course a move to putting through 2,000 kilogrammes a week in the manner suggested in your memo?

A. No, there wasn't because a pre-condition would be to have satisfactory clinical data. We wouldn't want to commit ourselves to doing something so enormous without suitable clinical results to justify it, and of course we didn't get that result because one of the patients experienced an adverse reaction.

Q. We are coming to that as well. But just before we drop for today the question of funding, do you have any memory of its also being an obstacle to being negotiated that money had to be found?

A. No, it didn't seem to me to be an issue. I thought this is so important that I thought, "If this is what it costs, this is what it costs and the money will come through," and I left that to Mr Watt and Professor Cash to sort out. It wasn't something that seemed to me to be an obstacle.

Q. So just reading on through your statement --

THE CHAIRMAN: Sorry, could I just follow that.

There are two possible situations in which you wouldn't recognise it to be an obstacle. One was that no one led you to believe that it might be an obstacle; the other is that, as a scientist, you weren't really concerned where the funding came from. Is it either of those or something else?

A. I was fully aware that funding had to be obtained and I knew the processes that we had to go through to get the funding. So I wasn't ignorant of that but I have no memory of this seeming to me to be an impediment. I was confident that Mr Watt and Professor Cash would get the funding. They were very good at doing things like that.

THE CHAIRMAN: I'm happy with having a clear answer on one

or the other.

MS DUNLOP: One of the things, which I hope will become clearer tomorrow when we are hearing from Professor Cash, is that around about this time, by which I mean May/June 1983, there is discussion both in the Blood Transfusion Service subcommittee and also in SHHD about funding for the pilot scale level. It almost looks as though you were working on the pilot scale project before that expenditure might formally have been authorised.

A. Yes, there are two issues here. One is the process equipment that we have talked about but also changes to the facility, because the pasteurisation step is carried out in the middle of the process. Then all the processing after that, to be absolutely sure that the product is going to be safe, has to be done in an area that's segregated, where there's no possibility of any recontamination occurring. And we had to build an area to do that.

So that required extra capital funding, of money to do building works and to design an area to do it and all of that. So that was the second aspect, which we hadn't progressed. So we were doing one part, which was doing the processing to get the pilot material to establish whether it would work in a patient, but to actually

prepare material that we would say was going to be prepared in the segregated facility, where there was no possibility of recontamination, that hadn't been put in place and that also needed funding.

Q. I see.

A. And it would need to be scheduled in as a building work and we would have to shut the factory to do it and stuff like that.

Q. I see. You mentioned Dr Johnson and I think we should pick up the story of that in subparagraph (f). When you met Dr Johnson, was it actually in Stockholm?

A. Yes.

Q. He was in Stockholm too? Right. He had a new idea, which he thought would achieve greater purity, and this is what you tell us but you have obviously envisaged that if this method were indeed successful, it would reduce the volume of material with which you were working hugely, which would make it much easier to carry out the pasteurisation process. Is that right?

A. That's correct.

Q. Yes. Can we move to the next page, please? You go on to tell us, however, that there was a patent problem. In fact, perhaps it should be acknowledged it wasn't specifically a patent problem, it was a problem caused by legal advisers, who said that they didn't want him to

disclose details of his procedure before the patent application was filed. You say:

"Dr Johnson continued to put off filing in order to add further information."

So he was still working on his process over the ensuing months. Is that right?

A. Yes, he was making improvements, although he told me when we first discussed it that he was very close to filing the patent, but it actually dragged on and on and on, much longer than he had expected and I had expected.

Q. Right. Did he know that you were waiting for details of the process?

A. Oh, yes.

Q. Right. And I appreciate you had a very good relationship with Dr Johnson, but in practice at this point he was holding you up?

A. Well, at this point we were actually putting in place what we call a "businesses arrangement", so contracts were organised through the CSA, so it was all done on a proper business footing and that took some time and Mr Watt took a lead in achieving that before he left.

Even if Dr Johnson had had no problem with patenting, if he had filed the patent, we couldn't have proceeded without the business agreement being in place first. So that did take some time also.

Q. So a number of things were happening simultaneously?
A. That's correct.
Q. Therefore it is not necessarily possible to say that any one thing delayed progress?
A. I think ultimately it was this issue of the patent because we had the business agreement in place and he still didn't come forward with the technical details of what it was and eventually we really became exasperated and said, "Look, we can't continue in this way," and then his legal advisers agreed that he could make the information available to me and that was on 14 June 1984.
Q. Did you go to New York especially?
A. I went to New York especially for that.
Q. Right.
THE CHAIRMAN: Was the business arrangement in place --
A. The business arrangement was in place, yes.
THE CHAIRMAN: -- by that stage? So you had in effect a joint venture that allowed the lawyers to treat this as other than disclosure to the public?
A. That's correct, yes. I think they were still very nervous that it might leak out.
THE CHAIRMAN: But, as Ms Dunlop is asking you, here was a legal structural problem, however one looked at it, standing in the way of implementation of Dr Johnson's

work at Edinburgh.

A. I would say that was the case, yes.

MS DUNLOP: And separately you then started analysing the details that he had given to you in June 1984 -- this is what you tell us in subparagraph (h) -- and you thought there was a slight snag in connection with the ion exchange reagent. Is that right?

A. Yes, I mean, it is often the case that scientists working in a research laboratory don't fully appreciate the implications of what they are doing in terms of a large-scale industrial process, and despite his wealth of experience, Dr Johnson still didn't fully appreciate -- because he didn't work in industry, he didn't have that appreciation. And I was able, in examining what he had done, to realise that it needed some improvement in order to fit it into an industrial process, and I suggested the kind of improvements that could be made.

Q. Right. You didn't just suggest, you actually arranged a meeting. You arranged for Dr Johnson to see somebody from, is it pronounced Pharmacia?

A. Yes, Pharmacia was the principal company at this time who provided this reagent to the fractionation industry. We knew Dr Curling well. He was a senior scientist in that company, and I arranged this meeting with

Dr Johnson and Dr Curling where Dr Johnson explained his requirements and Dr Curling identified this new material that the company were developing as being possibly the most appropriate, and it was named "Q-Sepharose" -- or "QAE Sepharose" to give it its full title -- and that is now a conventional reagent that is used in the manufacture of Factor VIII worldwide and this is where it originated, and that is what we began to work with.

Q. Right. Then you tell us that also you identified need for additional manpower?

A. Yes, I mean, having looked at what was going to be involved -- I mean, Dr Johnson had originally said to me, "This is very straightforward and you can do it in a few weeks," and I looked at it and I thought, no, it's a bit more than that. So I thought we need to bring someone else to work on this and I suggested Dr McIntosh, who was a scientist in my department who had been working on other projects and I thought he would be very good at this and he agreed to do that.

Q. Right. Then subparagraph (j), we find out that you obtained some Q-Sepharose, to give it its short name, in August 1984 and even then you realised that some further work would be required. Then you tell us in subparagraph (k) that when you had been talking to Dr Johnson and Dr Bernard Horowitz?

A. Horowitz.
Q. There is an extra "ro".
A. I have spelt it wrongly, I am afraid.
Q. Right, yes. You had had discussions at the ISBT congress in Munich and you had learned of a new viral inactivation procedure using solvent detergent treatment, is that right?
A. Yes, I think we were generally aware that the New York blood centre were beginning to make some progress in this area, but this was the first time I kind of discussed it with Dr Horowitz directly with Dr Johnson present. And this became the standard method that's used nowadays by virtually all fractionators.
Q. I don't want to go into something that's too scientifically difficult for me to follow, and that wouldn't take much, but I take it from this paragraph that this really would have been something rather different altogether; it would have been a combination of Dr Johnson's new idea for the chromatography with solvent detergents being used as the viral killers, the viricidal step?
A. That's correct. The problem that Dr Horowitz had was that he was using chemicals that had to be removed because they couldn't be injected into patients, and one way of doing that was the procedure that Dr Johnson was

devising. So that was another option that was opening up as a possibility that I was conscious of, if we wanted to go down that route.

Q. Right.

But at that time you didn't actually progress that particular possibility?

A. No, we didn't because the agent responsible for non-A non-B hepatitis hadn't been discovered. Hepatitis C hadn't been discovered and the solvent detergent treatment only worked against certain types of viruses, and it wasn't known if the Hepatitis C viruses would be affected by it or not.

Q. Right. I think you tell us in terms in subparagraph (k) that this was really more of a fallback plan, should the pasteurisation technology not work or should the pasteurisation project --

A. It was an alternative option.

Q. Yes. In (l), back to the matter of pilot batches, the pilot patches, these are the 1 litre bottles of pasteurised material, is that right?

A. The pilot batch would involve taking the equivalent of 100 litres of plasma but in terms of cryoprecipitate. So I think I said yesterday you would get 10 kilogrammes of cryoprecipitate from 1,000 litres of plasma. So we would take 1 kilogramme of cryoprecipitate from

production, so it was representative of the full production pool, and then process that. So it's an aliquot, if you like, of the production pool would be processed through this pasteurisation process to give it a small quantity of finished product that then could be evaluated.

Q. Right. Can we go back to page 1462, please? I just wondered if that matched subparagraph (d). You are talking about processing at pilot scale by dispensing the mixture into 1 litre bottles.

A. Yes, that's correct. The pasteurisation was done in a 1 litre bottle, but we had a number of 1 litre bottles so we had ...

Q. It was just when I was picturing the 1 litre bottles, presumably these would only be suitable for clinical trials, it was not something that a patient could take home and use as his normal --

A. No, this is not the final product. The 1 litre bottle is for the pasteurisation and then the material is taken out of that and processed further to be dispensed into vials aseptically and filtered and freeze-dried and all of that.

Q. So the material that ends up going for the clinical trials is, to all intents and purposes, the same sort of vials that are normally supplied for patients?

A. Yes, that's correct.

Q. Sorry, can we go back to 1464 then, please?

Subparagraph (m) refers to events in November 1984 and I think this answer really relates to a part of the question that focused on whether what happened when you did introduce dry heat treatment at the end of 1984, was essentially using the same equipment as was being used for pasteurisation in 1983/1984, and you explained, I think, essentially the answer is yes but you explained in a little more detail at (n):

"Specialist ovens for dry heat treatment had to be manufactured."

So for the first six month or so after November 1984, you were using the cabinets that you used to pasteurise albumin, and in fact if we move to the next page there was a degree of good fortune about that because the cabinet had been designed to function up to 70 degrees centigrade, so you were able to get higher temperatures than the 60 degrees for which you needed it to function for the albumin?

A. That's correct.

Q. That was a very long question, I'm glad you were able to follow it.

Right. Can we go back then, please, to the schedule which has the questions in it, [PEN0121531]. We have

covered 17 and 18 and then 19 is dealing with the contact with Professor Johnson, which we have just been discussing, and then question 20, we noted that you had written to Dr Smith on 23 August 1983. I don't think we need to go to that, but in that letter the intended collaboration with Professor Johnson was not mentioned and I think it's self-evident to us now that that will be because of the confidentiality that was necessary given that the patent was to be filed within the next few months. Is that right?

A. I think that's correct, yes.

Q. Right. We can see the answer, if we go back to your answers. You say that in your numbered paragraph 18, which is on page 29 of [PEN0121438]. Indeed, there seems to have been an unfortunate development involving the dean of New York University, who seems to have taken exception to Dr Johnson cooperating with organisations in Europe. Do you remember that?

A. I do. I do seem to remember that there was pressure brought on the dean that discoveries at the university should be offered to American companies first, and he was not entirely happy with Dr Johnson's arrangement with us. And there was, as I say here, a temporary breakdown. But by that point we had enough information that we could proceed without needing to have ongoing

communication with Dr Johnson and the situation was resolved eventually and normality resumed.

Q. Right. And your friendship with Dr Johnson and your collaboration with him survived?

A. Oh, yes. He was very keen to maintain the relationship with us. He just had to convince his dean that that was the appropriate way to do it.

Q. I see. You have already alluded to the departure of Mr Watt and we asked you one or two questions about that, Dr Foster. Can we go back to the questions document, please, at 1535? Can we just look at paragraphs 21 and 22:

"Meanwhile ..."

That is over the summer of 1983:

"... Mr Watt had tendered his resignation as scientific director of PFC."

He had written to Professor Johnson to tell him of his intended departure and he said in his letter that his decision was multifactorial.

Then paragraph 22, just trying to pinpoint these events in time, his resignation was known about by 15 July 1983, the issue was discussed at a meeting with Dr Scott and Dr Bell, caused a meeting with representatives of the CBLA to be postponed. Perhaps in passing we can just note that the meeting actually was

due to take place on 21 September, so obviously, as perhaps one would guess, a significant enough development that it required postponement of a meeting some two months ahead, and reading on that:

"The original plan was for Mr Watt to leave at the end of March 1984 but he left at the end of December 1983."

That reference -- we don't need to go to it -- but it's actually a memo from Dr Perry informing people that he is the acting director as from the beginning of 1984. Dr Cash described the circumstances of Mr Watt's departure as "unusual". I would like to look at that letter, if we could, please. That's [SNB0111346].

Plainly, this is material that we can put to Professor Cash and we will be doing that, but just perhaps to look at this letter, which is headed "Future Arrangements for the Replacement of Mr Watt", we can see in particular that Professor Cash is mentioning as decisions which will be required, subparagraph (b):

"Scaling up procedures for heat-treated Factor VIII concentrates."

And (c):

"Advancing studies on the heat treatment of existing Factor IX concentrates."

So I suppose, given that we were asking you whether

Mr Watt's departure had an effect on the heat treatment programme, it is striking that these two paragraphs occur in the letter of 5 January 1984. Does that not suggest that the heat treatment programme at this point was a crucial matter in the affairs of PFC?

A. Oh, yes, it was a very important project and I think here Professor Cash is listing that along with other projects, and he is seeking a period, he describes, of "reflection and stability" so that we can continue to progress these without disturbance, and I think he is in a sense wanting to try to maintain some kind of continuity as far as could be achieved.

Q. Right. Then, please, can we return to where we were on page 6 of [PEN0121531] That's the middle of paragraph 22.

So we have Dr Perry taking over as acting director, Dr Cash emphasising in that letter his view that the next director of PFC had to be unequivocally responsible to the national medical director, obviously Dr Cash.

Then we also referred you to another letter about the relationship as it then stood between Dr Cash and Mr Watt.

Can we go then to your answers on this matter, Dr Foster. Can we go back to the document [PEN0121438] at page 1466. You tell us firstly that Mr Watt did not

discuss his reasons for leaving with you and then you say that you don't believe the resignation of Mr Watt adversely affected the virus inactivation programme or influenced SNBTS strategy. As support for that view you highlight Mr Watt's continued participation in the biological subcommittee of the Committee on Safety of Medicines until 1986, and what you would see as Mr Watt continuing to display the same sort of approach to heat treatment viral inactivation as had been evident when he was the director of PFC. Is that right?

A. That's what the committee seems to have followed. Assuming that Mr Watt was in agreement with the committee, then, yes.

Q. Yes. But if we move on to the next page, you give us a little more detail about circumstances surrounding Mr Watt's departure. In fact you found out on Monday, 11 July, when you got back from Stockholm. Then subsequently, presumably at some point in the ensuing months?

A. Oh, no.

Q. No. Very shortly?

A. I think it was fairly shortly. I can't absolutely be sure but it seemed to me it wasn't very long afterwards.

Q. I suppose it was the talk of PFC?

A. I was told by the driver, he was the first person I met,

and if the driver knew about it, everybody knew about it.

Q. Was it also the driver -- I take it it wasn't the driver who told you that Mr Watt was planning to establish a company to fractionate animal plasma?

A. No, I think that was probably Dr McIntosh.

Q. And that Mr Watt was also seeking to recruit staff from PFC, and then you tell us in paragraph (b) and (d) that presumably Dr Cash was very disturbed by this?

A. Oh, yes, he was. And rightly so, I think. If a lot of people had left or even a significant number of key people had left, that would have been very harmful. But in the event that didn't happen.

Q. Right, and you told Dr Cash that you had heard of four people who had been approached by Mr Watt or who were planning to leave with Mr Watt?

A. No, who had been approached and were considering whether they would accept this offer or not.

Q. Right. And in fact Mr Watt's intended departure date was the end of March 1984 but he left at the end of December 1983. Was he asked to go earlier?

A. That would be my understanding.

Q. Yes. And did other staff leave with him?

A. At that time, no, because he didn't establish his new business for some time but eventually a couple of people

did leave and join him.

Q. Right. What sort of level of staff were they?

A. They were what we would call section manager level, which was senior technical level.

Q. So people who worked in laboratories?

A. There was a person who managed one of the quality control laboratories and also a person who managed one of the areas in production at a senior technical level. We did have a turnover of staff anyway. So these are things that do happen.

Q. So it was something that PFC could cope with?

A. Yes.

Q. Dr Foster, you, in your next answer, deal with four of our paragraphs and we need to go back and just establish the content of those paragraphs. So can we go back to the questions document at 1536, please?

In your next answer you deal with our paragraphs 23 to 27, excluding 26. So if we just take a moment to look at that section.

24, we referred to the position in England around about this time, in particular we referred to a Central Blood Laboratories Authority paper on heat treatment, which I think we should look at now. It's [DHF0024489]. Thank you. We can see that this is headed up "AIDS, progress with heat treatment of human plasma products".

We can see the introduction. If we look at page 2 of this document, please, I think we can see the extract that was included in the question, just to allow everyone to read that beginning section under the heading "AIDS". (Pause)

So it's being said that:

"The syndrome of AIDS is likely to include in its aetiology transmission of an infective virus and the possible phenomenon of reactivation of an existing virus in individuals concerned."

And an interesting remark that:

"This aetiological observation has promoted more activity in the area of blood products pasteurisation with the empirical view that a virus is involved and, as with hepatitis virus, is likely to be partially or completely inactivated by heat."

Then, the subheading "Means of Heat Treatment of Blood Products":

"Heat treatment is only one pathway by which viruses may be inactivated."

And I think we understand that from the rest of your evidence, Dr Foster:

"But it is the most favoured route at present."

Then the section that we quoted, that the options so far as heat treatment is concerned are really wet or dry

heating, so pasteurisation or dry heat treatment and then the paper goes on to say that:

"Heat transfer in the wet state is more homogeneous and efficient and to satisfy reliability in manufacture is to be preferred."

So a view with which you would have concurred?

A. Yes.

Q. But it says:

"Wet treatment is associated with more molecular damage of heat unstable proteins than occurs by the dry heat route."

What about that?

A. It depends how much heating you apply. And of course, as we have looked at, you have to add stabilisers to a very high concentration when you are involved with pasteurisation of coagulation factors, and that was much less so the case with dry heat because the process of freeze-drying is itself a stabilisation process.

Q. Right. So you would accept the second part of that sentence, would you?

A. I think it's a bit of a generalisation.

Q. Right. We then find some discussion of what's available at BPL. Wet heat pasteurisation of blood products is available for albumin, antithrombin Factor XIII and is likely to be successful with Factor IX. Then:

"Wet heated Factor VIII, however, is said to be likely to require a longer programme of work if a satisfactory reliable method is to be developed."

Then we move to dry heat:

"The majority of commercial manufacturers are currently depending upon dry heat of the finished Factor VIII concentrate. The associated claims, which are entirely unfounded in scientific and quality control term, are that the heat process will inactivate the putative virus transmission causing AIDS."

So a discussion of the different options that are around. Can we just scroll right to the bottom, please? The other document that we quoted around this time was a set of minutes from a CBLA working group on AIDS. That's [DHF0024834]. We can see this is a CBLA working group on AIDS October 1983. In particular, can we go to the foot of page 3 of this document, please? We see the heading "Treatment of Blood Products to Eliminate Micro-Organisms."

Then on to the next page, please.

Perhaps, as compared with the immediately preceding document, a slightly more negative view of dry heat treatment and perhaps unsurprisingly referring back to the chimpanzee results which seem to have been in everybody's mind around the summer of 1983. So possibly

slightly more equivocal as to whether the wet heat option should be pursued or the dry heat option? It doesn't really seem to record much of a decision, does it? I suppose just an acceptance that research is ongoing and that further evaluation will be required, which is all very sensible, is it?

A. Yes, I think they are probably leaving it to Dr Smith to work out what he thought was best.

Q. Yes, and I think Dr Smith has some views on these documents as well. So we will be able to ask him when he comes to give evidence.

Can we go back, please, to the questions document at 1536? We then said that the reference to the chimpanzees was presumably a reference to the knowledge that three chimpanzees had developed hepatitis and we mentioned Dr Walford's letter which we looked at yesterday.

Paragraph 25. A memorandum from Dr Smith to you in January 1984, setting out detail of work to date on dry heat treatment. Then 26 we can leave for the moment and look at 27, please:

"The information from England was referred to at the Factor VIII study group meeting of 12 January 1984 along with the information that the Hyland ... treated product was still infective."

Just to see that can we go to [SNB0074059]. This is the Factor VIII study group meeting in January 1984. We can see who attended and you were there. In particular, please, can we go to page 5 and we can see that reference in numbered paragraph 6(2)a.:

"Our report is being given ..."

Is this by you? Will you have been telling the group about news from England?

A. I don't know, I am sorry, I can't remember.

Q. Right. It doesn't matter. But anyway, the information is imparted that there is no yield penalty for dried Factor VIII if it is heated to 60 degrees for three days. This would be investigated:

"But it was noted though the current Hyland product made by this method is still infective."

So the study group is keeping in touch with what's happening in England but we asked whether there was any suggestion around this time of the possibility of changing tack; that is from pasteurisation to dry heat treatment. You then provided an answer, Dr Foster, to all of these paragraphs in your numbered paragraph 21, which is page 30 of [PEN0121438]. We don't, I think, need to investigate any further the knowledge that we know emerged in 1983 about the lack of success of the Hyland product, as far as viral inactivation is

concerned. That reference to Mannucci is in fact, although that's one possible reference to it, the article which is in our court book as [LIT0011101], but I don't need to go to it. Then you say:

"Further evidence against dry heat treatment was obtained by yourselves in late 1983."

That you carried out some dry heat research yourselves, and in particular looked at viral kill. Is that right?

A. That's correct.

Q. Or viricidal results.

Dr Cuthbertson was involved in those experiments, and plainly we will be able to ask him next week but just to go to the reference for that, which is a kind of state of play report from December 1983, that is [PEN0121500]. You say this is actually a report that you prepared for the study group meeting in January 1984. If we go to page 5 in this document, please, I think this is actually the very last item in your report and we can see that you are telling the group that various experiments have been carried out on freeze-dried product but the initial results were suggesting that the viral kill was less successful than the pasteurisation method.

Can you just explain to us, Dr Foster, what the

nature of the experiments was? You were using, as it were, surrogate viruses, is that right?

A. Yes, some people call them "model viruses", other people call them "marker viruses". These are viruses that are -- they can be worked with, so you can actually measure whether they are dead or alive and you can get a known amount of the virus, add it to some Factor VIII, freeze-dry it in a research freeze dryer and then heat it under different conditions and then reconstitute it and find out how much virus is alive or how much is dead.

Dr Pepper had the freeze dryer, because at that time I did not have a laboratory freeze dryer, and Dr Cuthbertson did all the virology work. So it was really their experiment. But I was aware that the experiment was taking place, and when I was writing this report, I wanted to know what the results were and they hadn't completed the analysis of the data. So all they could give me was a general answer, that it was looking as though it was much less kill than they had previously in the earlier experiments with pasteurisation. So that is what I recorded in this note.

And Dr Cuthbertson can probably describe the experiment better than I can.

Q. Right. Thank you.

Can we go back then, to the answer, please? That's page 31 of [PEN0121438]. You actually explain that as far as you were concerned, the information from Dr Smith lacked that sort of material; in other words, comparative viricidal analysis, as it were?

A. Very much so. There was no information at all from BPL on that kind of analysis.

Q. Right.

A. In fact they didn't have the capability to do that and we did the work for them subsequently.

Q. Right. Can we move on to the next page, please? I think this is really your answer to your changing tack question when you say:

"The information from Dr Smith did not alter the opinion in Scotland that pasteurisation should continue to be the main focus of research on virus inactivation."

So not only did you feel that nothing had been said to displace you from your main goal, there was also interest, you tell us, from England in what you were doing by way of pasteurisation and Dr Smith came in June 1984 to see what was happening with your pasteurised product and took some photographs?

A. That's correct.

Q. And sent you copies?

A. Yes, which I still have.

Q. Right. You say -- and again this is something we can ask Dr Smith -- that you think there were accommodation considerations that were relevant to which method was going to be chosen for England as well?

A. Yes, I think that's probably very important. I was aware that they were perhaps giving more priority, or more emphasis I should say, to dry-heated than to pasteurisation but I wasn't entirely sure why that was the case but later on I understood that it was very much because the pasteurisation process has a much bigger footprint, if you like, and they just couldn't imagine they could fit it into the BPL facility at that time.

Q. Right. We can pass over your answer 22 very quickly, just to note that there is a question in the questions document about what happened with Dr Ludlam's patient, when batch 761 was tried, and you say you are not in a position to provide information about that.

Then, moving on to the next answer. Can we go back to the question, please, question 28? There was a costing prepared for the production of heat-treated Factor VIII, that is pasteurised Factor VIII, that shows a total cost of £90,000. The date towards which PFC were aiming was April 1985 and we asked you if there was any suggestion that this might be too long a timescale and your answer is contained in your numbered

paragraph 23. You say that rather than being too long a timescale, you think it was actually extremely ambitious?

A. Yes, I would still take that view, yes.

Q. Right. In subparagraph (b) you contrast the more technically straightforward introduction of dry heat treatment.

Just to confirm that information about the costing, can we look firstly at [SNB0074276]? We can see that this is a covering letter from Dr Perry to Dr Cash in February 1984 saying he is sending a paper for transmission to the Blood Transfusion Service subcommittee. That's a subcommittee of the Common Services Agency?

A. That's correct.

Q. Yes. So for their meeting on 22 February, a paper is being written with a costing in it and the costing is [SGH0020068]. Did you coordinate the preparation of that?

A. I can't remember.

Q. Right. Fair enough. We deal with this in the preliminary report, I think subsequently it was tweaked because there was a question of increased money being required for the reagents or something like that?

A. Yes, I noticed that.

Q. Yes. But perhaps we should ask others about what happened to the costing and the authorisation of the funds and so on. Would that be reasonable?
A. Yes.
Q. Right. Can we go back then to question 29, please? Again this is something you answered very briefly. We simply referred to a memo from Dr Craske, which I don't think we need to go to, but Dr Craske was talking in early 1984 of an Edinburgh product being available shortly and you say you do not know how Dr Craske obtained his information and that as at March 1984 there were five pilot scale batches which had been prepared. So it does seem to be slightly over optimistic to say the product would be available shortly, although perhaps there is no quantification of "shortly".
A. It depends what he means by "available shortly". He might mean available for clinical trial shortly, and that's what the intention was with the pilot scale batches.
Q. We know that the funding was in fact approved -- or least approved in principle at -- the meeting of 22 February 1984 and we can perhaps develop that with other witnesses.
The next subject I want to talk about crops up really from now on in the questions, Dr Foster, and it's

concerning the events of the autumn of 1984. I would like to try, if I may, to deal with this period chronologically because there are a number of different strands around this time. So if you will bear with me, I'm not going to work systematically through the questions and answers.

I think the first matter we should deal with is something you refer to in your statement, which is a suggestion that was made to Lord Archer's Inquiry, that it was known that the AIDS virus could be inactivated by heat treatment by May 1983 and I think that was something on which you did some work for the Archer Inquiry. Is that correct?

A. Yes, I didn't think that comment was correct and I prepared a short note for the Archer Inquiry to try to explain the situation, what was known and what was not known.

Q. Right. So can we look firstly, I think, at the paper that you prepared, just to check that this is the correct reference. I'm not sure actually if this is the correct reference but can we look at [PEN0121506], please? Slightly confusingly it does say "response to questions raised at the Inquiry" but that's not our Inquiry, that's the Archer Inquiry. Is that right?

A. That's correct.

Q. Can we just look then at the text of this? You have highlighted an extract from a submission actually from the Haemophilia Society and it's the point that I was just making, this suggestion that in May 1983 it was discovered that the HIV virus could be inactivated by exposing it to dry heat at 68 degrees centigrade for one hour.

Perhaps the first reaction of those of us who have sat through the first 41 days of this Inquiry would be that that really would be surprising, given that that might almost pre-date the article by Barre-Sinoussi and Montagnier?

A. Exactly.

Q. But you think that this is to do with the Hyland product, about which we have heard so much, and indeed material was published in relation to the lack of seroconversions in connection with the Hyland product. So we know that a lot of research was done, or studies were done, in connection with hepatitis in patients who were given this Hyland product but there was also some monitoring in relation to AIDS and there is a publication on that point, which is [LIT0010436].

This is a letter to the Lancet in February 1985. Can we just look at the authors of the letter, please, if we can go to the next page? We can see that this

comes from plainly some French researchers, also somebody from Milan and Rolland. Is he something to do with the company? I think he may have been something to do with the company? You probably don't know. We can actually see, not as an author, but Dr Savidge mentioned and then obviously Professor Mannucci.

One of the questions I have asked myself is what is the relationship between this piece of research and the hepatitis research which we know Professor Mannucci was coordinating in connection with the Hyland product, and this looks perhaps to have been a satellite of that?

A. Yes, Professor Mannucci explains it in one of his memoirs in that, from the hepatitis study, they had retained samples from the patients and he was approached some time in late 1984 by Luc Montagnier, who said they had an assay for HIV, and he volunteered to assay these samples to see if these patients might be infected or not, and these are the results of that study. So it was the same patients, some of whom were infected with non-A non-B hepatitis, and this shows that they were free from infection with HIV.

Q. Right. So can we just go back to the previous page then, please? We can see the description of what the research had been and as you say, they had been using LAV, which at that time was the name for the French

isolate. Can we scroll a little bit further down, please? It says:

"None of the 18 patients ..."

This is just the second last paragraph on the right-hand side:

"None of the 18 patients in the test group were anti-LAV positive before or after treatment. Five of the 29 controls were seropositive. No patient has any symptoms of AIDS or AIDS related diseases.

"5. Anti LAV positive controls have no risk factor for AIDS other than treatment with Factor VIII concentrates."

So I think this is one of the points you are making in your paper to the Archer Inquiry, that it was this which was the first publication of that research, rather than anything being published in 1983 or 1984?

A. That's correct.

Q. Yes. So can we go back to Dr Foster's paper on this, please? That's [PEN0121506]. If we can just look again, you make a number of different points which you say are necessary to consider in assessing the merits of the claim. If we can perhaps just read through them.

So the first point you make is that the Hemofil product was heated at 60 degrees, not 68 degrees, and then some material with which we are now familiar.

Perhaps noting specifically that a UK licence application for Hemofil T was rejected by the Committee on Safety of Medicines.

Then the fourth bullet is the reference to that report in February 1985. In January 1986 a manuscript concerning inactivation of viruses in clotting factor concentrate is submitted by Dr Gomperts. Then over the page, please.

Then taking a slightly different tack, you point out under a subheading "Dry Heat Treatment at 68 degrees" that:

"At the time in question ..."

So that will be in May 1983:

"... the only company which was heating its concentrate at 68 degrees was Bayer, also known as Miles Cutter, and that their product Koate was licensed by the FDA in February 1984."

Then you go on to talk about other research, which we are going to look at too. Then can we go on to the next page, please?

You point out that evidence that HIV was relatively heat sensitive and could be inactivated by heating in solution was first published in January 1985 with a caution from the authors that:

"The data cannot, however, be extrapolated to

lyophilised products since our experiments were conducted in liquid medium."

So, in essence, Dr Foster, the thrust of your paper is to suggest that it was known in May 1983 that the HIV virus could be inactivated by a particular heat treatment protocol is a misconception?

A. I think it was a misunderstanding, yes.

Q. Sir, before we return to autumn 1984, perhaps this is a good time for a break.

THE CHAIRMAN: It might just be.

MS DUNLOP: Right.

(11.00 am)

(Short break)

(11.25 am)

MS DUNLOP: Thank you, sir.

Dr Foster, just before we stopped, I had asked you about that paper that you did for the Archer Inquiry and we had looked at that and I did so because you refer to it specifically in your statement. That's at page 34 of [PEN0121438] at subparagraph (c), which we don't need to go to but just for the references.

The next document that I want to look at is a publication from the Lancet in September of 1984. This is [LIT0010434]. You refer to this as well in your statement. Simply trying, as I said, to work through

the different references in chronological order. This is to do with mouse retroviruses. Is that right?

A. That's correct.

Q. Yes. These authors are sending what's called a preliminary communication to the Lancet about work they have been doing with retroviruses in mice. So in essence what they are doing, it's dry-heated material, so using dry-heated material, heated at 68 degrees, and then injecting it into mice and seeing what happens to the mice? Is that --

A. No, that wouldn't be it.

Q. Sorry. I'm completely wrong?

A. They are taking, their company, Factor VIII -- and this is Bayer. And we know already that Bayer were heating their Factor VIII at 68 degrees for 72 hours in an attempt to inactivate the agent for non-A non-B hepatitis, and they are trying to establish whether or not that process would be effective against a retrovirus, because by now it is known that HIV is a retrovirus.

They don't actually have the human retrovirus, HIV, so as an alternative they have taken this mouse retrovirus which is available in a laboratory as a culture that they can add to the Factor VIII. They can then heat that to 68 degrees and establish whether

or not that retrovirus is inactivated. But I think they also added it into the process to see how it distributed in the process as well. So they could get a measure of what was happening to the virus all the way through their process.

Q. Yes. Can we just scroll down to look at the text of the first page of this, please? Actually I put it exactly the wrong way round because we can see that they recovered a virus, possibly not "they", somebody else recovered a mouse retrovirus from a New Zealand black mouse kidney. Then it seems the virus was grown in mink lung cells.

People are very creative in your line of work, Dr Foster.

Can we then look on to the next page, please? Because I'm interested in the time periods.

Just to direct attention, if we look at the table and then a little bit below the table, it says:

"No infectious virus was detected in the samples heated for 96 hours at 68 degrees."

So a particularly long period of heating. And then in relation to the 72-hour heating, which is immediately above:

"Virus was detected in two out of three lyophilised samples but only at a concentration of ..."

I think a hole has been punched just at the wrong bit but I think it's under one particle per millilitre. I think we possibly have that data in another --

THE CHAIRMAN: It looks like the same unit of measurement as is in the second last line of the paragraph.

MS DUNLOP: Yes:

"Infectious particle per millilitre", yes.

I think the other thing to note about this, if we can go right down to the bottom, please, is the connection with Cutter Laboratories, so that's the Bayer/Miles Cutter?

A. Yes, and one of the authors is a person that I knew reasonably well.

Q. Right. So this is the murine retroviruses research and this is also referred to in MMWR, which is a publication we haven't looked at for a while. [LIT0010460]. This is one of these weekly bulletins with which we are now all familiar. It's 26 October 1984 and it's an update on AIDS but if we look at the bottom of the first page, in the third last line. I'm directing you to this but you, I think, directed us to it in the first place. So it won't come as a surprise:

"A recently published study evaluated the thermo-stability of murine retroviruses inoculated into factor concentrates using a cell transformation assay."

Then, after 48 hours at 68 degrees, viral titer has dropped from 10 -- I don't know, is that 10 to the power 8?

A. Yes, it would be.

Q. To two infectious particles per millilitre. Then:

"In studies done at CDC in cooperation with Cutter Laboratories ..."

We can all read it for ourselves, that this is the same research.

The date of that being 26 October is interesting for our purposes because we know that it was around about that time that news broke in Edinburgh of the infection of a group of patients treated at Edinburgh Royal Infirmary. That's correct, isn't it?

A. Yes. I think Dr McClelland has actually said the 26th was the date that he was informed.

Q. Yes. Can we go, please, to a set of minutes from that date, which are [SNB0103479]. These are the minutes of a meeting of heads of department and section managers, held on Friday, 26 October 1984. You are there. Dr Perry, Dr Cuthbertson. We can see that various matters are discussed. If we can scroll down, some practical points, and then on to the next page, please. These meetings, were they a regular event? Was it every Friday?

A. Yes, I think at this time they were, yes.
Q. Can you remember, was it a morning meeting?
A. This would be a morning meeting.
Q. Right. Can we just scroll right through the document, please. I think it's towards the very end there is a reference to AIDS. It's actually under AOB:

"Dr Perry was concerned that there may be a possibility that PFC would be asked in the future what plans had been made to reduce AIDS infection in blood products. He proposed and it was agreed that it would be useful to collate all information and data on heat-treated products and that Dr Cuthbertson, Dr Foster, Dr MacLeod and Mr McQuillan should meet with him to discuss this matter."

Do you remember that actual discussion at the meeting?

A. Only vaguely, very, very vaguely, and I think it is no more than is stated here.
Q. Right. Could we return, please, to Dr Foster's statement. That is document [PEN0121438]. And go to 1471. Just so that we are not losing anything that's in the statement, there is a reference to what Dr Mannucci said at a meeting in Cardiff. We have tried actually to find the exact date of the meeting in Cardiff but we are not very clear when it was. It was certainly around

about this time but you point out to us that that research, which is the research that we looked at in the Lancet in 1985, wasn't published in fact until 1985, and also you are referring to a publication in connection with Hemofil T, which was first made in 1987. Paragraph (c), we have dealt with because that's the submission to the Archer Inquiry.

Then paragraph (d), back to the report of the meeting in Cardiff, which you heard about on 6 November 1984 but I'm interested in going a little bit further back into the end of October. In paragraph (e) you make a reference to data that were presented at Groningen and you correct something that's in your report of Groningen and we will come to that in a moment, but if we can move on to look at the next page, where you are answering more specific questions about your awareness of the infections in Edinburgh, you tell us in answer numbered 27 that you think you heard the news from Dr Cuthbertson, or at least from overhearing a conversation Dr Cuthbertson was having, probably with Dr McClelland?

A. Yes, it might even have been Dr Boulton, now I have seen that Dr McClelland was ill. So it could have been Dr Boulton, but I didn't know who Dr Cuthbertson was talking to but I got the gist of the conversation.

Q. Right. You say that you immediately called Dr MacLeod to your office and asked him to identify all the R&D samples of Factor VIII concentrate that were already available and which could be used for heat treatment experiments. By "immediately" I take it you mean within, what, minutes or an hour at most?
A. I mean that they were already prepared. We didn't have to go away and get cryoprecipitate and process it and freeze-dry it. We actually had some freeze-dried material -- some freeze-dried samples that we could heat and then assay to see what effect the heat had.
Q. But in terms of how quickly you contacted Dr MacLeod --
A. That was immediately.
Q. As in minutes or maybe an hour at most?
A. It was immediate. I think he was in my office before Dr Cuthbertson had put the telephone down.
Q. We need to turn on to the next page, please. WeD are talking about the research information that we have looked at. That's the Levy publication and the reporting of that. I don't think you mention it here but the further report in MMWR. We take up the story of Dr MacLeod's involvement in subparagraph (e). So he comes back to you with a list of available samples. That's samples available for research. You drew up a plan. Do you think that that was on the Friday,

26 October?

A. At one point I thought that might have been the case but it can't have been because there is a report from Dr McClelland, which was written at the time, where he is quite clear that he didn't have this information until that evening. So it seems to me more likely that that was the Monday morning and that it was Dr Boulton who was phoning Dr Cuthbertson on the following Monday and that then led us to carry out these further heat treatment experiments. And I do have a set of results of some of these experiments, which are dated Tuesday, 30th, which would be consistent with that.

Q. Yes. Indeed, you go on and tell us with great clarity about that in the ensuing paragraphs but I'm just interested in your own recollection. When you first thought about it, before you had seen other people's material, you did think it was the Friday, did you?

A. I did and I think I must have been mistaken but it's so vague. I really would be wrong to give a specific date without anything to verify it by.

THE CHAIRMAN: Dr Foster, what about the atmosphere, as distinct from the precise date? You are in a different room and yet you pick up enough, from what you have said, whether it's the Friday or the Monday, immediately to call Dr MacLeod, who reacts very, very quickly

indeed, probably back before Dr Cuthbertson or Dr Boulton has put the phone down, and then you are giving instruction as to tests. What was it that informed you of the need for as urgent a reaction as that?

A. Well, it was the possibility that the HIV was actually in the Scottish blood supply and we hadn't known that before that.

THE CHAIRMAN: Yes, and how did people react to that around you?

A. I don't think it was broadcast at that time. It was kept fairly confidential because it was very preliminary and I think people didn't want to talk about it very widely at that point in time.

THE CHAIRMAN: And the narrow group of people who did know? How did they respond?

A. I really can't remember. But we did -- I mean, I'm sure I had discussions with Dr Cuthbertson and we did start to do these dry heat treatment experiments and it was, of course, immediately after that that we went to this meeting in Groningen and we discovered the data from CDC and we came back and implemented that.

MS DUNLOP: Yes. Can we just look, please, at the next page.

You are not sure if that discussion at the heads of

department meeting on 26 October -- we looked at what is perhaps a slightly cryptic paragraph at the end of the minutes. You are not sure if that discussion was taking place in the context of there now being known to be infections in Edinburgh.

A. I think the more I think about it, I would say it wasn't to do with that. I think Dr Perry was simply beginning to anticipate that this was obviously something that was of great concern and he was going to be questioned about it and he just wanted to bring together all of the data that we had, so he was in a position to answer questions.

Q. Dr MacLeod obviously acted with great alacrity and you say that the results of these dry heat experiments were available on the Tuesday. So if it wasn't the Friday, it wasn't during the working day on the Friday, there is no alternative, other than to say it was during the working day on Monday that you learned about it?

A. I think that's probably correct, yes. But the data from my discussion with Dr MacLeod, actually those samples were examined over a period of time. It was the first information that I had, that was on the Tuesday, 30th, it wasn't samples which had been modified in any way, it was the standard product, that was there to be heated and to test.

Q. Right. You say that the results were available on the Tuesday. It will have been very quick work to have learned about the infections on the Monday and to have results from further experiments by the next day?
A. Yes, I think -- it is just possible that -- I mean, there were two things done here. There is the experiments that I discussed with Dr MacLeod, which involved samples that I had prepared with different additives. But then there was also heat treatment studies with the existing product, and they weren't done by Dr MacLeod, they were done by Mr McQuillan, who was in the quality control department, and it is his results that I'm talking about that we had on Tuesday, 30th, not the results from Dr MacLeod's discussion. And it's possible that those experiments were discussed on the Friday afternoon, following our meeting on the Friday morning, in light of the publication with the murine virus, that it was worth going back and seeing what our product would tolerated at 68 degrees. Or that might have been done on the Monday morning. And the heating was only for a few hours. So it would have been a few vials heated for a few hours and then the Factor VIII assay is done and a short reported written and given to me on the Tuesday.
Q. Just so that I'm not misunderstanding, Dr Foster, none

of these results was something that you already had on the books, for example. It wasn't a question just of going back and looking up something that had been done a month or so before?

A. No.

Q. No. So it was all starting from scratch?

A. The previous work we had done was virtually 12 months earlier, the December 1983 experiment of Cuthbertson, where we had not done any further work with dry heat treatment until this point in time.

Q. Right.

A. And of course, the 68 degrees follows on from the -- I think it must follow on from the publication with the murine virus from Cutter and that I chose to include that temperature.

Q. Yes, and the different samples you were trying out were ones that had been treated, if that's the right word, with various different additives or potential stabilisers?

A. Yes, and that was studies that I had done to try and improve the yield of Factor VIII and I had put some vials aside for long-term stability studies, because that was something that was needed for licensing. You had to show that the product would retain its activity after two years but it seemed to me that this was more

pressing. So I took those samples to be used in this experiment. And one of the difficulties at this time was that our production operation was shut down for building renovations. So there was no way that I could actually do new experiments. I couldn't get fresh cryoprecipitate to do further experiments. That would have taken a number of months. All I had was what was already on the stocks, if you like, to work with.

Q. A very stressful few days, I imagine, Dr Foster?

A. A stressful 30 years, I think.

Q. Indeed.

So the focus at this point, you have the help of Dr MacLeod and Mr McQuillan, and the focus is to find out of your library of samples what is the most robust in the presence of heat, really?

A. Yes, that's right, and we did heating at 60 degrees, as well as 68.

Q. Right. We travel to Groningen. Just for completeness, as lawyers keep saying, just noting that on a previous page, 1472, you do say that prior to leaving for Groningen, you had received results from Mr McQuillan that indicated that the Factor VIII concentrate could withstand dry heat treatment at either 60 degrees for 24 hours or at 68 degrees for about three hours.

Groningen. You tell us in paragraph (h) that the

Wednesday, Halloween, you travelled to Groningen and as I think was your practice, you wrote a report about that meeting, which is [SNF0013373].

This event in Groningen, was it a regular fixture?

A. The transfusion centre in Groningen held a conference every year but each year they would have a different topic, and in this particular year the topic was plasma fractionation, which was almost a unique event. There were very few conferences dedicated to plasma fractionation.

Q. Right. Here are your notes from the meeting. I think this is one of these documents where every second page is blank but I think we need to go to what is our page 3, please. We can see that page 3 has quite a bit of information about AIDS, in particular AIDS in haemophilia, and then at the very bottom of the page you have recorded information about heat inactivation studies, and you have said:

"Probably by Cutter."

Then starting level of the virus. Over the next page, please. Then "conditions", 68 degrees wet heating and 68 degrees dry heating. You corrected that, and drew attention to the passage in your statement, where you have corrected that. The pasteurisation experiments that were being spoken of were actually 60 degrees

heating?

A. That's correct.

Q. So we should correct that first reference from "68 degrees" to "60 degrees", where we see it there. Is that correct?

A. Yes, yes.

Q. But the 68 degrees dry heating is said to have fewer than ten viral particles per millilitre after one hour, complete inactivation at 24 to 78 hours. So is this different from the information that you had had in your mind before you went to Groningen from the CDC and the Lancet publication.

A. The Lancet publication was concerned with the mouse retrovirus. I'm not a virologist but I didn't really know how relevant that was to the human virus. So there was some uncertainty. But the Lancet paper did suggest that dry heating might have some effect and might be therefore worth picking up again, which was what we were starting to do. The MMWR that was dated 26 October, although we subscribed to that, we hadn't received our copy by that date because it took a couple of weeks to arrive. So this was the first knowledge I had of these findings. In her presentation, Dr Jason actually said this is hot from the press, and gave the impression that she had just had these results by telephone the previous

day.

Q. I suppose the other thing that appears to me to be strikingly different is the shortness of the period of time because the Lancet paper had spoken of much longer periods of dry heating?

A. The Lancet paper does have a time point of one hour, if you go back to the table in the paper. It had the time period of one hour and it goes up to 96 hours. So they had a lot of time points.

Q. Right. Well, perhaps we should just look at that table because, I'm sorry, I have missed that reference to the one-hour heating. That's [LIT0010434]. It seems a slightly different result. You had better explain it to me. It looks like more particles were still present after one hour?

A. That's right, and that tells us that the mouse retrovirus is more resistant to heat than the human HIV.

Q. Right. I suppose in a nutshell, the newness of the information being imparted in Groningen is how successful even as short a period as one hour of dry heating could be?

A. That's right. That's what brought it into our terms of reference, almost, that we could apply that.

Q. Right. At this point I would like to return, if we could, please, to Dr Foster's paper, which is the

document numbered [PEN0131309]. Go to a passage I skipped over yesterday. That's on page 17 of [PEN0131309]. Just to look at the information that's on the three pages that we missed yesterday. I think most of this we have already covered. In the second paragraph, Dr Foster, you are crediting Dr Gallo with discovering the virus responsible for AIDS, are you?

A. Yes, I would say that the earlier French publication concerned the isolation of the virus but proof that this was actually the virus responsible for AIDS wasn't fully established, I would say, until the Gallo publication and of course, a discovery, you have to know what you have discovered.

Q. Yes. Of course, what happened in that year, May 1983 to May 1984, and whose virus exactly Dr Gallo was working with, seems to be a bit murky?

A. That's a very interesting story.

Q. Yes. Fortunately I don't think we have to probe that. Although we will be looking perhaps in a little more detail at it in the next topic.

But you mention the CDC experiments and the collaboration with Cutter and then the publication in the MMWR on 26 October, which we have looked at, and just in case anyone wants to do some further reading, the further article by Levy et al, 1985 is -- and I'm

not wanting to go to any of these but just to give the references for the transcript -- [SNB0085852] and the McDougal paper. I can say this because Mr Stempt isn't here to hear it. The McDougal paper is a duplicate in court book, and has two references, which is not supposed to happen, it's [LIT0010826] and it's also SNB0106169.

Information on the effect of dry heating Factor VIII concentrate for one hour at 68 degrees was presented at Groningen. We have looked at that, and also you say in September 1985 in a brochure that Cutter published. Then you refer to further evidence about the heat sensitivity of HIV and then the Mannucci et al research published in February 1985 in the Lancet.

On to the next page, if we could, please. Again, this is information that we have come across before, that commercial heat-treated Factor VIII concentrates were first licensed for use in the UK in February 1985:

"Supplies were insufficient for some months with the result that 40 per cent of UK haemophilia centres were still using unheated concentrates as late as May 1985."

Then a further reference to research on dry heat treatment at 60 degrees, a reference to some difficulty, some infections caused by heat-treated Factorate, an Armour product, which is dealt with in the preliminary

report. Then you go on to summarise that material by telling us that there were questions asked about the effectiveness of dry heat treatment and a resort by most manufacturers to solvent detergent treatment. You say:

"It is likely that the early heat-treated products were largely successful in destroying HIV, evidenced by the fact that in a major USA study there were no cases of HIV infection in people with haemophilia born after 1984."

Then you have provided for us a table, which is on the next page, and we can see that by international standards or on an international survey, Scotland was not just prompt but first to distribute heat-treated Factor VIII and recall unheated Factor VIII.

That's that section of your paper. Can we move forward in the paper, please, to 1344. Again, just to confirm that much of this has been covered but if we can go to the bottom of the page, please, reference to the American research. Then you make a point in the next paragraph about concern about neoantigens and there is a trio of letters that I wanted just to look at in that regard. Can we look, first, please, at [SNB0064708]?

Here we have Dr Ludlam writing to Mr Watt on 24 March 1983. He is very interested to hear of progress of both the new Factor VIII preparation and its

heat treatment but -- and this is the second paragraph -- he is concerned about the possibility of neoantigens developing following heat treatment. And neoantigens are, I think we covered this yesterday, basically that the heating will do something to the Factor VIII which will actually create something that will adversely affect the patient?

A. Yes, it would be a new site on the Factor VIII that would be recognised as being foreign and would cause an immune response in the patient.

Q. Yes.

A. We talk about inhibitors, which you have heard about. It would be a type of inhibitor that would stop the Factor VIII from working.

Q. Right. I think he is proposing a small study. Is that right?

A. That's correct.

Q. He is also worried about sorbitol as an irritant.

The next letter is [SNB0073601]. Mr Watt is writing to Dr Cash on this topic. That is Dr Ludlam's letter of 24 March. He is saying he finds it difficult to follow Dr Ludlam's logic.

This seems quite technical, Dr Foster.

A. Yes, Mr Watt is talking about the test system that Dr Ludlam has proposed, because there was no known way of

actually determining whether anything was going to be a neoantigen. So the question they were addressing was: how can we make these measurements? What measurements can we make that might tell us that the product is going to be harmful or is not going to be harmful? So they are having a debate about the possible approaches that can be taken to that.

Q. Can we look at the second page, please? So Mr Watt is thinking that the type of study proposed by Dr Ludlam is either unnecessary or premature:

"I believe the latter to be most probable."

Can we next look, please, at [SNB0073625]? This is Dr Cash coming back to Mr Watt. He seems to be more supportive of Dr Ludlam's position than of Mr Watt's position. Is that right?

A. Yes, that's correct.

Q. Yes. So Dr Cash thinks there are some investigations that can be carried out that would be meaningful. These letters certainly illustrate your point, Dr Foster, that there was concern about the possible formation of harmful neoantigens. Did anything very much come of this exchange, do you remember?

A. Yes, as a consequence of this, we did some work with Dr Joan Dawes, who was working with Dr Pepper who reported to Dr Cash, and she had developed some test

systems to look at the integrity of the Factor VIII molecule and associated molecules to see if they were altered in any way by the heat treatment, and basically the answer was that it looked fine. This was the pasteurisation.

Q. Yes. Right. Can we go back to Dr Foster's paper then, please?

A. It is just worth pointing out that some years later two pasteurised products did cause abnormal inhibitors in patients and had to be withdrawn. So it did turn out to be actually a real issue some years later on.

Q. Right. I suppose these concerns, which are certainly, obviously, evident in 1983, wouldn't then have been restricted to pasteurisation; they would have applied to concerns about dry heat treatment methods?

A. Yes, very much so.

Q. Yes. So we were on 1345, if we could look at that, please.

After your reference to neoantigens you tell us that two hours was specified for the initial dry heating protocol at PFC because this was the longest period of heating that samples of the existing concentrate would stand. You must also have been comforted by the fact that it was double the period that had been reported to substantially inactivate the virus?

A. Yes, it did seem to be -- it made it worthwhile.
Q. Then you tell us about the oven angle, which I think we have mentioned before, and then three months' supply was heated immediately and the product issued as soon as the necessary clinical evaluation of efficacy and tolerability had been completed. So you were able to supply all of Scotland and Northern Ireland with sufficient dry-heated Factor VIII concentrate for all patients on 10 December 1984.

Then this is something that we have discussed before, that adding a bit of sugar enabled the heating period to be increased from two hours to 24 hours. And you explain the rationale for the release of the two-hour product, which I think we can follow. Then on to 1346. I think you are basically telling us that although you had some information about the possible tolerance up to 24 hours, you didn't wait and actually proceed with that protocol because you want to get on with issuing heat-treated product immediately?
A. We made the change to the formulation as soon as we started manufacture because at this point we weren't manufacturing Factor VIII. We had stopped production due to building renovations. So it was the first day that we started manufacture that we put sucrose into the new formulation.

Q. We will be going back to the paper, I think, so if we could perhaps leave it open but if we could return to the questions document and look at the last batch of questions, which is on [PEN0121531] at 1538. We can work our way through the remaining questions. Fortunately we don't have to look at all the documents that are listed at the end of 35 because I think your answer in a nutshell is that you didn't at that time require to obtain any additional equipment. That is at the end of 1984?

A. That's correct.

Q. Yes. The last question we asked you, Dr Foster, is as follows:

"In retrospect the infection of the group of people known as the Edinburgh cohort would have been prevented if PFC had moved to dry heat-treated product at the beginning of 1984. It appears that the equipment necessary to do so was either already installed or easily obtained. What are the reasons why this did not take place?"

Just to clarify, obviously, any prevention by such a step would have had to encompass product recall, and I think you make that point in your answer. So what we are really asking you to envisage is what happened in December 1984 but envisage it happening

in January 1984, say. We asked you to explain in your view why that didn't happen and you have answered that very fully. This is [PEN0121438], Dr Foster's statement, at 1475. You have a number of reasons and indeed some further comment in response. Just to go through these, you say:

"The cause of AIDS was not known."

And you refer to the preliminary report:

"The virus had not been discovered."

And I suppose that links back to the answer you gave a little while ago about the linking up that was done in America between the virus and the disease?

A. I think even Luc Montagnier has agreed with that in some of his publications.

Q. "That the virus could be inactivated by heat treatment was not known; that it could be inactivated by dry heat treatment under conditions that SNBTS Factor VIII concentrate was not known."

You were hard at work and we know this. You were hard at work preparing pilot batches of a heat-treated product, a pasteurised product, indeed ZHT, for clinical evaluation, as were a number of other manufacturers.

You make the point that no manufacturer in the world had switched from unheated to heat-treated Factor VIII concentrate, although some manufacturers were

heat-treating a small proportion of their Factor VIII and it was known that dry heat treatment had not inactivated agent or agents responsible for non-A non-B hepatitis.

Then you also mention a concern about an adverse reaction in patients.

A. There is another way of looking at this and that is to put to one side what we know now, and in January 1984 it was conceivable that heat treatment would not have inactivated HIV. It was conceivable that it might have caused adverse reactions in patients and if we had proceeded to do what you suggest, and it hadn't inactivated HIV and it had caused adverse reactions in patients and serious adverse reactions, I might be then asked questions as to why we had made that change that damaged patients when there was no evidence to justify it.

Q. Yes.

THE CHAIRMAN: That's the reality of life, Dr Foster.

MS DUNLOP: You refer, indeed, in the very next paragraph to the then Dr Hann's letter and we looked at that when we were examining concentrate treatment. It's a handwritten letter. We don't need to go to it but he had misgivings about the swiftness with which your heat-treated product was introduced.

A. That's correct.

Q. That's an example of somebody who wasn't completely in favour. Then you say:

"A similar concern was published by Bird and others in the Lancet."

And we have referred to that in the preliminary report.

Then you make other points, which we can read at (d) and (e) and so on. You didn't have evidence in a peer reviewed journal that HIV was relatively heat sensitive until January 1985, and we have seen that referred to before. Then also the continued use in the UK -- for practical purposes, I think we do mean England and Wales here -- the need to continue to use unheated domestic Factor VIII continued within the UK. The position in BPL. Then in (h) you refer to applying the heat treatment to the stock that was held. You say it was discovered subsequently -- this is reading from subparagraph (i) -- that:

"A number of HIV positive donations from this period are contributed to batches of SNBTS Factor VIII concentrate that were subsequently dry heat-treated. One HIV positive donation having been collected as early as 24 March 1984."

I think the information that exists about the

donations that went into batch 0090, if we can call it that for shorthand, actually reveals that the donation must have been collected in the spring of 1983?

A. That's correct.

Q. Yes.

A. I would probably say later than that. It might have been summer to autumn 1983.

Q. But the manufacture was November 1983?

A. November, yes.

Q. That gives us a cut-off date. You say:

"The heating of a 12-month stock of Factor VIII concentrate did not extend back to the batch of Factor VIII concentrate that was implicated in the transmission of HIV to the group of people known as the Edinburgh cohort."

A. It's worth pointing out that the heating of the 12 months' stock probably did include material that was manufactured in January 1984. So in fact you could say we did heat-treat material that was prepared in January 1984.

Q. Yes. But in fact it's not really the cut-off date for the retrospective heat treatment that is determinative here, it is the fact that actually this batch was transfused between March and May 1984. So it had gone out anyway?

A. That's right.
Q. Yes. Of course, the question was actually framed on the hypothesis that there was only one infected batch, which we have been over to a considerable extent already, and the picture is not as crisp as that. But you say in subparagraph (k) that:

"In retrospect, the infection of the group of people known as the Edinburgh cohort would not have been prevented if PFC had moved to dry heated product at the beginning of 1984 unless stocks of Factor VIII concentrate had also been subjected to a speculative heat treatment procedure."

So that would have had to have been a similar kind of retrospective treatment?
A. That's correct.
Q. And you refer to harm that was done by the formation of inhibitors.

Would it be fair, Dr Foster, to add as an additional reason why this wasn't done -- that is dry heat treatment at the beginning of 1984 rather than the end of 1984 -- that it was not known that the agent responsible for AIDS had entered the blood supply in Scotland?
A. Certainly that was not known.
Q. Yes.

A. I'm not sure if I would include that as a reason or not. I can't really remember that far back as to what was our thinking. I doubt if we would have done something based on speculation. I mean, you know, in science you like to do things based on evidence.

Q. I appreciate that this question may well break down on the detail, but if one imagines that at the beginning of 1984 you had somehow had knowledge that one of the batches that had already been manufactured was infectious, surely that would have altered the course of events? I'm not saying you should have had knowledge, just with the luxury of hindsight which is afforded to us, if we look back on that and say, if you could have known in some way --

A. You could make the same analogy with non-A non-B hepatitis, and we knew that was being transmitted but we didn't know how to prevent it. And in January 1984, even if we had known that the HIV was in the blood supply, we didn't know how to prevent it, and what you are suggesting is based on hindsight. It is the knowledge that was gained later, with what worked.

Q. I appreciate that.

We have rather neglected Factor IX. So to correct that, I would like to go back, please, to your paper, which is [PEN0131309]. Turn to page 1358.

THE CHAIRMAN: Could I follow just a little bit about what might have happened. I'm sorry to take time to think about it.

MS DUNLOP: Yes, certainly.

THE CHAIRMAN: Dr Foster, we know that in the last days of October 1984, when the word broke that there was an infected batch out there, there was a very swift reaction and you did call in things. I appreciate that by then you had quite a lot of additional information, but if you had known at the beginning of the year that NY0090 was out in circulation and was infected, don't you think there would have been immediate action taken?

A. There might have been a change to cryoprecipitate.

THE CHAIRMAN: Well, no. I'm thinking about the product that was out and in circulation. Would it not have been recalled, so far as possible, immediately?

A. I think if it was known there could have been a link to any batch, yes, that would have been recalled, and we did that with hepatitis. But to recall, to stop issuing Factor VIII, is putting the lives of all the patients at risk because they need some kind of treatment.

THE CHAIRMAN: I appreciate that but of course it was recalled, so far as possible, as soon as the knowledge was available?

A. The batch that was implicated was recalled, yes.

THE CHAIRMAN: And the implication, of course, arose from an examination of the treatment records of patients and the distribution records of PFC, and that information was available early in 1984, as it was later on?

A. Yes, I agree with you. If there had been some association with a batch, or more than one batch, those batches would have been recalled.

THE CHAIRMAN: So there would have been a situation surely in which such material as could be found would have been taken out of circulation?

A. Yes.

THE CHAIRMAN: And PFC would have had at that point a body of material that was at least suspected, to a fairly high degree of suspicion, to contain infective particles of HTLV-III or HIV, would it not?

A. Yes.

THE CHAIRMAN: What would you have done?

A. In what respect?

THE CHAIRMAN: In PFC. You have this stuff, you have grounds for believing that it's infected. I don't believe you would have done nothing, so what would you have done?

A. If we use the hepatitis analogy, I think what Mr Watt did with batches that were implicated like that would be to send them to a virologist to see if they could

isolate the virus.
THE CHAIRMAN: And once you had made that attempt, you would be trying to do something about it?
A. If the virus had been isolated, yes, but I don't think anyone did isolate HIV from Factor VIII at that time, even for some years.
THE CHAIRMAN: I appreciate that if one uses all of hindsight, we have to get up to Professor Simmonds in 2005 and his philogenetic trees to find out exactly what was in it, but I just find it difficult to imagine a situation in which you would not have done something.
A. I'm sure we would have sat down and done everything we could have thought of. I doubt we would have done something speculative in terms of some treatment that we had no knowledge would or wouldn't work, which might harm patients.
THE CHAIRMAN: I think that's as far as I can go in provoking Dr Foster, but you take over.
MS DUNLOP: Thank you, sir. As you appreciate, it's a question that we put to everybody.
THE CHAIRMAN: I know.
MS DUNLOP: So we will have a number of opportunities to reflect on it.
THE CHAIRMAN: Absolutely, and Dr Foster mustn't think he is the only person who is going to be asked these

questions. It is an area I have to look at very carefully.

A. I understand that and it's a question that has been put to the whole industry.

MS DUNLOP: So back at Factor IX, we are in the paper, [PEN0131309], at pages 1358 and you have a subheading, "The development of heat-treated Factor IX concentrate". You tell us, which I hope we can manage to remember from yesterday, that you have been engaged in research aimed at eliminating the risk of hepatitis transmission by Factor IX concentrate since 1970.

A. SNBTS have.

Q. Yes, not you personally. But you joined in when you arrived?

A. At some point, yes.

Q. Yes. You mention on the following page Supernine. So was Supernine a product then in which some viral inactivation was expected to have occurred?

A. It was expected to remove some virus, not to inactivate it but to physically remove it.

Q. Sorry, yes.

A. Whether it was sufficient to remove all the virus to make the product free from infection was a debatable point.

Q. And then 5.2. The application of heat treatment to

Factor IX concentrates, you point out that SNBTS research on the application of pasteurisation was undertaken about Factor IX as well Factor VIII, but of course -- and we have heard this before -- there was this concern with Factor IX about thrombogenicity. And we have already looked at Dr Cash's article from 1975 on that topic. Just for reference, although we are not going to it, it's [LIT0010959].

Then on to the following page. We know that this was an area in which you worked with BPL/PFL. So you worked both on the Scottish product, DEFIX, and on the English product, which you say was called "9A", to discover whether heat-treating was posing an additional risk of thrombosis?

A. Yes, I mean, they agreed with us, and with Dr Cash, that this was a very important study to be carried out with their product as well as with ours.

Q. Yes. Fortunately the animal safety studies were completed in August 1985 with no increase in thrombogenicity being observed:

"Clinical trials proceeded and heat-treated Factor IX concentrate was issued routinely from the beginning of October 1985. As soon as adequate stocks were in place, the SNBTS recalled all stocks of its unheated Factor IX concentrate, DEFIX, which were

destroyed."

Then you take us forward and tell us about a high purity Factor IX concentrate, HIPFIX. I should have said, of course, that all of this -- I think it's clear from your paper anyway -- is heat treatment at 80 degrees for 72 hours. Factor IX is just generally rather more obliging than Factor VIII, isn't it?

A. Yes, I would say that's a good way to put it.

Q. Yes.

A. Apart from the thrombogenicity risk.

Q. Yes, well, there is that.

1361, the next page. You have a section entitled, "Clinical safety of SNBTS heat-treated concentrates", and you say:

"All the heat-treated concentrates are considered to have been free from transmission of HIV ... Two patients are known to have developed antibodies to HIV after receiving SNBTS heat-treated Factor VIII concentrate but both patients had previously received unheated concentrates at a point in time consistent with this being the most probable source of infection."

Your reference for that is a letter from Dr Forbes, which I think we should just look at. That's [SNB0047732], Dr Forbes to Dr Cash in February 1986:

"We have become aware of three seroconversions in

the past year in patients receiving blood products."

He is enclosing details. The first is a patient who's Factor VIII-deficient.

The first positive test is October 1985 but it certainly would have been possible for the previous negative test, in October 1984, to have been during a window period, and I think that may be a view which has been taken in relation to this individual. I'm not sure if you are in a position to comment, Dr Foster.

A. This is not really my area of expertise. I would refer that to Professor Cash or Dr Forbes.

Q. But if we look at patient 2, we see that patient 2 is actually a Haemophilia B patient and he looks to have seroconverted during 1985. Do you see that? Of course, the heat-treated product, we have just said, wasn't issued routinely until the beginning of October 1985, so it's likely that that was unheated Factor IX that is implicated in the case of patient 2. Does that seem a reasonable inference?

A. Yes, I would agree with that.

Q. And then patient 3 is somebody who has received FEIBA, only, and FEIBA is, I think, a commercial product anyway?

A. It's manufactured by Immuno.

Q. Yes. Can we go back to the paper, please? You tell us

that when donor screening was introduced in October 1985 and the Blood Transfusion Service, therefore, was able to pick up donors who screened positive, investigations were done to determine what had happened to donations that they might have provided earlier, and you say:

"It was discovered that a number of batches of Factor VIII concentrate which had been heat-treated had been prepared from plasma donations where either the archive sample tested positive for antibody to HIV or where infectivity was implied because the associated red cell donation had transmitted HIV. None of these batches transmitted HIV."

Indeed, you have tabulated those donations and the donors for us. Then you say:

"The absence of HIV transmission via unheated Factor IX concentrate suggests that the infectivity was eliminated by the manufacturing process or that the recipients were not susceptible to infection."

But I think, having looked at Dr Forbes' letter, it isn't a total absence in relation to Factor IX, is it? It does looks as though there is --

A. No, I think there is evidence that Factor IX did transmit, and it may depend on the titer of virus in the particular batch concerned.

Q. Right. Then over on to the next page. You say:

"The fact that an infective donation from March 1984 did not infect people with haemophilia demonstrates the value of dry heat-treating the stock immediately in November."

Dr Foster, the rest of your paper consists of a detailed chronology, which I hope people will find doesn't contain anything of significance that we haven't discussed, and then a series of numbered references and also a further series of references for literature which was primarily referenced in a work that you prepared with -- you had better help me with the pronunciation -- Bienek?

A. Dr Bienek.

Q. You have provided a great deal of material for us on heat treatment and it has obviously been enormously helpful to us in our preparations on this topic. So we are very grateful to you. Thank you.

A. Thank you.

THE CHAIRMAN: Mr Di Rollo? Do you want to start or do you want time or --

MR DI ROLLO: No, I don't want to ask any questions --

THE CHAIRMAN: You do not want to ask any questions.

Mr Anderson?

MR ANDERSON: I have no questions, sir.

THE CHAIRMAN: Mr Johnston?

MR JOHNSTON: No, sir, I have no questions.
THE CHAIRMAN: I don't know if Dr Foster is coming back. Is he due to be arraigned again?
MS DUNLOP: I'm afraid he is. I'm sorry, Dr Foster, I think you know that, though.
A. I do, yes.
Q. Yes.
THE CHAIRMAN: I will leave my final thanks until then.
MS DUNLOP: Once more.
THE CHAIRMAN: But thank you very much.
MS DUNLOP: Once more.
A. Thank you.
THE CHAIRMAN: Now ...
MS DUNLOP: Well, I had anticipated we might take all of two days so I'm afraid I haven't lined up anybody for this afternoon.
THE CHAIRMAN: Quel dommage. Very well, we will rise.
MS DUNLOP: It gives us more time to prepare for Professor Cash tomorrow.
(12.37 pm)
(The Inquiry adjourned until 9.30 am the following day)

I N D E X