Tuesday, 10 May 2011

(9.30 am)

(Proceedings delayed)

(9.54 am)

THE CHAIRMAN: Good morning.

MS DUNLOP: Good morning, sir. We are sorry for the delay but we have been printing out Dr Foster's paper so that people will be able to follow it in hard copy as well as on the screen, and that has taken slightly longer than anticipated.

DR PETER FOSTER (sworn)

Questions by MS DUNLOP

MS DUNLOP: Dr Foster, good morning. We generally begin by looking at a witness' curriculum vitae and I would like to do that with you, if I may. We have it in our system and its number is WIT0030389.

On the first page you have narrated your education. We can see your school education and that you studied at Heriot-Watt. You took a first-class honours degree in chemical engineering in 1968 and then you proceeded to University College London, where you did a PhD. We can see the subject matter of that almost in the middle of the page.

Your membership of professional bodies reveals that you are a clinical scientist, regulated, I take that to

mean, by the Health Professions Council?

A. That's correct.

Q. And you are a chartered scientist under the Science Council. What's the difference between those two?

A. The Science Council is more like the Engineering Council and it's a relatively recent development of the engineering Council to accommodate science as well as engineering. So my membership of that is really through the Institute of Chemical Engineers.

Q. Right. And does it have any regulatory function?

A. No, it doesn't. It is a professional body.

Q. If we look on to the following page, please, we can see your appointments listed. Really your whole working life was spent within the Scottish National Blood Transfusion Service. Is that correct?

A. That's correct.

Q. Yes. You started as a research scientist in 1973 and you became the head of research and development, and although your grading or the name of your grade seems to have changed, that was the position you occupied until you became development manager in 1991. Is that right?

A. That's correct, even then it was essentially the same job, just a revision of the titles.

Q. Right. You have management experience and we note from that section that -- this is about half way down -- you

were a member of the PFC, Protein Fractionation Centre management team between 1974 and 2008. You tell us -- and I'm reading up the way now, two bullets above that -- that you were responsible for maintaining awareness of scientific knowledge and protecting intellectual property. So not just your own awareness of scientific knowledge but a certain amount of dissemination as well?

A. That's correct. We had a library and I tended to take responsibility for that at the time.

Q. I notice that too, that you were responsible for the library, so you were responsible for planning and managing the PFC library, which must have been a useful way for you personally to notice recent developments?

A. Obviously one has to keep up with the field. So that was a good way to do it.

Q. You were responsible for line management and financial management of PFC development department between 1974 and 2008. You had responsibility, reading from the first bullet, for planning, managing and reviewing PFC product and process developments and contract research and development activities from 1974 to 2008.

The section headed "Scientific contributions" reveals that, among many, between 1973 and 1975 -- and I need to go to the next page because I'm starting again

at the furthest point in time -- responsible for development of automated continuous flow technology for cold ethanol fractionation of plasma. Leader of SNBTS team concerned with increasing the Factor VIII content of plasma supply to PFC. Developing methods and technology to increase Factor VIII yield and process capacity, enabling Scotland to achieve self-sufficiency in Factor VIII supply, 1981 to 1986. Developing a method for stabilising Factor VIII, now used by all major manufacturers to enable virus inactivation; further purification to be carried out without an unacceptable loss of yield. Developed a method for precipitating fibrinogen from Factor VIII solutions.

Then back to the previous page, please:

"1981 to 1986, development of heat treatment methods for inactivating HIV and hepatitis in Factor VIII and Factor IX."

Then again reading up, 1990 to 1994, I noticed, project manager for the development of high purity Factor VIII, which is Liberate. Many of these things crop up in the paper which you have prepared and in which we are going to look in more detail, but certainly we recognise a number of themes in that list.

Going to page 3 again, please, we see that today's is by no means your first experience of giving evidence

in this area. Looking at around the middle, you were a witness to the independent public inquiry under Lord Archer. You were the author of SNBTS evidence submitted to investigations by the Scottish executive and the Scottish Parliament. Author of papers for the SNBTS concerning evidence to the Scottish public inquiry under Lord Penrose. Invited expert witness to the tribunal of Inquiry in Ireland, the Lindsay Tribunal. Witness in USA, multi-district litigation.

Then towards the bottom, some more regular scientific activity: as a PhD supervisor and external examiner, and then of course at the very top, your invited reviews, scientific papers, 70 letters and abstracts and eight patent applications. Speaker at many conferences or symposia and lectures and seminars. The next page lists the patent applications. Successful patent applications?

A. Successful in that, I think, most of them were granted. I wouldn't say they made any money. Certainly I never saw any.

Q. Intellectually successful but not perhaps --

A. That's a good way to put it.

Q. -- but not enriching financially.

THE CHAIRMAN: Did they all stand the test of time or were there revocations?

A. I think some of them have stood the test of time and some have not.

MS DUNLOP: Then you have a long list of publications, Dr Foster, entirely as one would expect. I'm not going to take you through them. I wonder if it's fair to say that in general they relate to processing matters; things like yield, to heat treatment, to viral inactivation and then gradually as we read through them chronologically, we see VCJD appearing and some work on prions, and also from time to time the history of how these matters have developed, particularly in Scotland. Have I left anything out?

A. No, that's a reasonable summary, yes.

Q. Right, thank you.

One that struck me, if we just look at the third page of these, number 28, it was just the use of a different term from the term "self-sufficiency", I saw the term "self-reliance" being used there, which perhaps is an interesting alternative description of what at least I understand people to have been trying to achieve.

A. Yes, that was the term that the Swedish government or the Swedish authorities used when Dr Perry was invited to give that presentation. So that was the terminology that they applied.

Q. Were they the only ones who liked "self-reliance" as a term?
A. It's the only time I have come across it, I think.
Q. Right. 34 is an example of the phenomenon I alluded to of documenting the history of matters. "Plasma fractionation in Scotland: the first 30 years".

Then going on, we can see 66 is a contribution to a book, "Blood, blood products and HIV." some of these book titles, Dr Foster, I recognise because we have them on our shelves. We have quite a library of our own, which might not surprise you.

I noticed, if we go on to number 122, that you had also written an obituary of John Watt. When did Mr Watt die?
A. That was last year.
Q. It was last year. Then your presentations are listed as well. Constant outflow of academic work as well as, presumably, your day job?
A. I'm not sure I would call it "academic". You do get invited to talk to students from time to time.
Q. Actually I was going to ask you that as well. Have you done much teaching?
A. Just a little bit and it's listed here in these presentations.
Q. I'm comforted by that because you may have to do some

today. We are all obviously coming at this as non-scientists essentially. Although I don't want to demean anybody who might have a first degree in science, but I suppose, speaking for myself, starting from a low knowledge base, so, as I think we have said, please feel free to explain things in basic terms as the questions demand.

You have prepared for us both a witness statement and a separate paper, Dr Foster. The witness statement is [PEN0150101]. You explain the structure of your response. You were sent a standard schedule, which was prepared by the Inquiry team last summer and you responded to that. But probably more importantly, if we go on to the second page, we can see that you took up the invitation to provide any additional information you thought was relevant and you did so by preparing a paper, which is entitled "Self-sufficiency and the supply of blood products in Scotland, with particular reference to the treatment of Haemophilia A."

You say what's included in your paper and if we go on to the following page, please, you say:

"Although the preliminary report addresses this topic there is material in my paper which has not been included in the preliminary report and which may be of assistance to the Inquiry."

Dr Foster, I don't think there is any doubt of that and because of that, it's my intention, sir, just to go at this point to Dr Foster's paper and spend some time looking at that.

THE CHAIRMAN: Well, Dr Foster, I think I would have been surprised if there hadn't been omissions from the preliminary report given that it was a paper exercise and depended largely on what we could find, but I badly need to have your input so that I can understand the way things did develop. So please do make sure that we get the proper and full story.

A. Okay. I must say the preliminary report was very excellent. So I think it was really quite impressive.

THE CHAIRMAN: I know that there are large gaps in it, not least that it was published before I had taken on board fully the 1972 joint symposium of The Royal College here in Edinburgh and the College of Physicians, which set a sort of position at 1972, which is not properly reflected at all. But there will be a lot that you can fill in for us.

MS DUNLOP: Dr Foster, your paper is [PEN0131125] and I think you have a hard copy of it as well. You and Professor James should have hard copies in fact.

When you started in SNBTS in 1973, the name PFC, Protein Fractionation Centre, was already in use, as

I understand it? Is that right?

A. Yes, that name was adopted in 1970, and prior to that the unit had been called the Blood Products Unit, but there was some possibility of confusion with the Blood Products Laboratory at Elstree and it was decided to adopt a new name, and it was proposed that it should be called the Scottish Protein Fractionation Centre, and that took effect from 1 April 1970.

Q. Right. I should say you have dealt in your paper with the history of matters but that's quite a bit further on and it's certainly my intention to return to that and also to look at an article you have provided, which is a useful addition to our knowledge on the history of matters, but for the moment I think we really need to look more at the science.

So can we turn through your paper. You do provide, as is the custom nowadays, a sort of executive summary but we are going to bypass the executive summary because we are looking at the full text and if we can look at the introduction, which is page 10, please, so that's PEN0131134. You refer to previous consideration of self-sufficiency and to the opening of PFC. You say:

"Some 20 different plasma products were manufactured at PFC. Of these, Factor VIII concentrate presented the greatest challenge to the SNBTS, as it was the most

difficult product to manufacture and growth in demand was high."

Dr Foster, it is my understanding that Factor VIII is a very complex molecule. Is that correct?

A. It is quite a large molecule; that is correct. And because it co-purifies with other molecules that are also large and difficult to work with, the whole mixture that you are dealing with is really very difficult. I have to say, in all of my career, it is far and away the most difficult material I have ever had to work with.

Q. Perhaps you could explain what you mean by co-purify?

A. For example, you have heard a lot about cryoprecipitate, and that contains other proteins compared with Factor VIII. It contains predominantly fibrinogen and another protein called fibronectin. They have all, if you like, in that one step come together as a group. So if you regard cryoprecipitation as a purification step, then in that one step those proteins have all followed the same path, if you like, and kept together.

Q. Right. So there isn't any one physical step, as it were, that is an easy way to get Factor VIII on its own?

A. There isn't and perhaps it might help if I explain just how much Factor VIII we are dealing with. Because I think you have heard that it's actually a trace

component in plasma, and to put that into perspective, if you want to know what proportion of the protein in plasma Factor VIII represents, it's approximately 1 part in 150,000. That is like trying to find one person in a crowd of 150,000 people, which is about twice the size of Murrayfield stadium.

Q. So you have a big needle in a haystack problem.

A. That puts it very well, yes. So when one starts to try to find that needle, you get chunks of haystack as well.

Q. Right. Is it more complicated than Factor IX?

A. What do you mean by more complicated?

Q. Right. Is Factor IX a needle in a haystack or is the haystack smaller?

A. The haystack is smaller with Factor IX, so it is not so difficult, and Factor IX has properties that make it easier to find the needle, if I can put it that way.

Q. Just leaving that page, page 10, and moving on to page 11, if we could, please, you give us a bit of history here too:

"In 1959, it was discovered that a residue which remained in the bottle following transfusion of thawed plasma contained antihaemophilic factor, Factor VIII, activity."

That's Dr Judith Pool, whose name we have heard before:

"Factor VIII activity was able to correct haemostatic defect in Haemophilia A."

There is perhaps some potential for confusion, Dr Foster, in the references that we have had so far to freezing and thawing. In other words the haemophilia clinicians, when they have spoken about treating patients with cryoprecipitate, have spoken about thawing bags of cryoprecipitate in water baths at 37 degrees before you get something that you can inject into a patient, but obviously there are two freezing steps involved here, and to get the cryo in the first place, you start with frozen plasma. Is that correct?

A. That's correct, and what you are describing is the procedure that we used in the blood bank to prepare cryoprecipitate from a single donation, and that would begin with frozen plasma. The plasma would be thawed. During the thawing process the cryoprecipitate would form in the bag and then the cryoprecipitate would be extracted and then frozen down again.

Q. Yes.

THE CHAIRMAN: Sometimes, Dr Foster, it might help us to have a sort of physical picture painted. It might help our understanding of it. For example, you talk about fractionation quite a lot but people generally may think of fractionation in terms of the oil industry and of

very large columns that we see all over the place, or they might not know what it is at all. Similarly with the isolation of cryoprecipitate, it's sometimes helpful to have a picture of the actual physical process. It might communicate things.

A. Okay. In the blood bag that you are talking about, simply, when the block of plasma in the bag is thawing over a period of time, during that procedure there is a kind of sticky residue that forms that doesn't dissolve. It will dissolve if it gets warm enough but if you keep it cold it won't dissolve, and that residue can be harvested, if you like; it can be taken out and separated from the rest of the plasma. And that is what Judith Pool discovered, that she had this sticky stuff at the bottom of tube and she found it contained Factor VIII activity.

MS DUNLOP: If that's going to go to treat patients as cryoprecipitate, then you want the sticky stuff, you package it separately and then it's refrozen until it's needed for treatment. Is that right?

A. That's correct. I have to admit I have not worked in a blood bank, so I have never actually handled cryoprecipitate in that way that we are talking about. If you wanted somebody more expert it would be somebody like Dr Prowse or Professor Cash.

Q. I think that will do for now, Dr Foster. Just to say that when Dr Foster comes back as a witness in topic B3, we intend to do a more elaborate investigation of the different scientific processes. By that point we will want to take in viral inactivation as well.

THE CHAIRMAN: Yes. I don't want to get out of line but it's just this picture of Judith Pool's big step forward really; and there was a bit of background to that, wasn't there? She was trying to do some work for another laboratory and wondered where the Factor VIII was?

A. I can't say that I fully know the history of this but as far as I understand, it was kind of an accidental disclosure, that there was this gungy stuff left behind and she took a look at it and found that it contained Factor VIII activity.

THE CHAIRMAN: Because the Cohn process had been different before that.

A. Yes, that was quite different and Edwin Cohn had been given the task of developing a substitute for plasma and he had identified albumin from plasma as a possible option for this, and he set about working out a means of recovering the albumin from the plasma, and to do that he had to remove the other plasma proteins and he used various techniques, basically based on solubility

differences between the different proteins, to remove, say, the proteins that were the at least soluble and the proteins that didn't have an intermediate solubility, and he was left with albumin, which is one of the more soluble proteins, and he called those different groups of protein fractions.

THE CHAIRMAN: That's something that I think we do all have to understand, that it was a progressive removal of proteins with different characteristics, ending up with Fraction V, which was albumin.

A. That's correct. And Cohn examined the different fractions and he looked at them to see if they would be effective with haemophilic plasma tissue, if they could correct that defect, and he found that Fraction I would correct that defect and that became the basis of the very first Factor VIII concentrates that were the Cohn Fraction I.

THE CHAIRMAN: And Fraction I is what drew out these relatively large molecules of fibrinogen and fibronectin at the same time.

A. It's basically a heavy version of cryoprecipitate.

THE CHAIRMAN: Then Judith Pool comes along and accidentally, or otherwise, realises that she might get to the end product of the cryoprecipitate rather more quickly.

A. It was a simpler procedure than Cohn Fraction I and the cryoprecipitate was a slightly better material.

THE CHAIRMAN: It had a better Factor VIII content, relatively?

A. It probably had a better Factor VIII content and it was less difficult to work with. It was slightly more purified.

THE CHAIRMAN: I know there is a great history which I thoroughly enjoy reading, but perhaps that sort of picture that you have painted helps us to get the context right.

MS DUNLOP: I wanted to pick up the thread with the gungy stuff or the gloopy stuff, whatever you want to call it, that is the cryoprecipitate, and we are now looking at the paragraph beginning:

"Intermediate purity concentrates ..."

That that's not the end of the story, that you are going to go on and make concentrates. You are going to work with cryoprecipitate to do that, as I understand it. Is that right?

A. That's correct. Cryoprecipitate could also be obtained at what I'll call the industrial scale, where you are dealing with large quantities of frozen plasma and when you melt that plasma, the same material that you would get in the single blood bag would form in all of that

plasma, and it can be collected because it has a heavy mass. You can separate it in a machine called a centrifuge, which is like a spin dryer, and the solids settle in the spin dryer, and it's essentially the same type of material as Judith Pool had discovered but it could be the basis for beginning a further purification.

Q. What I had trouble picturing when I read this paragraph was the large-scale freezing. I think we can all imagine lots of donations of plasma mixed altogether in a pool but how did you --

A. The freezing is the same. The individual donations of plasma are frozen and then they have to have the plastic pack removed and then they have to go through a melting process, either by putting all the lumps into a big tank, and it's at that point that the cryoprecipitate forms.

Q. Right. And then with the cryoprecipitate, which you have obtained on an industrial scale, as I understand it, that is redissolved. Is that correct? Perhaps you should explain to us, rather than my trying to paraphrase it, but in simple terms, the next step to get to Factor VIII concentrate?

A. First of all you would collect the cryoprecipitate in the centrifuge and then when you had completed thawing all the plasma and you had all the cryoprecipitate in

the centrifuge, which is refrigerated because it has to be kept cold -- if it gets too warm it would redissolve and if it is too cold it freezes, so it has to be a controlled refrigeration. Once that is completed, the centrifuge is brought to a halt and the cryoprecipitate is removed, put into a vessel and various chemicals are added to redissolve the cryoprecipitate, and we called that a partial extraction because not everything dissolves; there would be some proteins that you would want to leave behind.

So a slight purification takes place at that point. Once that extraction has taken place, there are various other adjustments: you adjust the pH, you add in a chemical, which is a reagent to which some of the other coagulation factors that are still present stick, and can be removed.

Following that, there is another centrifugation step to clarify the material and some further adjustment, by adding chemicals, to stabilise the Factor VIII, and it's basically at that point that you get to what we call an intermediate purity Factor VIII.

Q. The last bit of this I want to ask you about is another freezing step, and it's the freeze-drying. That's presumably very near the end of the process?

A. Yes, once all of this chemical processing that I have

described is completed, the solution is filtered through a very fine filter to remove any bacterial contaminants, and it is dispensed aseptically in a sterile area into vials, then it would be loaded into a freeze dryer. Then within the freeze dryer, the material would be frozen, because the freeze dryer has a number of shelves which carry refrigerant, so you could freeze inside the freeze dryer and then carry out the freeze-drying process thereafter, which is the process for removing the water by a process of sublimation, where you miss out the liquid phase; you go straight from the solid to the gaseous phase by doing this under a vacuum.

And then at the end of the freeze-drying process the bottles or the vials would be sealed, still inside the freeze dryer because there would be stock rows that would be pushed home inside the freeze dryer to close everything inside the freeze dryer to maintain sterility inside the vial.

Q. One of the questions that I have seen, and I have to confess, on the Internet, but out there there are a number of different theories still around, and one of the questions is how a virus can survive after freeze-drying. But I suppose the answer to that is some do?

A. Well, freeze-drying is to preserve labile materials and

viruses might be labile materials. So you use freeze-dry to preserve viruses as well as proteins. Vaccines might be freeze-dried to preserve their activity.

Q. The other point I wanted to ask you, Dr Foster, just so we can understand, as his Lordship says, a little bit about the practicalities of it, trying to picture what happened, can we suppose a person gives a donation of blood, it would be, in Glasgow in 1980, that donation might have gone towards the treatment of people with haemophilia in one of two ways. It could have gone to the manufacture of cryoprecipitate or it could have ended up as Factor VIII concentrate. I just wondered if you could explain the practical steps that would have applied in relation to each. If you take the cryoprecipitate first. Suppose this is a donation somewhere in the centre of Glasgow?

A. If it was in the centre of Glasgow -- and I think the centre at that time probably was in St Vincent Street in Glasgow -- once the donation had been taken, the donation would be transported to Law Hospital, where the processing centre was, and the bag of blood would be centrifuged to sediment the cellular components, so you would have -- and I think Marc Turner has described this to you. At the bottom of the bag there would be the

cellular components that really would look red and above that there would be the straw-coloured liquid, which is plasma, and then the bag would be squeezed to squeeze out the plasma, which would go into another bag, and there were a number of bags interconnected to maintain sterility. Then the bag with the plasma in it would be taken away and frozen, still in Law Hospital. At some point it could either be taken to make cryoprecipitate in Law or it could be dispatched to PFC. And when bags came to PFC they would be boxed, I'm not sure how much there would be, 20 bags in a box, and we would get a lorry with a load of boxes that were all frozen. We had a refrigerated truck so that it would be kept frozen between Glasgow and Edinburgh and then it would be stored at PFC, frozen.

Q. So up until this point, the flowchart, as it were, it just has one stream and is it up to the people at Law to decide whether they are going to send the plasma to PFC or use it to make cryo?

A. Entirely.

Q. Right, okay. And suppose the former; suppose they are going to use it to make cryo?

A. That's not an area that I was involved in so I can't really go into --

Q. Okay, but they would do the whole process at Law?

A. They would do that themselves, yes.
Q. Then the plasma that they decide they are sending to Edinburgh comes through to Edinburgh. Still in 1980, it would have come through frozen?
A. That's correct.
Q. Does all Scottish plasma go in together?
A. Yes.
Q. Right.
A. There were periods when we actually separated Glasgow from Dundee or from Edinburgh; it goes back to the time when I was looking at investigating the quality of the plasma from different centres and we were trying to understand how to improve the Factor VIII contents of plasma, and we did, for a period, segregate the plasma from each centre but that was something we couldn't really do routinely. It was a special exercise.
Q. That would be the exception not the rule?
A. That's correct.
Q. On this page you have mentioned the commercial preparations, and from a table which you yourself include -- on page 46, but we don't need to go there, table 11 on page 46 -- it is pretty obvious that the first two commercial preparations licensed in the United Kingdom were a Hyland one, Hemofil, in February 1973, and a preparation from

Immuno-in March 1973. I just wanted to ask you, because I have asked several other witnesses, if you actually know why, given that Hyland seemed to have brought out a concentrate in America 1966, it was seven years before it was marketed in Britain?

A. I really have no answer for you other than to say that perhaps this was a learning process and it was a difficult manufacturing process and it took them that amount of time to learn how to do it to the extent that they could then distribute product around the world rather than just in the United States.

Q. I suppose what would have been particularly interesting would have been if there had been any attempt to introduce it in the United Kingdom which had failed, but you are not aware that that ever happened?

A. No, I have no knowledge of that.

Q. We have also seen reference, Dr Foster, in the Reverend Black's medical records to his being treated with four flasks of AHG in 1965. I don't know if you have seen that reference. I think that's maybe something which we could just note for the moment and go back to when we come to your more detailed history section. But in outline that's likely to have been an early Scottish product, is it?

A. I think that's most likely, yes.

Q. On the last paragraph on that page you record what I think now doesn't surprise any of us, that the problems from the commercial products really related to the size of the pools and to the nature of the donors. So the fact that the donors were paid for giving their plasma and that the pools were very large.

Can we move on to the next page, please? You narrate some developments in 1973, and we have actually already looked at these. We looked at the establishment of the expert group and at the minutes of its first meeting. Self-sufficiency. You describe government policy, and we have looked at Hansard for January and indeed February 1975. I don't think there is any material difference, indeed what Dr David Owen said seems to be word for word the same on two occasions, and then you also refer to policy statement in December 1980, by Sir George Young, and I want to come back to that.

"The department of health has confirmed that the British Government supported recommendations on national self-sufficiency from the World Health Organisation and from the Council of Europe."

Next page, please. We have the World Health Organisation, and again we have looked at this, at the beginning of this block. Its

recommendation, the resolution adopted in 1975.

Then you tell us about a WHO group of experts and they met in December 1975. You set out for us the final recommendations of the group. Again, we see emphasis on relying upon "voluntary unpaid donors", and then you mention also erythrocytes. Erythrocytes are the red cells?

A. That's correct.

Q. The reference to something called "component therapy" which I think we understand to mean, in crude terms, making good use of every single part?

A. Yes, that would be correct.

Q. Yes. Obviously using whole blood could be very wasteful because if the patient only really needs the red cells, then the other bits of the donation could go to treat somebody else?

A. That's right, yes.

Q. They could be used in a different way.

If we move on to the next page, please, I just wanted to ask you about the first bullet. On page 14; this is obviously a caution which is being expressed here:

"The long-term effects of repeated plasmapheresis ..."

And we understand what that is. That is about

taking blood from the donor and then having the plasma but returning the red cells to the donor, as I understand it. Is that right?

A. That's correct.

Q. And hyperimmunisation. I just wonder, how does the donor become hyperimmunised?

A. These are people who are deliberately given some injection to boost something like anti-D for example. That's my understanding of what that would mean.

Q. So you have obviously set out the relevant material from that report for us and then you have moved to a Council of Europe recommendation. I thought we should just look at that so that we have seen that. I don't think we have looked at that one before. It's [DHF0010507]. You have quoted, Dr Foster, the first of the recommendations, which we can see there on the first page, it seems to be 1A, that:

"The governments of member states are to establish minimal criteria."

Do you think "minimal" is a slight mistranslation? I suppose "minimal" tends to connote that there is as little as possible. Do you think it may be minimum?

A. That may be what was intended.

Q. "... criteria for the quality, packaging, labelling and control of blood products for the treatment of

haemophiliacs."

In terms of what's easily available, I couldn't find any legislation until the Blood Safety and Quality Regulations, but were there specifications in the United Kingdom relating to quality, packaging, et cetera, that were propounded by other bodies?

A. There is the British Pharmacopeia, that has a specification of Factor VIII and Factor IX concentrates, and I think there were also World Health Organisation guidelines that were published in 1978, although I can't remember offhand if they covered all of these details.

Q. But for Britain you would suspect that the mechanism would be the British Pharmacopeia?

A. At that time I think that's correct.

Q. Then 1(c):

"The WHO are recommending the governments of member states to inform all concerned in haemophilia therapy of the problems arising from the procurement and rational use of blood components concerned in order to balance the needs and resources ..."

I found that slightly delphic. Do you have a feel for what that's really saying?

A. I think it means try and make everyone work together to achieve this objective.

Q. Perhaps that it's not an unlimited supply and it's necessary to make the best use of what there is?
A. I think it was always recognised it was going to be a very difficult aspiration to achieve and therefore one would have to work closely right across the board, from the transfusion service to the haemophilia doctors, to make progress.
Q. Then in (ii) there is the reference, which you have quoted, to reaching, as far as possible, self-sufficiency of the member states, both in respect of anti-haemophilia products and blood plasma required for their preparation. So an international goal being expressed, I daresay not for the first time, but certainly being recorded in this 1980 resolution.

If we could go on to the second page, please. Dr Foster, we have seen from the 1970s quite a lot of material showing that haemophilia clinicians in Britain very much ranked concentrates higher in their scale of preference than cryoprecipitate for treatment, and that last bullet looks to reflect the same sort of point. Is that right?
A. That would seem to be the case, yes.
Q. Then further down on the second page, if we see a paragraph beginning "quality control", we can note that there is a reference to the need -- and you have

quoted this -- to reduce the risk of transmission of hepatitis.

THE CHAIRMAN: Could I just ask a question at this stage? The use of British Pharmacopeia as the way of disseminating definitions of Factor VIII/Factor IX, I rather understand that the Pharmacopeia is normally used for the benefit of pharmacies. Is that your understanding?

A. I'm not really sure about that. Certainly in terms of the blood products, the Pharmacopeia does lay out the specifications of what ought to be achieved. So it gives, for example, a purity and potency, and all of these characteristics are defined in the Pharmacopeia. So that for us would be the guideline that we would be working towards.

THE CHAIRMAN: You would quite happily resort to it for the specification?

A. We would, yes. Could I add that I think Mr Watt was on the Pharmacopeia committee at the time. So he was well aware of the discussions.

THE CHAIRMAN: Writing his own definition?

A. I wouldn't say that, no.

MS DUNLOP: Can we go back to Dr Foster's paper, please, and we are really on page 15. So that's [PEN0131125] at 1139. You have set out the other two Council of Europe

recommendations that we know are relevant in this area, R(81)14 and then R(83)8, which relates to AIDS. The third bullet from R(83)8 reads:

"To avoid importation of blood plasma and coagulation factor products from countries with risk populations ..."

I have to confess, Dr Foster, I did check and that is certainly, word for word, what it says, perhaps not the best translation in the world. But I suppose it just means populations where the risks are thought to be higher, something like that.

A. I think at this time there was concern that blood was being collected in countries with populations that might have a higher level of hepatitis in their population and that that wasn't a desirable thing to do.

Q. Or, at this time, AIDS?

A. That's correct.

Q. Yes. Can we go on to the next page, please? You have referred to a statement of policy that's really quite a bit further on in time. Perhaps we can look at a document that seems to record this, [SGH0050501]. You do mention this later on in the paper, so we will be looking at it a second time, but it is interesting to see what was being said by the Department of Health in October 1990. I think what you are quoting,

Dr Foster, is a different reference but it's the same formulation. Your reference is a letter to Mr Watters at the Haemophilia Society but we can see that the last sentence of this statement from the Department of Health says that:

"The principle of self-sufficiency, therefore, means that the supplies of domestically sourced blood products should be sufficient, both in range and quantity, to meet the needs of all patients whose clinicians prefer these to other available products."

So really quite a change from what seems to have been the understanding of self-sufficiency in the 1970s, and probably 1980s.

A. Yes, that was certainly different to the understanding that we had in SNBTS and I think it was something that Professor Cash was quite concerned about.

THE CHAIRMAN: There two aspects to it. There is the policy of community self-sufficiency. What do you understand that to refer to?

A. That refers to the European Community.

THE CHAIRMAN: So that, so long as there was enough of a blood product in the community as a whole, self-sufficiency was met, irrespective of whether individual states were --

A. You could interpret it that way, yes.

THE CHAIRMAN: That may be the interpretation of the first paragraph. The second is that self-sufficiency seems to depend on some sort of residual demand, after each individual clinician has decided whether or not he wants to use alternative products.

A. That's certainly how it reads, yes.

THE CHAIRMAN: How do you work within that sort of framework?

A. I think that's why Professor Cash was so concerned about this.

MS DUNLOP: Was it around about 1990 that was the first time you had ever heard it expressed in this sort of way?

A. Yes, it was. It was certainly the first time we had seen anything in writing along these lines. But this is really an aspect you should ask Professor Cash more about than myself.

Q. We shall, but you mention the timing of this later in your paper and it may be that it has some relationship to the government reporting that it had achieved self-sufficiency around about this time -- in the UK Government?

A. Yes, there was a survey carried out by Professor van Aken for the European Community shortly after this, in which he was dealing with what had been achieved in different countries, and he quoted this

definition of the UK and saying that the UK had declared that it had achieved self-sufficiency according to this definition.

Q. Yes. We will come back to that, I think, Dr Foster. Then you have dealt in your paper -- perhaps we could go back to that, please -- with VCJD. Then can we move to the next page, please, "Policy into practice". You say:

"Achieving national self-sufficiency using local plasma from volunteer, non-remunerated donors is not straightforward."

Easy to state, difficult to achieve, doctor?

A. I think the evidence on that is very clear, that if you look worldwide, I'm not really sure any country has really ever achieved that with Factor VIII concentrate.

Q. Then can we go on to the next page, please? You make at the top what I understand is perhaps an important difference, that national organisations have an additional hurdle that commercial companies don't face, namely that national organisations are trying to achieve use of only volunteer donations and produce all products in quantities sufficient to treat their whole population, which, obviously, commercial companies don't have to worry about. They, presumably, just make as much as they think they can sell?

A. There is a different framework completely, obviously,

from the two types of operation. But there is one other aspect that is really fundamentally important and that is the different way in which plasma is supplied, let's say, in Scotland in the volunteer system, compared to the United States, and I think that was discussed earlier in this paper, which is really the volumes that can be obtained by plasmapheresis from a commercial donor in the United States, where the donor could give 600 millimetres twice a week, which is 1.2 litres a week, every week, compared to the Scottish situation, where we had a whole blood donor, who at best would give twice a year and you would get half a litre from that donor.

So there is a difference in terms of productivity of the donor, if I can put it that way. The commercial donor is 100 times more productive than the Scottish Dover. By that I mean the commercial donor in the United States because no other country in the world takes plasma in that volume from its citizens, and that was unique in the United States then and it remains so today.

Q. And you have dealt with that also later in your paper. You have set out these specific limits. You make a point too in the last sentence of this paragraph that they, that is national organisations:

"Lacked a team of sales and marketing representatives to promote their products and offer clinicians support for research and attendance at meetings."

Even simple things, Dr Foster, packaging has been mentioned; I think there was a reference to some of the commercial manufacturers producing a little box which had in it everything the patient might need. Presumably that sort of thing is easier for a commercial company?

A. Well, commercial companies were competing in a marketplace and they were doing their best to provide attractive products. So I think it's understandable they would be doing a lot of work into packaging as well as the product.

For us in the health service, we would just have to be quite clear about it. We didn't have budgets that would cover that kind of thing and we were hoping or expecting that haemophilia centres would provide appropriate bits and pieces that were required for the treatment of the patient over and above what we provided. If someone had come to us and said, "Look, we really need this, can you give it to us," we would have addressed that but I'm not aware that that happened.

Q. You mention, obviously, in this sentence support for research and attendance at meetings. That's financial

support, so paying for doctors to travel to conferences abroad and that sort of thing. That's what you mean?

A. I think that's generally what happened, yes.

Q. What effect does that have in your estimation?

A. I don't really want to comment on that.

Q. Then I wanted to note from the next paragraph "forecasting product demand". You say that what was not readily predicted was how the availability of concentrates would change practice and drive up demand. And I think we understand that it was a situation in which success bred success really?

A. I think that's a very good way to put it, yes.

Q. And then on to the next page, "Supply of plasma". I didn't want to ask you anything specific about this page, Dr Foster, but you are making points to do with, firstly it's only really the freshest plasma, fresh-frozen plasma, that was suitable for the manufacture of concentrates. So quite an important time factor that comes in really from the start?

A. Yes, that's correct. There was a time when the transfusion service would send blood out to hospitals and if it wasn't used it would come back, and you could recover the plasma but you couldn't make Factor VIII from it because it was too old. You could recover albumin but not Factor VIII. So to get Factor VIII you

have to process the plasma much more quickly.

Q. Then you make the point you have just explained at the bottom of that page:

"The volume of plasma that could be obtained by a plasmapheresis from a donor restricted to 12 litres per annum."

In practice, I think, from what you said a moment ago, it would be unlikely to achieve 12 litres per annum?

A. This was in the UK. If we were to use plasmapheresis, those would have been the guide allowance that would have been followed in the UK. In practice, prior to 1990, we didn't collect fresh plasma by plasma pheresis; we just used the whole blood donor.

Q. So you are just at the two donations a year, which is 1 litre per year?

A. Half a litre.

Q. I thought it was half a litre each?

A. Quarter of a litre each donation.

Q. Half a litre in total?

A. From one donor in a year.

Q. Then you say that in the United States of America, it was possible to collect up to 60 litres per annum per donor.

On to the next page. Look at the section on

manufacturing capability. Many different products from a complex starting material, needing dedicated facilities, specialist facilities, temperature control, use of specialist equipment, reagents, other materials. A research and development capability too, and that's the area in which you have worked prominently.

A. That's correct.

Q. You refer in the last paragraph to what was done in some countries, for example, Norway, that they achieved self-sufficiency but not by doing it themselves. They collected the donations and sent them elsewhere to be processed?

A. That's right.

Q. But the difficulty with that would be that essentially you would be mixing plasma from your own country with the plasma from whatever country the facility --

A. That's correct, yes.

Q. I suppose one of the ideas, or one of the less desirable aspects of that is that you are opening up the possibility of viruses, which may be contained within a particular country or confined within particular borders, mingling on a much wider geographical scale?

A. Yes, there is that possibility, yes.

Q. Then "Management processes (Scotland)", if we move on to the next page, please. So here you are telling us how

matters in Scotland were organised and you say that:

"There were meetings between officials of the SHHD haemophilia directors and SNBTS directors."

We have seen those. Obviously slightly sporadic, a bit of a gap between 1977 and 1981 and then between 1981 and 1983. Perhaps we could have a look at the 1977 meeting. I don't think we have looked at that. It's [SNB0015033].

You are not at that. I suppose the directors of SNBTS and the haemophilia directors with government involvement. We can see that it's around about the time when Major General Jeffrey had died, he having been the National Medical Director. If we just scroll down page 1, please, we can see what's on the agenda. Look in particular at page 2 and section 7 at the bottom, please.

Mr Watt. Presumably from the time you started there will have always been a hunger for supplies. This sounds as though Mr Watt has been pleased to receive some more from the West of Scotland but Dr Wallace is saying that that has really only been possible because he has purchased a substantial amount of commercial concentrate to help overcome the initial transitional phase.

So a certain paradox, I suppose, Dr Foster, in that

PFC is wanting more plasma to assist in achieving the goal of self-sufficiency, and that's the production of more plasma or the sending of more plasma from west to east, has been achieved because in the west, some commercial product has been purchased. But I suppose that may have been seen as a transitional arrangement, something that might not be a permanent policy?

A. This situation is really just after the start-up of PFC, which we began in 1975 and we were commissioning the plant, and PFC, it may not be appreciated, was actually designed to provide albumin and when it was built, Factor VIII wasn't really on the agenda because the big MRC working party hadn't decided what was required.

The real drive to begin with was to provide albumin, and because there was a shortage of albumin in Scotland, Glasgow BTS were providing freeze-dried plasma in quite large quantities, and it wasn't until we could provide them with albumin that they could stop providing freeze-dried plasma and that plasma then became available to recover Factor VIII as fresh-frozen plasma.

So there was this knock-on effect, that we first had to provide the albumin then they could stop making the freeze-dried plasma and then we could get more plasma to make Factor VIII. That's why this, what might appear to be a prolonged start-up phase of PFC, took place and of

course this was at the time when in Glasgow Royal Infirmary there was a keenness to start patients on home therapy and this correspondence that shows that they want to start home therapy, so they go and buy commercial, so they can do that.

THE CHAIRMAN: I have a problem trying to sort out in my own mind where the blockages might have been round about this time, Dr Foster. I see from what you have said that there is a tension between getting PFC into full commissioning and operation and the effect on the supply of plasma. I am also of the impression that there was a preference for particular approaches to therapy in the West of Scotland that might be different from the objectives of PFC, and that cryoprecipitate in particular was a favoured therapeutic material. Do you remember that as a factor?

A. I have noticed that coming out in some comments, that there seems to be a view that Glasgow were keen on preparing cryoprecipitate and they did have a programme, after this actually, for trying to develop a freeze-dried cryoprecipitate. But the clinicians weren't really that interested in cryoprecipitate, they wanted concentrate. So I think there was a period here where people were trying to understand what was required because the demand and the use was actually going into

territories that nobody had predicted.

THE CHAIRMAN: Yes. It may be one of these things it's very difficult to disentangle retrospectively from the odd recorded comment but I would like to try to get the atmosphere if I could.

A. I think, unless the participants can be brought back from the grave, then I think it's impossible.

THE CHAIRMAN: My powers are extensive but they don't cover that particular method of getting information. Yes.

MS DUNLOP: Can we just go on to the following page, please:

"Dr George McDonald of Glasgow Royal Infirmary complimented Mr Watt and his staff on their achievements over the past 12 months."

The word "optimistic" is actually used in paragraph 7, Dr Foster. Would it be right for us to think of this as a time when people were optimistic about what could be achieved?

A. PFC had only just opened and it was opened with some kind of an expectation that this was going to solve everyone's problems, and of course that didn't happen because the targets that had been set turned out to be not what happened. The demand went up and up and up and up and really we were just chasing this ever-increasing demand as hard as we could and Dr Cash was banging the drum to get more and more plasma, and we were doing

everything we could to produce more and more, but of course the aspirations of the doctors and the patients, which one can understand, is that this was so successful that they were running ahead of us all the time.

Q. Yes. We can see this particularly Dr Foster, I think, when we come to look at some of tables, it certainly has the feel of a race in which you are trying to catch the person in front of you and it's very difficult even to draw alongside because they are always pulling ahead.

A. That's exactly right, yes. They were kind of always disappearing over the horizon.

Q. Yes. Can we go back to the paper, please? We have already looked at the minutes of the joint meeting in January 1981 and just to note that, as you say, at that meeting the Council of Europe recommendation was discussed. So even if it might be difficult -- and we haven't really gone into this in any detail, it might be difficult to find express statements of the policy of self-sufficiency for Scotland by politicians or by government; there doesn't seem to be any doubt that everybody knew that that was the aim in Scotland?

A. Certainly I would say that 1981 meeting there seemed to be quite a consensus and complete agreement that that was the objective we were all working towards.

Q. Right. From national management processes you go on to

discuss SNBTS management processes, and you explain that there was a blood transfusion subcommittee of the Common Services Agency and then that the directors met themselves with SHHD in attendance, and you explain about the organisation of the chairing of the meetings of the directors. Can we go on to the following page, please?

Just to note that you also have a section on management at PFC and we have noticed -- and it's discussed in the preliminary report -- that there was a Factor VIII study group created -- and I think that's 1982 -- and that that itself had various subgroups.

A. That's correct. That was John Cash's initiative and it began in January 1982.

Q. Yes. Section 3 is Factor VIII demand and you have looked first at forecasts of demand.

THE CHAIRMAN: Ms Dunlop, are we having a break this morning?

MS DUNLOP: Yes.

THE CHAIRMAN: I know that timing has got out of line a little but I'm still anxious that we should break the morning up in a way that suits the stenographer best and if you are going on to another major new topic, it might be better. I'll take your guidance on it.

MS DUNLOP: I'll try and stop at a natural break, sir.

Factor VIII demand. You refer to the forecasts of 1973. Then reading on to the next page, the MRC working party:

"An assessment of the total amount of Factor VIII likely to be required for all types of treatment puts the total in excess of 500,000 blood donations for about 40 million units of Factor VIII."

Dr Foster, I worked out, so it might be wrong, but I worked out that this arithmetic suggests that you would be expecting about 80 units per donation. This is the 40 million units from 500,000 blood donations. That would be 80 million units from 1 million donations, which would work out at 80 units per donation. That's the assumptions they are making.

A. There is an assumption here about what's in cryoprecipitate. And one of the difficulties with cryoprecipitate is that you couldn't actually assay it, you couldn't measure the Factor VIII content every time. You could only go on some samples that might be taken. I think it may be -- and I'm not sure it is clear in any of these documents -- that that was the assumption, that that was the yield in cryoprecipitate at that time from one bag of cryoprecipitate. I have to say, I think cryoprecipitate was quite variable in its content. So they might have assumed the local level just for safety

purposes in terms of making sure that the patient got an adequate treatment.

Q. Thank you.

We can see at least steadily rising targets. Sometimes targets are expressed as absolute numbers of donations, sometimes as numbers of international units per head of population. Would it be correct to think of the end point of this -- and this is the race with the runner disappearing over the horizon again, but the end point, I suppose, was going to be when all those with severe haemophilia in the United Kingdom were on prophylactic treatment and there was also enough to supply the additional requirements for people with moderate and mild haemophilia and for acute incidents requiring specific treatment as well?

A. I'm not really sure that that had been thought through at this point in time because people were still learning what they could do with this stuff and thinking, "What more can we do with it?" I'm not really sure that even at this time these working parties really fully understood how far it was going to go.

Q. But I suppose if they had had a crystal ball they would have been able to say to themselves, "This is, in the end, what we are going to be required to satisfy"?

A. If they had had a crystal ball, yes.

Q. I noticed in Professor Hann's statement that he urges the Inquiry to bear in mind, when considering self-sufficiency as a topic, that prophylactic treatment in a child with severe haemophilia would take 6,000 units per kilogramme of body weight per year. So just working that through, and thinking about 1980 -- if we could move down the page and look at forecasts of demand for Scotland.

Just to give ourselves an idea of how the figures panned out, if you imagine that the 55 Haemophilia A patients who were registered at Yorkhill in 1980, suppose 25 of them had severe haemophilia, then that would be 25 at whatever would be a reasonable weight to take, and I'm unashamedly going to give evidence here and say that a reasonable weight for an average 9 or 10-year old child, so a mid-aged child, might be 30 kilogrammes. So you would be talking about 25 children at an average of 30 kilogrammes all needing 6,000 units per year and that actually works out at 4.5 million units. So that would be just that very small group of patients with haemophilia in Scotland. So I think that just gives us some sort of idea of how far ahead the runner was perhaps going to pull.

A. Yes. It also indicates how far ahead that type of treatment was compared to the thinking that was taking

place at this time. The people actually hadn't -- the thinking hadn't gone that far. I suspect that what was happening is that they were tending to look at what had been used in the past and then extrapolating from that without trying to calculate -- or looking into the future and saying, "What do we think would be required in the future?" And I think the first person who sat down and did that was probably John Cash.

Q. Right. So indeed, having done that calculation, and worked out that you would need 4.5 million units just to meet that portion of the need at Yorkhill, it's then interesting to juxtapose it with the estimate that equated to a total of 4 million units of Factor VIII per annum for Scotland, which is from the mid 1970s.

But we can see that the target did increase and you have taken us through that. Moving to a different measuring system, moving from a target of 1.8 units per head of population per annum, 1981, 2.75 units per head of population per annum, 3.75 units per head of population by 1996. If we look at the table, which is on the next page, table 1, you have given us the amount of Factor VIII used each calendar year in the United Kingdom since 1970, and we can see the figures. Over that 35-year period, 1970 to 2005, if we just look at the column on the furthest right, which is

international units per head of population, it has gone from 0.15 in 1970 to 4.73 in 2005. So very roughly, in a 35-year period it has increased about 35-fold; a big increase.

A. You could say that, yes.

Q. Yes. So the runner behind wouldn't just feel that he was trying to catch someone in front, he would feel he was running uphill at the same time?

A. Running uphill and trying to sprint faster as well.

Q. Yes. We move to the next page where you note a number of points from this table. Those of us with hard copies can unpick them and put them side by side, if that's easier.

You say that:

"An almost continual year on year increase in the treatment with Factor VIII ... reduction in the use of cryo ... marked use of imported commercial concentrates from 1974 ... year by year increase in the use of commercial concentrates from 1974 to 1982."

Of course this is a UK table:

"A decline in the use of commercial concentrates, 1983 and 1984 ..."

Substantial reduction in the supply of NHS Factor VIII in 1985 to do with heat treatment. Then back to an increase in the use of commercial

concentrates in 1985 and so on.

You say:

"A reduction in the use of cryoprecipitate was consistent with guidance in the 1970s from expert advisory committees and UK haemophilia directors, whilst importation of commercial Factor VIII concentrates was recommended by haemophilia directors and by the UK Haemophilia Society."

Then, an amount of Factor VIII used in Scotland. You say:

"The UKHCDO does not normally provide a breakdown of the treatment of people with haemophilia in different parts of the UK."

But you have some data for the period 1978 to 1984 and we can see that on the next page, table 2. Again, an almost year on year increase, reduction in the use of cryoprecipitate, some use of commercial concentrates. We can always look back and see how these figures compare with the United Kingdom. You have gone on to do that. You said:

"A direct comparison between Scotland and the rest of the UK can be made for that period."

That's table 3. Go on to the next page. There didn't seem to me to be anything particularly worthy of note in the comparison, Dr Foster, save perhaps that in

1980 and 1983, the totals for Scotland are more than they are for the rest of the UK, and for the other years it is really the other way round but not huge differences. This is looking at at least the first two columns of numbers. I think that would be all that one would take from that perhaps.

A. Yes. I think you will see this later on in table 16, where there was a doubling of use of Factor VIII in one year in Scotland.

Q. Yes. 1980, in fact.

A. That's right.

Q. But what is remarkable in this table are column 3 and column 4. They really speak for themselves. I think, as usual, Dr Foster, you have said what I'm trying to say in your text --

A. I could point out the footnote to the table. That includes cryoprecipitate.

Q. Yes, indeed. But you have said that the total amounts are not that different but the difference in the origin of Factor VIII was more substantial, with 88 per cent. You have just averaged the seven years that you have tabulated, have you?

A. Yes.

Q. That:

"The 88 per cent used in Scotland being obtained

from the NHS compared with 44 per cent in the rest of the UK. With 12 per cent and 56 per cent being imported from commercial sources respectively."

That seems to be a good point at which to break, sir, if that's suitable.

THE CHAIRMAN: Yes.

(11.18 am)

(Short break)

(11.45 am)

THE CHAIRMAN: Can I ask just a little about plasmapheresis?

MS DUNLOP: Oh, right.

A. There is a big section in the paper on plasmapheresis, sir.

THE CHAIRMAN: On the history of it? If we are coming back to it? If we are, I won't bother.

MS DUNLOP: A little further on, there is a section on plasmapheresis. Section 4.2.1.

THE CHAIRMAN: I'll ask my few questions when I get to there. I think they fit in quite well. I have some references to 1981 and the study of plasmapheresis in Belgium, for example. Did you take part in that?

A. No, I didn't take part in that.

THE CHAIRMAN: We will come back to it in due course.

MS DUNLOP: Dr Foster, I think just before we stopped we were looking at forecasting on page 27. So back to your

paper. [PEN0131125] at 1151, section 3.6, "Accuracy of forecasts".

You have tabulated for us the particular forecasts made and essentially how long they lasted. So the DHSS expert group who made a forecast in 1973, their forecast was exceeded in 1977. Likewise, the MRC working party, the DHSS working group who made a prediction in 1977, theirs was exceeded in 1982 and so on.

Look on the next page, 1981, the haemophilia directors, their forecast wasn't exceeded until 1990. Then the one of 2.6 million international units per million members of the population was exceeded in 1996. Then the ones for Scotland, certainly the one made in 1981 by Professor Cash seems to have lasted for a reasonably long time, 1981 to 1997.

Your commentary on these is at 3.6.2. You say:

"The first set of estimates, either for the UK or for Scotland, failed to anticipate long-term growth in usage."

One of the problems was that the collection of data necessarily, I suppose, retrospective, and only usually available some ten months later:

"At a time of strong growth in usage, reliance on these data could be misleading. This is illustrated by an editorial in the BMJ."

We do have that. That's [PEN0160239].

At the beginning there is a contrast drawn between cryoprecipitate and freeze-dried Factor VIII. The advantages of the latter being highlighted. Haemophilia centre directors generally agree that most if not all of the material used to treat haemophilia in Britain should be freeze-dried concentrate, preferably made within the NHS. Nothing we haven't heard before, Dr Foster. Then on to the next page, the amount still falls far short of the needs of haemophiliacs. The writer of this is making the point that:

"Commercial concentrates are costing about 10 pence per unit of Factor VIII activity. This is money that many experts think would be better spent in promoting the manufacture of Factor VIII and other important plasma fractions within the NHS."

But I think the particular reference you make to this editorial, Dr Foster, is further down this page, where the writer is wondering why self-sufficiency hasn't been achieved. We can see that:

"Why is this? It is not lack of skill, it is not lack of fractionation facilities."

It is really that phrase that you have highlighted for us:

"... though, to meet the target of 40 million units

of freeze-dried Factor VIII per annum ..."

I think the point you were making was that the writer of this is talking about the problem of not producing enough but actually they are talking in terms of a target which is itself inadequate.

A. The point I'm making is that when this was written, the actual use was 45 million units, so the author was already out of date.

Q. Yes. Do you agree with the author's explanation? Even with adequate financial support it is difficult to switch from relatively small scale to very large-scale production in under five years?

A. I think there were different difficulties in different parts of the UK. Certainly in Scotland, the greatest difficulty was obtaining plasma, whereas in England the greater difficulty became having facilities for fractionation as well as plasma.

Q. So both north and south of the border, as we always say, having enough plasma was a constant problem and then the lack of facilities in England was an additional difficulty.

A. That's correct.

Q. Yes. Can we go back to the paper then, please, at page 28?

You make the point that to calculate the amount of

plasma required, it was necessary to know the yield of product. I think we can understand that, that essentially this is a process of working backwards. If you know the number of units that you want to achieve to treat patients, and you know what the starting material is, obviously you have to have an assumption for what proportion of the material you want, you can derive from the starting material. I think you go on to tell us that the estimates that were used for yield, or the assumptions that were used for yield, were a bit over-optimistic. Is that right?

A. That seems to be the case, yes.

Q. You instance the MRC working party, their assumption of a yield of 37 per cent, Colonel Jeffrey assuming a yield of 40 per cent, and you go on to say that:

"The actual yield was much less than had been assumed. So estimates of the amount of plasma to be collected and the processing capacity needed were both about half of what was required."

And that was before the growth had been taken into account?

A. Yes, and of course, this was at a time when manufacturing intermediate purity Factor VIII in the UK was really a new activity and people didn't really have the experience to know what the yield was going to be.

Q. Can we go on to the next page, please? Two main reasons for the overestimation of yield. One was an under-appreciation of how much would be lost in the simple scaling-up of the work. You say it was a greater loss during the additional time needed to process larger volumes?

A. Yes, I think everyone understands that Factor VIII was a sensitive material and therefore the longer you took to carry out the process, the less you would have at the end, regardless of other difficulties that you come across at increased scale of manufacture.

Q. Yes. Then the second reason was a change to the method, the assay used in the UK by which the activity of Factor VIII was measured. I think it would help, Dr Foster, if you explain this reason to us a little more fully because I certainly didn't find it particularly easy to grasp: why a change in measurement made a difference.

A. Yes, we are talking about the assays that were used to measure the Factor VIII activity. I think you have heard that there were basically two types of assay. One was called a one-stage, the other one was called a two-stage. You don't need to know the details of that, except to know that there was a great deal of variation. These are not very precise measurements and at this

time, even in the best laboratories, there was an error of about 40 per cent in the assays and there were differences between laboratories. At NIBSC they were very keen to try to have some standardisation so that there would be more uniform measurements; and this would be in haematology laboratories as well as in fractionation centres.

So there was this workshop of all the people brought together in the UK by NIBSC, where each group carried out the assay using their own procedure and comparisons were made, and they gradually worked out where the differences were occurring and tried to come up with a more standard procedure. In doing that they changed some of the reagents that were being used and also, what is called a standard, which is the reference material that you use to calibrate the assay. That was changed. Putting all these changes together, the outcome for us and for BPL was that we apparently had a reduction in the value of Factor VIII that we measured, which was seen as a reduction in yield.

Q. That was true even though there might not have been an absolute reduction in yield. The same sample measured before and after the change of methodology might in fact have the same proportion in it --

A. That's exactly right. We would have exactly the same

material measured both ways and you would have one value that was, say, 100 and one value that was 120 and therefore the value that was 100 would be taken, not the value that was 120, whereas in the past it would have been the 120 that you would have taken.

Q. Right.

A. So this is actually a more conservative assay than the previous assay.

Q. Yes. You go on to tell us what the net effect of all of this was. This is the paragraph we can see on the screen:

"Instead of a yield of 40 per cent assumed by Colonel Jeffrey in 1976, the overall routine yield by 1976/1977 was only 20 per cent. This in turn fell to 15 per cent when the full impact of the change in assay procedure was experienced. This resulted in the amount of plasma needed to meet the targeted output of Factor VIII being increased 2.6 fold."

A. There is one thing that I haven't explained in this paragraph. I do mention samples for quality control but it might help you to appreciate the quantitative impact of that. Because at this point in time we were manufacturing a batch of Factor VIII that would contain about 150 vials of Factor VIII, and to carry out the quality control sampling that was required we would have

to remove about 25 vials from that batch. So you are actually consigning, for quality control, quite a significant proportion of the batch.

Q. Yes.

A. And the only way to reduce that impact, because this number of samples is fixed, was to increase the batch size, which is something that we went on to do.

Q. But you say that this resulted in the amount of plasma being increased 2.6 fold. That's just because, to get from 15 up to 40, you need to multiply by two and two-thirds.

A. That's right.

Q. That's the process?

A. Yes.

Q. Yes. For Scotland, the demand predicted in 1975 was exceeded in 1980, and you go on to give us some more detail on estimates and when they were exceeded. Read on to the next page. This is both UKHCDO estimates and SNBTS estimates that were more accurate:

"They predicted continued growth in usage over a long period of time, however, in both cases the actual rate of growth was much slower than predicted."

So the rate of growth in fact was slower?

A. I'm going back to the table earlier where there was John Cash's estimate, where he said we would expect to

have 2.75 million units by 1986. In fact that was a bit of an overestimate because the actual amount reached that point some years later.

Q. Yes. Actually that was table 4, that his prediction was 2.7 by 1986 and that wasn't in fact exceeded until 1997?

A. Yes, that's what I'm getting at here.

Q. Section 4 "provision of plasma". You alluded to this earlier. There might have been three different types of plasma but only one of them, fresh-frozen plasma, could be used to prepare Factor VIII concentrate. And no doubt Factor IX as well?

A. That's correct.

Q. Because you were working with the same stuff. So you go on to tell us that given that restriction, there were a number of strategies used to obtain fresh-frozen plasma, the first of which was to increase the number of donations. We can understand that. I don't know if you call it advertising. It sounds funny to call it advertising when you are trying to encourage people to give blood but I suppose it's of that sort?

A. We would call it advertising, yes.

Q. You would call it advertising?

A. Yes. You see it on the television, "Give blood".

Q. Promotion, perhaps. I don't know.

Then on to the following page, "Component therapy".

So making use of the different elements as far as possible. Splitting the blood up. I think we can understand that too. You say you began to provide red cells for transfusion in 1960. And you are right, we have heard evidence from both Professor Turner and Dr Norfolk about the most economic ways of using a donation of blood, particularly this emphasis on only using red cells.

It says:

"Eventually SNBTS actually ceased to supply whole blood routinely."

So that became the default, that people were just given red cells?

A. That's my understanding. I think it is important to appreciate the effort that was required to achieve this, because you were trying to educate doctors in every hospital in Scotland virtually to change their clinical practice, and I don't think that was at all easy.

Q. No. I'm sure. Then on to the next page, you go into this topic of producing enough albumin. So when enough albumin was being produced at PFC, it was possible to stop freeze-drying plasma in the West and send the plasma to PFC instead?

A. That's correct, and just to finish the equation: what was happening at this time was while PFC was being

constructed, outdated plasma was being stored, frozen, so that there was a stockpile of plasma. So once PFC was functioning, we could process the stockpile of outdated plasma to albumin and that would then release plasma that was fresh-frozen that had otherwise been used to make freeze-dried plasma in Glasgow.

Q. Right. So really another example of the most economical use of the different bits?

A. Yes.

Q. Yes. Just at the end of that section you have talked about the use of a freeze-drying plant at Glasgow for the preparation of freeze-dried cryoprecipitate, but that that plant was closed. Just to look at a couple of references we have to this part of the story, SNB0015064. I think there is a reference to the second page. This is a meeting of the Haemophilia and Blood Transfusion Working Group on 4 March 1981. It says:

"The production of freeze-dried cryoprecipitate."

We have looked at this before as well. So it does look as though, at least in March 1981, it was thought that this might have some future as product. If we look at [SNB0015160], at the third page, please, which is SNB0015162. Right at the bottom of the page, please, there is a reference to freeze-dried cryoprecipitate:

"There has been a successful clinical trial in the

west. Notwithstanding this work, it had been decided to abandon production of freeze-dried cryoprecipitate in the meantime, having regard to the closure of the plasma freeze-drying plant at Law and the cost of meeting the standards demanded by the medicines inspectorate."

I suppose it is essentially the other way round, that the cost of meeting the standards demanded by the Medicines Inspectorate had contributed to the closure?

A. I would say that was the overwhelming point. It is not just the cost; it was actually more than that. It was actually working out if it was possible to meet those demands at all with this type of product. I was familiar with this because I was present when the medicines inspectors inspected the plant at Glasgow. So I understood what their concerns were. It wasn't just the plant, which was elderly, it was the notion of how can this particular type of product comply with what they regard as good manufacturing practice. Because it wasn't what we would call the aseptic product; it couldn't be filtered to remove bacteria. It couldn't be sampled easily with the number of samples I have mentioned already. 25 samples from a batch; you couldn't do that with cryoprecipitate. So it didn't comply with any of these aspects that were regarded as important to good manufacturing practice.

Q. So, notwithstanding that there may have been a successful clinical trial, there were all these problems earlier in the sequence which were almost impossible to overcome?

A. I think if doctors had come back and said, "This is a brilliant product, we must have it, it is absolutely essential," then I think the medicines inspectors might have reviewed their position but that didn't happen.

THE CHAIRMAN: I would like to be sure I do understand this. There are a number of different strands that come out of the documents. One is that it might have been useful for some particular clinical applications and there was discussion of that, but this seems simply to have disappeared into the background. The other is that I think the predominant feature that one sees in the documents is the cost of meeting the medicines inspectors' criticisms of the Law plant. But you were there and you say that there were many more fundamental issues really, the inability fully and properly to test the material. Why was that?

A. That is because when you have a batch of a pharmaceutical product, you have to carry out testing to ensure that it is uniform and a specified number of samples must be taken, and the size of the batch of freeze-dried cryo wasn't big enough to allow that sample

to be met.

THE CHAIRMAN: There were basically five donations that they were working on.

A. That's correct. There wasn't enough in the batch to meet all the sampling requirement, never mind treat the patient. So you are in between the pharmaceutical product and what was a blood component, and it was trying to find the balance. And because it was being manufactured and freeze-dried in a what was a manufacturing environment, the inspectors saw it more as a pharmaceutical product than a blood product that you would get at the blood bank. And that might have been a debate that could have carried on if there had been a huge demand for the product, but it didn't, it ended there, and of course, the financial cost of building a new freeze-drying plant was not small.

THE CHAIRMAN: So it really was a combination of factors and the debate really was brought to an end rather than fought out.

A. I would say so, yes.

THE CHAIRMAN: I think that's very interesting about the final stages in Law's history, at least on this topic.

MS DUNLOP: Yes. We are still about how to increase fresh-frozen plasma, Dr Foster. Can we go back to your paper at page 32, which is 1156. Thank you.

You had been working to a time limit of six hours, which you say is a significant constraint especially for donations collected in the evening or at locations far removed from the processing laboratories. You looked into whether plasma frozen within 18 hours of donation would be suitable, if there was any possibility of relaxing the time constraint but there was a yield penalty. You say:

"18-hour fresh-frozen plasma was introduced routinely in 1975 and enabled the supply of plasma to be increased by about 30 per cent."

We can understand the thinking there. Then:

"Optimal additive solution."

As I understand that, that was to reduce the amount of plasma that had to be retained in a packet of red cells, as it were?

A. That's correct.

Q. To make the red cells usable?

A. That's correct, yes.

Q. So you put something else in with the red cells and that increases the amount of plasma you can take out?

A. I think the motivation was originally to benefit the red cells but the knock-on effect was that you could recover more plasma.

Q. Onto the next page, we come to plasmapheresis. I should

ask you at the start, Dr Foster, why was plasmapheresis not used in the United Kingdom at this time? We seem to have been very slow --

A. I'm perhaps not the best person to ask because collecting plasma wasn't the area that I was working in.

Q. No.

A. But I think at first there was certainly a reliance on the normal blood donor. I think if you go back to General Jeffrey's paper from 1976, he notes the importance of plasmapheresis and this might be needed, but he points out that it is expensive and time-consuming, but he doesn't dismiss that as a possibility. He does identify it. And I think certainly by the late 1970s, early 1980s, that was being explored and we were doing studies in Scotland. Certainly at PFC we were studying plasma collected by plasmapheresis in my department to establish that it would be appropriate to manufacture Factor VIII from it, but the bottom line really is that it is an expensive technique and it requires funding and that funding wasn't made available until 1990.

THE CHAIRMAN: This is where I would like to fill in a little bit of the history.

I have a note of a meeting of the SNBTS directors on 17 March 1981, when Dr Urbaniak reported on the work of

the Jenkins working party, which was trying to put together a code of practice for plasmapheresis. Did you know about that?

A. I don't know about the details but I did know that Aberdeen did some work to collect plasma by plasmapheresis, which they sent to us to investigate to see if it was appropriate. Similarly, in Leeds in England they were doing something similar and they sent us the plasma to explore but I think it was after that that the funding wasn't available.

THE CHAIRMAN: The reference to that minute is [SNB0022623] or 26289. I don't think we need it, it is just to get its place. The next reference I have after that, I think, does take us into a wider sort of context, but I also have a note from March 1981 of the SNBTS directors talking about it and proposing to send a team to Belgium, which is what I mentioned earlier.

A. Yes.

THE CHAIRMAN: That is [SNF0010210]. A group of SNBTS staff were to go to Belgium, where there was an extensive programme of plasmapheresis at the time, but you don't remember that, or you weren't involved?

A. I wasn't involved in that. I wasn't a member of that committee but I have seen documents since and a team went and they did write a report. I think

Brian McClelland was probably the author of the report and I think that probably did lead Professor Cash to make bids for plasmapheresis which weren't funded.

THE CHAIRMAN: That's where it comes to an end really at that stage. The lack of funding put an end to that project.

A. That would be my explanation but you need to check that --

THE CHAIRMAN: We will ask Professor Cash. I think that is the story, Ms Dunlop, but clearly we want to make sure that we get it rounded off since plasmapheresis could have been quite important had if taken off.

A. It could have provided considerably more plasma, yes.

MS DUNLOP: In your paper, Dr Foster, you take us back to the generous provisions in the United States of America. 60 litres per annum per donor. And a maximum of about 12 litres per donor per annum in the UK, but in the period in which we are principally interested, which is late 1970s, early 1980s, none at all in practice.

A. Not by plasmapheresis, no. Not for fresh-frozen plasma.

Q. And you have indeed quoted in your paper that section from Major -- I'm calling him Colonel Jeffrey?

A. Major General.

THE CHAIRMAN: I think if there is one word it has to be General rather than Major.

MS DUNLOP: Major General.
THE CHAIRMAN: He is a Major General. A very model one, I'm sure.
MS DUNLOP: Yes, General Jeffrey in 1976. Time-consuming for both donor and operator and involves expensive equipment. On to the next page, you say:

"Plasmapheresis. To collect normal plasma wasn't available to SNBTS until 1990."

A number of other avenues were explored to obtain additional plasma, and there is the Kansas proposal, 1979. Mr Watt thought he could import plasma from unpaid donors in Kansas. It was not used for Factor VIII concentrate manufacture but by putting it in at another stage of your work, you were able to free up plasma to go towards concentrate manufacture, as I understand it?

A. One of the difficulties throughout this period was actually getting enough plasma to do research because there was so much demand by the patients, and obviously you wanted the plasma to go to the patient, the products to the patients. So getting an alternative supply of plasma that could be used for research was quite helpful at that time.

Q. Right. So at that point you weren't competing with those who were actually manufacturing product directly

to get plasma for research?

A. Well, it was up to Mr Watt to allocate resources to the best of his judgment, but clearly if there was an enormous pressure to produce the product, then the plasma would go in that direction, and we actually had to encourage our staff to give plasma by plasmapheresis to provide material for research, and we had quite a number of staff signed up for that.

Q. So the staff at PFC themselves?

A. That's correct.

Q. So they were the exception to the proposition that plasmapheresis wasn't being used in Scotland?

A. That's actually a good point, yes. I had to do that myself to show a good example.

Q. Yes. Thank you.

The second illustration you give us of another effort that was made was to try to squeeze more Factor VIII from the cryo but that wasn't so successful because the potency of trial batches was too low?

A. That's what transpired, yes.

Q. Yes. Then thaw siphon technique is the third one. Basically, as I understand this, this is to get more Factor VIII in the cryoprecipitate, which was going for cryoprecipitate, because then less plasma would be required to make cryoprecipitate?

A. Yes, you made the point earlier that at some points one has to decide, does the plasma go to cryoprecipitate or does it go to PFC, and if you have a higher yield in the cryoprecipitate at the blood bank, then you can provide more plasma to PFC.

Q. Yes, I think we understand that, thank you. Then you say:

"As a result of these strategies, the amount of FFP supplied by SNBTS increased greatly from 1974/1975."

You have put that in a table for us and we can see for ourselves that indeed from 1974 to 1975, where you had 1,934 kilogrammes per million people, in 1997 to 1978 you had 13,019 kilogrammes per million people.

So on any view, a significant and steady increase. It is also interesting to look at this table and see that breakdown, the amount of fresh-frozen plasma that was going for the preparation of cryoprecipitate and the amount that was going to concentrate. And we can see the cryo is declining. Then there are three years, Beginning 1977, 1978 and 1979 where it seems steadier. Indeed, there is a slight increase in 1978/79, but then after the year 1979/80, a decline again. One or two blips but the amount going to concentrate is steadily increasing. Do you remember Dr Howard Davies?

A. I never met him, no.

Q. Was it well-known in Edinburgh in the 1970s that he didn't want to use commercial concentrates?

A. I didn't know that.

Q. Right. In your commentary, if we could go down, please, you say:

"The data demonstrate both the magnitude of the year on year increase and the increasing emphasis on the preparation of Factor VIII instead of cryoprecipitate."

Then on the next page. Although the increases in the amount of fresh-frozen plasma to PFC fluctuated, there was always an annual increase in the amount of FFP to PFC, well, until 1984/85, we can see there is a decline, but up to the end of 1984, including some pretty significant year on year increases in the amount of FFP going to PFC. You explain in your bullets under the table why some particularly significant increases occurred.

Then on to section 5, SNBTS manufacturing capability. Some more historical material, Dr Foster, blood products unit between 1950 and 1974. This is the one at the Royal Infirmary actually in the basement. Is that right?

A. Yes, it was in the same block as the regional transfusion centre, and the regional transfusion centre was on the ground floor and

the blood products production unit was in the basement.
Q. Right.
A. Next door was the haematology department.
Q. And you say:
"The first plasma products prepared there were immunoglobulin for the prevention of measles and Cohn Fraction I."
THE CHAIRMAN: Could I ask one question? There is something I'm not at all clear about and that is whether the Cohn fractionation was limited to Edinburgh or whether it happened in other transfusion centres. Can you help me?
A. Cohn fractionation didn't happen in transfusion centres, it only happened in what we would call fractionation centres, and there were only three of those in the UK, one at Elstree, one at Oxford and one at Edinburgh. And Oxford only focused on coagulation factors.
THE CHAIRMAN: So what was happening throughout the rest of Scotland until PFC was established at Liberton? What was happening locally?
A. In what respect?
THE CHAIRMAN: In respect of the preparation of any sort of therapeutic material.
A. Blood products would be had at the regional transfusion centres and then this was the national unit. Edinburgh was the national unit for plasma products.

THE CHAIRMAN: So what would they do at Aberdeen, for example?

A. They would obtain material from the national unit in Edinburgh.

THE CHAIRMAN: Right.

A. This Cohn Fraction I that was manufactured at this time actually was distributed as far south as Newcastle?

THE CHAIRMAN: Did everybody make cryoprecipitate?

A. From 1966 onwards, yes.

THE CHAIRMAN: Thank you.

MS DUNLOP: Just to go back, and this is, I think, quite basic, but just so that we understand, at the beginning of your evidence we talked about cryoprecipitate as a starting material that can go and be used in the treatment of haemophilia as cryoprecipitate, or it can be used as the starting material for the production of Factor VIII concentrate at PFC. In that process, as we understand it to have been occurring, particularly in the early 1980s, where, if at all, does Cohn fractionation feature?

A. Cohn fractionation is the procedure devised by Edwin Cohn, which I don't need to go into the chemistry of, but at PFC, once we had removed the cryoprecipitate from the plasma, we would then apply the Cohn fractionation process.

Q. Right. So when we spoke about the freezing and then taking the gloopy stuff or the gungy stuff from the cryoprecipitate, at that point you used Cohn fractionation in obtaining what will eventually become the powder which is going to be the freeze-dried Factor VIII. Is that right?
A. No.
Q. No? Sorry.
A. The cryoprecipitate is then processed to be an intermediate purity product that comes to Factor VIII as a concentrate; it doesn't involve Cohn fractionation at all.
Q. That's why I'm asking actually, because I think it is possible to get distracted by Cohn fractionation.
A. It is the liquid that is left after the cryoprecipitate has been removed. We called it cryo-depleted plasma, if you like. That then is subjected to Cohn fractionation, and the objective of Cohn fractionation is to produce immunoglobulin and albumin.
Q. Yes. So in fact, in the whole of the process, going from cryoprecipitate to Factor VIII, you don't need Cohn fractionation to get the Factor VIII?
A. No. You only need that to process the residual plasma to obtain albumin and immunoglobulin.
Q. Thank you. Thanks. That was my impression but just so

that we are clear.

THE CHAIRMAN: It doesn't clarify everything for me since Fraction I contained Factor VIII, as I understand it.

A. That's correct. And the early concentrate was made from Fraction I --

THE CHAIRMAN: Indeed, and I think history is part of the problem here, that we do have to know what was happening over particular periods of time, rather than the generality.

A. When cryoprecipitate came along, that was a better starting material for Factor VIII production than Fraction I. So Fraction I was only used to prepare fibrinogen after the cryoprecipitate had been removed.

THE CHAIRMAN: When we hear about antihaemophilic globulin in the early days, what was that?

A. Factor VIII.

THE CHAIRMAN: And that came from Cohn Fraction I?

A. Yes. That was in Cohn Fraction I. Today we would call it Factor VIII activity.

MS DUNLOP: Yes. I think it's possible, Dr Foster, as we said at the start, for us to misunderstand something which is absolutely basic for you but it isn't for us.

THE CHAIRMAN: You must assume that nothing is basic for us.

MS DUNLOP: Yes.

Having told us about the era before the opening of

PFC at Liberton, you then go on in 5.1.4 to tell us about the opening of PFC at Liberton in 1975, and we know from our background reading that there was quite a debate about whether PFC would be used to process English plasma, and that that in the end never happened. In fact, from your article, which I think we will go to later on today, you think that in retrospect that was very unfortunate for PFC. Is that correct?

A. It was certainly John Watt's view that PFC -- John Watt was advising a number of countries and he understood that the fractionation process was very expensive and in order to afford it, if you like, you had to have a certain population to sustain that infrastructure that was required, and Scotland, he thought, was too small and really he thought it needed a bigger population to keep the facility working economically. And of course, that kind of analysis was delayed slightly because the demand became much greater than he had imagined. So I think the economics weren't quite what he imagined it would be but ultimately PFC was judged to be not economic for Scotland alone.

Q. You say that the DHSS decided not to use PFC for the fractionation of plasma for England and Wales and this was judged wrongly to be more expensive than the construction of a larger and newer facility at the BPL.

We are not investigating in any detail what happened in England and Wales, but really in the early 1980s there was quite a saga about the construction works at BPL, was there not?

A. Well, BPL facility was inspected, I think, around about 1979 and the outcome of that was that they really needed a new facility to comply with the standards that were needed and also because the demand for the product had exceeded their capacity. So there were two reasons for building a new facility and the discussion then was what size should it be built to. Should it be built to handle the whole of England and Wales and send half to Scotland or should they build a large plant, and the decision ultimately was to build the large plant for the whole of England and Wales and not to send plasma to Scotland, and that was justified on some costings that I think, looking at now, could be seen to be quite wrong.

Q. Given what was destined to unfold, in the shape of the AIDS crisis, it was not a good time to realise that you needed a new factory. Or is that not fair?

A. I think a new factory was required but I think if people had known of the problems in the future, then they might have taken a faster track to getting that off the ground and part of that would have been to make better use of

the Scottish facility.

THE CHAIRMAN: Dr Foster, I would have very much liked to ask John Watt about the period when processing for England seems simply to have disappeared into the sand. I know that some plasma did come from England and was held in store for quite a period of time, but it wasn't processed because I think Mr Watt wasn't satisfied about the procedural arrangements that would be made for its distribution in England. I rather think he wanted to be sure that the product went back to the plasma source. Do you have any feel for the debate that was going on over this time?

A. Yes, I have a reasonable understanding of it, partly because of documents that have been released more recently that tell me the story because I didn't at the time understand it all. But really, when PFC was being planned, there were discussions with different departments and it was agreed that PFC would process plasma from the north of England as well as Scotland, and that was actually written into my job description I have to say when I began work there.

Once PFC was constructed, John was quite keen to begin this process of handling English plasma but to do that, we needed more equipment because we had only been funded to handle Scotland and we also needed new

staffing arrangements to handle this extra plasma. And at that time this was for albumin, it wasn't for Factor VIII and really the staffing arrangements that were needed failed to be achieved because, although a system for staffing was negotiated and was approved in Scotland, it wasn't accepted by the Department of Employment because it was judged to contravene the government's incomes policy at the time -- not incomes policy. The Callaghan government had a pay policy and it was judged to contravene that.

THE CHAIRMAN: The overtime couldn't be worked?

A. It was more of a shift system. It was seen to contravene the government's policy and then the issue came back around about 1980/1981 when there was this question about what they were going to do to rebuild BPL, and we did receive plasma from England and we did process it in an experiment to show that we could actually handle that quantity and that from our point of view that experiment was quite successful.

So we had actually proved that we could handle it if we had the proper staffing arrangements but then this analysis that I mentioned earlier, the economic analysis, the costings that were carried out, that showed that it would be cheaper to build BPL at the larger size, took precedence and we can see that that

was incorrect.

THE CHAIRMAN: It turned out to be incorrect but we can understand what was going on, thanks to the explanation.

Thank you very much.

MS DUNLOP: You also mention on the following page, Dr Foster, page 38, that the design of PFC was essentially completed in 1970 and then government guidance on the construction of and operation of the facilities for the manufacture of pharmaceuticals in the UK was first published in 1971. Certainly when one reads that, it sounds the wrong way round. You would presumably, in an ideal world, choose to have the government guidance and then you would design your building accordingly.

A. The government guidance followed the Medicines Act that was introduced in 1968, and the creation of Medicines Division and Medicines Inspectorate and they produced guidelines. And they weren't dealing with us specifically, they were looking at the whole of the pharmaceutical sector in the UK.

The decision to build a plant in Scotland had been taken before any of that started and didn't wait to see what was going to happen. But the design was drawn up to what was thought to be best practice at the time, based on World Health guidelines and what other

manufacturers were doing around the world. And we can only see now, looking back, that these things were happening in parallel: the plant was constructed and in parallel with that the inspectorate was getting going and beginning to look at the standards and change the standards in the UK. But I think the same thing affected BPL because they had a major reconstruction at this time and they were really in the same position.

Q. No doubt that sequence of events led to what you go on to discuss, that PFC later had to carry out modifications to comply with Medicines Control Agency guidance. You say you also carried out work to increase the capability of the centre. So an extension in 1982 and 1983 and another extension in the early 1990s?

A. I think by the time PFC opened, John Watt was well aware that standards were moving and the earlier designs were becoming out of date. But to justify funding to make these improvements, he needed a medicines inspection in order to have something in writing to say this is what is required. And I know from personal experience he was nagging the inspectorate to come and visit PFC, really from 1975 onwards, but they had other priorities. So they didn't get to us until about 1980. By that time a cumulative number of things had to be done to make the improvements needed that had been accumulating over that

ten-year period, and that all kind of focused in on the period in the early 1980s.

Q. Right. Can we move on, please, to the next page at the top. You say that PFC closed in 2008. And bearing in mind that this is all still within section 5, which is dealing with manufacturing capability, you move on to talk about the regional blood transfusion centres and I think we all know where these were based. The Glasgow one from 2001, I think has been based at Gartnavel. Yes, you do go on to say that. And you have then given us, in table 8, a breakdown of the fresh-frozen plasma according to transfusion centre. Unsurprisingly about 80 per cent of the FFP was provided by Edinburgh and Glasgow combined.

We can see really not a lot of change between 1974 to 1975 and 1983 to 1984; very similar sorts of percentages.

Then on to the following page. You deal with the centres individually. Law Hospital, you say, which opened in 1939, according to some reading that I have done, at that time was anticipated to have a ten to 15-year lifespan but plainly it lasted longer than that. Large number of pre-fabricated buildings in an open rural location.

Dr Foster, the one in the West of Scotland, Law,

rather stands out from the other four. If you think of the Aberdeen one being based at Aberdeen Royal Infirmary at Foresterhill, Dundee based at Nine Wells, Edinburgh based at the Royal Infirmary in Edinburgh and Inverness based at Raigmore, the centre for Glasgow was rather out on a limb, was it not?

A. My understanding was that Law Hospital was built in Carluke because Glasgow was thought to be the focus for bombing during World War II and they wanted it out of the city centre and it remained there. As you say, it took a long time to replace it.

Q. I don't suppose you know why a decision was taken to put the regional transfusion centre there as well?

A. I don't know the answer to that, no.

Q. There must have been practical inconvenience in its being situated so far from Glasgow city centre. It is not quite half way to Edinburgh but it is a decent distance from Glasgow city centre?

A. I think you need to put that question to Dr Mitchell.

Q. I don't suppose he decided to build it there either.

Right and you have charted for us the various moves that took place in Edinburgh as well. Then in section 5.3:

"Know-how for the preparation of SNBTS coagulation factor concentrates."

Just at this point, Dr Foster, I wanted to share your article that you have given us. We have some hard copies. I'm hoping that people have hard copies of this, sir. I can make more available if people are wanting to take one away and we will obviously put it into court book. It is just that I have only seen it since yesterday and it's an article by Dr Foster from the SNBTS Blood Letter, is that what it's called, the publication?

A. That's correct, it's an external publication within SNBTS.

Q. From the spring of 2008, pages 21 to 23, and you no doubt wrote this because of the closure of PFC. Was that the stimulus?

A. It was, yes.

Q. Yes. We can see for ourselves the origin of PFC: The underground site at the Royal Infirmary, the move to plasma fractionation premises at the Royal Infirmary, opened in September 1950, Dr Robert Cumming and Dr Drummond Ellis and then between 1951 and 1974 Dr Ellis went to the United States to study plasma fractionation at the laboratory of Dr Edwin Cohn and, no doubt influenced by that, came back and planned the installation and designed much of the equipment to produce Scotland's first fractionated plasma product.

That's the immunoglobulin for the prevention of measles infection, 1952, and then an early version of Factor VIII, Cohn Fraction I.

Sir, this is maybe where the four flasks of AHG come in?

A. If you look at the photograph on the first page, the top right-hand photograph, there are a number of bottles. The top right-hand bottle, which actually has a blue cover that you can't see in your copy, is actually the antihaemophilic fraction that we call Cohn Fraction I. I would imagine that was the product that the Reverend Black received.

Q. Right. A picture is worth a thousand words, Dr Foster?

THE CHAIRMAN: Only if you can see it.

MS DUNLOP: It's a great deal better than no picture at all.

What are we looking at? Are we looking at a bottle of white --

A. It's freeze-dried, yes.

THE CHAIRMAN: -- powder? Right. So you don't know where flasks would come into it. It might just have been done in flasks rather than --

A. It was manufactured in -- I would say it was a jar, if you like. It held about 3 litres of material, so I would guess it was about 12 donations of plasma in the pool.

Q. Then you say:

"Demand continued to increase."

I think we know about that.

Mr Watt came. Mr Watt had previously worked on the fractionation of animal plasma at the Royal (Dick) Veterinary College, which I think helps to explain what might have been slight puzzlement on our part as to his background in veterinary medicine. But it was really his background in fractionation that was important, I take it?

A. Yes, that's correct.

Q. Then you mention the close collaboration with Dr Alan Johnson. Then, 1975 to 1983, 35 staff moved from the Royal Infirmary and a further 90 were appointed to operate the new centre, and you mention Dr Jim Smith, who we will be hearing from in September.

Then your reference to the design being to accommodate plasma from the north of England, but obviously we know that that didn't happen.

Then, on to the next page, you say:

"The success of Factor VIII concentrate led to demand greatly exceeding all projections."

And Mr Watt's departure at the end of 1983.

Then, 1984 to 1994, you discuss heat treatment.

But thank you for providing this, Dr Foster. It

seems a useful story of the history of matters, sir, and that's why we want to put it into court book.

THE CHAIRMAN: Yes, I think it's very useful indeed. Glasgow didn't try the Cohn fractionation process at all, did it?

A. I don't think so, no.

THE CHAIRMAN: No.

A. It needed special facilities and I think Edinburgh was chosen as the place.

THE CHAIRMAN: Yes. And Glasgow clung on somewhat tenaciously to cryoprecipitate for a period after that?

A. Yes, that's true, yes. I think the decision to site fractionation in Edinburgh actually came from Dr Robert Cumming, who was the Edinburgh transfusion regional director, who joined, I think, about 1948, and he perhaps had the vision to see what was needed and made the progress in Edinburgh.

MS DUNLOP: Just to mention this, Dr Foster, because it's another interesting historical document which is in fact referred to in the preliminary report, but we have "Fifty years of an organised Blood Transfusion Service in Scotland", which is [SNB0101836], and a bit more information about some of those involved.

Particularly, if we read through it, we can see that from page 4 onwards there is the section headed up "The

separation of plasma". You, presumably, are very familiar with this piece as well, Dr Foster, are you?

A. I have read some articles by Girdwood. I think I have glanced at this one, yes.

Q. Mention of Dr Cumming on page 5.

A. This looks like the draft was published eventually.

Q. Yes. It was published, I think, in the Scottish Medical Journal?

A. That's right.

Q. Yes, you are right, this is not a copy of the text as published.

More information about Dr Cumming, who had been a Japanese prisoner of war, and some more discussion of the products on to the next page.

Plasmapheresis, although not suggesting that that was actually happening.

Then some discussion of the different centres around Scotland.

So your section on know-how, to which we need to return, Dr Foster. Section 5.3 on page 40 of [PEN0131125]. You refer to a chance meeting in 1966 in Australia between Mr Watt and Dr Alan Johnson, and his is a name we see quite frequently over the ensuing decades in fact. There was obviously a connection established there which lasted some time. Is that

right?
A. Yes, it lasted really for many, many years. I became good friends with Dr Johnson. Really from the 1950s and 1960s he became probably one of the word's leading experts in the development of Factor VIII concentrate and it was really out of his work in part that the concentrates actually were ultimately developed.
Q. And that's why you named one of them "NY", wasn't it?
A. Exactly, because we used his method and his advice. I don't know who came up with the term "NY" but it reflects New York and that's where he was based. So it was an acknowledgment of his contribution.
Q. Move on to the next page. You explain that it was really a global network of contacts, presumably with a view to sharing information about R and D. That must be difficult at times, Dr Foster, because -- we have seen your patent applications listed. We may come on to this far more in the autumn, but there must be a balance to be struck between sharing information and not giving away some development that you alone have perhaps identified?
A. I think, certainly in the not for profit sector, I never found any impediment. We would reasonably get to know who was doing what in which place, and particularly BPL, and if you had a question or a comment, we could phone

them up and they would talk to us and sometimes they might say, "I'm not supposed to speak to you but I'm going to talk to you anyway."

So there was quite a lot of exchange, certainly at my level, without any difficulty whatsoever. There might have been the occasional thing where there was a patent application pending, or some agreement with some other third party, that precluded discussions, that required confidentiality, but that was really quite rare.

Q. You now take us to section 6, which is "Blood products for the treatment of haemophilia", and you give us a introduction, a lot of the content of which we are, I think at the moment, reasonably familiar, thank you.

On to the next page. You do mention purity and potency. Can I ask you to have a look at [PEN0150445]? This is Professor Ludlam's statement. Can we go to page 13 of this, please? Sorry, I'm not sure that we are at the right section. Can we go on to the next page, please? Sorry, I have forgotten my hard copy, sir. There is a section on purity and potency in this. Can we scroll through until we come to it? I think it's suggested in the index it's page 13 but it doesn't look to be.

Yes, here we are: "Clotting factor concentrate,

purity and potency".

I think I should ask you, Dr Foster, because we have found this slightly challenging: do you agree with the way Professor Ludlam has set it out? Don't worry, I'm sure he would defer to you, but is this a reasonable explanation?

A. I think I might have put it slightly differently. I tend to refer to a textbook from the same period, where there was a chapter written by Dr Smith, where he gives his definition, and for me it's slightly different but I don't know that we need to get into details of decimal points.

But, generally speaking, the products that we were manufacturing -- and I think this is said later on in the document -- what we called "intermediate purity concentrate" -- and that was the general term that was used -- was of the order of half a unit per milligramme in terms of its specific activity, and the main issue -- and it leads into potency and dose size and everything else -- really comes back to something we discussed earlier, which is this source of plasma and the way that is provided.

We have seen that in Scotland we had blood from ordinary blood donors, who would donate maybe half a litre of plasma a year; we have seen that in the

United States they have what from our perspective looked like a reservoir of plasma available. In order to achieve the further purification that did exist with the commercial products, you had to carry out further processing and that had a yield penalty. There were a number of reasons for that, which I can go into if you like, but ultimately, if we had done that, we would have either needed more plasma or we would have reduced our output and because we didn't have enough plasma, the bottom line is we would have reduced our output, at a time when we couldn't make enough.

The commercial companies, on the other hand, had this large reservoir of plasma. So, for them, they could accommodate a reduction in yield without any great difficulty and produce what was a more purified material. To give you a feel for it, our product would be of a purity of about 0.5 or slightly less units per milligramme of protein and the commercial products might be up to 1 or even 1.5 units per milligramme of protein. So it was maybe a doubling or tripling in terms of specific activity. But the reason for that was that they could afford to do that because they had access to this plasma. If we had as much plasma as that, there would have been no difficulty in doing that.

There were a number of implications that that has

because, in terms of potency, which is the strength of the product, if you want to make it stronger, you have to dissolve more and you can only do that if you have the greater purity, that we didn't have.

Also, in terms of the dose size, the availability of plasma made it much easier to provide a greater dose size. I have already explained to you that we had to take a number of samples for quality control and if we had increased our dose size, the proportion that would have gone to quality control would have been even higher.

For example, to go back to the point I made where we had 150 bottles in a batch and we were taking 25 bottles for quality control, if we had increased the dose size and doubled the dose size to what some of the commercial companies were doing, then we would have only had 75 bottles in the batch and we would have been taking 25 bottles for quality control; that's one third of the batch.

So it's those kind of considerations made it really virtually impossible for us to compete, in terms of potency and purity, with the commercial companies, and that was really entirely down to the availability of plasma, that they had and that we didn't have.

Q. Are you describing the state of affairs around about the

early 1980s?

A. I'm describing the state of affairs right through the 1970s and 1980s. If you go back to the availability of plasma and work it through, the commercial companies were providing 70 per cent of the world's needs. They had huge quantities of plasma because of the system that they had, which was unique to the United States. They had this reservoir, we had a dripping tap, basically, and we had to make the most we could of that.

Q. Are these definitions in paragraph 51 of purity and potency the ones that we should be using as our working definitions?

A. I said earlier that I would perhaps check with the article that Jim Smith wrote in the textbook at the time but, roughly speaking, yes.

Q. Right. Can we go back to the paper, please? So in that second paragraph, which is page 42, it looks as though the Pharmacopeia were specifying a lower limit for the product in 1980 as well. We saw Professor Ludlam's gradation of low, intermediate and high purity but to be described as the product at all, according to the Pharmacopeia, it would have to contain a concentration beyond a certain lower level. Is that right?

A. That's correct.

Q. Yes. Then you have explained in the next paragraph the

point you have just made, about all the elements that are in tension all the time and I think we can understand that, that additional processing to increase purity has a yield cost or a yield penalty and in the end you are obviously going to have to find a compromise between those. But in the result, commercial products often tended to be somewhat more concentrated and more potent.

Then you tell us that that changed. So that problem improved or the possibility of solving that problem or striking a better balance increased. Is that right?

A. Yes, there were some changes made in 1979 which increased the specific activity and increased the solubility of SNBTS product, quite a major step change, I think, in the convenience of the product.

Q. I think I should just ask you -- and perhaps I can do this before we stop for lunch, Dr Foster -- about some of the comments made by haemophilia clinicians so far. To do that, we need to go to the transcript. Could we go first to Professor Forbes on 28 April at page 27? Have you read some of the transcript?

A. I have read this one.

Q. Have you read it all?

A. Yes.

Q. Good. That may save some time.

Look at this page 27, from 28 April. It's four pages to a page. Yes, here we are. It's this section where I say.

"Question: Can I just backtrack a moment?"

Can you just have a look at that section and actually we go on through the next page and on to page 29. Let us all look at it in fact. (Pause)

Can we go on to 29, please? (Pause)

There is mention there, Dr Foster, of putting these points to people from the protein fractionation centre. Well, can I do that now?

A. Maybe we can take them one by one. If we start off with specific activity, I think I have gone over that one already, that, in order to achieve the purity, if you like, of the commercial products we have been provided, we would have had to undertake further processing, which they had done, and that had a yield penalty. In order to do that, we would need more plasma and we didn't have that plasma.

The same applies to the potency because, in order to increase the strength of the material, you can only do that if it will dissolve and, to make it dissolve, you have to have the further purity. So those two things went together.

There is quite a lot of talk about solubility.

I think, generally speaking, this is the reconstitution of the product, how long it takes to do that. I would again agree that the commercial product would dissolve more quickly than our product, again for the same reason, that it was more purified; you had removed some of the less soluble material.

I'm a little bit less sure about some of the figures that are given here and I should say that in the Pharmacopeia, that we've talked about, the limit on reconstitution time is 20 minutes. We would not have released a batch for use if it had been greater than that.

As I mentioned a minute ago, we actually made improvements. For example, I have looked back at some of the data and in the 1970s the typical reconstitution time for our product was of the order of 12 to 15 minutes and after 1979 it was down to 6 to 7 minutes. I haven't checked every batch, so I can't rule out the possibility that there might have been the odd batch that might have been longer than that, but that certainly wasn't typical.

Q. Can you just look at Professor Ludlam as well, please, from 3 May? It's page 42. Can we go towards the foot of the page, line 11, on to the following page? A comment:

"Question: The initial clotting factor concentrates were relatively impure and contained large amounts of other plasma proteins. Are we talking about only NHS product here or about commercial product too?

"Answer: Commercial product as well."

Then could you just read on to --

A. Could I just comment on that, just to put that into some perspective?

Q. Yes.

A. You have talked earlier in these proceedings about albumin and the product that we manufactured called Stable Plasma Protein Solution, that had a purity of 90 per cent. The immunoglobulin that we have talked about had a purity of about 99 per cent. When we look at Factor VIII concentrate, the purity is 0.01 per cent for our product, 0.02 per cent for the commercial product.

Q. That's back to the needle in the haystack?

A. It is not Factor VIII, it is Factor VIII concentrate and "concentrate" is the operative word, not "Factor VIII".

Q. Right. These early concentrates were very difficult to solubilise, if we go on to the next page. (Pause)

So he is making a point about dissolving the material, which I think you have just dealt with in fact, about your compliance with the specifications.

I suppose, comparatively speaking, people might have found the products from PFC slightly harder to dissolve than a commercial product. There is also the point you make about there may have been odd batches that were particularly difficult to dissolve.

A. I think there is no doubt that overall our product would take longer to dissolve than the commercial product because it was less pure. My comment about there might have been the odd batch that took longer was simply speculation, to try to accept the points that have been made here. Maybe there might have been a batch that was like that.

Another aspect to bear in mind is that this material is derived from cryoprecipitate. "Cryo" means "cold", "precipitate", it's insoluble. It actually doesn't dissolve if it is cold. These products are stored in the fridge. So, in order to dissolve them, you have to allow them to warm up and if somebody tried to dissolve it when it's cold, then it won't dissolve. That maybe is something that has happened from time to time, if people are not doing this properly.

Q. I wondered in a sort of low-tech way actually, when Professor Ludlam was talking, whether it would be permissible to heat the water.

A. It would be, yes, and I think you find reference to that

in the preliminary report, where Mr McIntosh, who was our general manager much later on, said:

"This problem can be solved for the price of a water bath."

Q. Right. I think, sir, that would be a good point to stop.

THE CHAIRMAN: Very good.

MS DUNLOP: If that's all right.

(1.11 pm)

(The short adjournment)

(2.00 pm)

THE CHAIRMAN: Yes, Ms Dunlop?

MS DUNLOP: Thank you, sir. I think, Dr Foster, we had been talking just before lunch about purity and potency and then you were looking at what has been said by two of the haemophilia clinicians about PFC products.

Can we return to your paper, please --

A. Before we move on, could I just make one further comment on some of the points that have been made previously. One of the issues that has been raised is that our product didn't always work, and I think that Dr McClelland began to talk about that last week. I have really tried hard to think why anyone would make that comment because our product was licensed, it had been evaluated in patients before it received a product

licence. It was tested by an approved method by NIBSC. So really I can't understand why it wouldn't have worked. The only explanation I can come up with is that we did provide a product that might have a variable quantity from batch to batch in the vial.

We aimed to have a vial that would contain in the range of 200 units to 250 units, and that variation was simply a reflection of the type of plasma that we obtained. We have seen earlier how our plasma might be frozen within six hours or even 18 hours, and because Factor VIII is very sensitive and loses its activity over that timescale to some extent, then that meant the batch of Factor VIII from 18-hour plasma might have less in it than a batch of Factor VIII from six-hour plasma.

Compared to the commercial companies, that wouldn't be the case, because where they are collecting plasma in a fixed location, by plasmapheresis, they can freeze that material almost immediately after it has been collected. So their product would be more uniform because their plasma was more uniform. Our products might be less uniform because our plasma was less uniform, and that led us into a position where we might have this variation from batch to batch. And therefore, to accommodate that situation, we would print on every vial the amount of Factor VIII in the vial, but it would

be incumbent on the doctor or the patient to read the label to work out how much to treat themselves with or how much to administer. If they didn't do that, if they just took a vial and assumed what was in it, it's possible that they might have got that wrong. That's the only explanation I can come up with for that comment that was made.

Q. I can remember Dr Forbes saying something about a lack of correspondence between what was on the bottle and what was in the bottle, and Dr Ludlam referring to the product not working in one patient, but you are alluding to a comment by Dr McClelland, are you?

A. No, Dr McClelland began to answer that question.

Q. I see.

A. And he said you would refer it to me and he gave half an answer, if you go back and check the transcript.

Q. I see.

A. So I'm trying to imagine what it was that led to these comments from Dr McDonald and Dr Ludlam, and that is the only explanation that I can come up with, that we did have a wider variation from batch to batch in terms of what was in the vial.

Q. I'm just clarifying so that I know when I go back and look at the transcript, when I come to that part I need to read this section of your evidence so that

I understand what the link is. So, thank you.

I think we need to go back to table 9, which is shown on [PEN0131125] at 1166. This is page 42. Different types of blood product. You can go on to the following page. This is really again picking up some of the points you made when we talked about purity and potency. Indeed, we can see what was ultimately achieved with Liberate, for example, Liberate and Replenate.

A. Yes.

Q. Really very much higher than, for example, Cohn Fraction I. And no doubt these sorts of very high purity products require much smaller infusions, do they?

A. You are able to put more Factor VIII into a smaller volume, yes.

Q. Yes. We have had some reference to the need for small infusions when treating small children, for example. Is that a factor?

A. Yes, I think these very high purity products would have that advantage in children because of that, yes.

Q. Then in section 6.2, you chronicle for us the introduction of different products, and we see mention of Dr Johnson again at the bottom of the page.

If we look on to the next page, there is a reference to requirements being uncertain and we understand about

that. I suppose in doing the necessary predictions when planning manufacture, we have already discussed the constantly spiraling demand, but there must also have been difficulty -- and I think you are alluding to this here -- in knowing how much cryoprecipitate was going to be used and how much plasma would then be sent for the making of the concentrates. So that would be an added difficulty when you were trying to predict what was going to happen in future. Is that fair? Even the breakdown was uncertain?

A. I think to some extent it was uncertain but there was certainly obviously clear indications from haemophilia directors what their preference was. But I think there were times when Professor Cash was saying to them, "Would you like more cryoprecipitate", and the message coming back was, "No, we don't".

Q. Right. Then you mention this freeze-dried cryo on this page and we looked at that before lunch as well.

THE CHAIRMAN: Ms Dunlop, do you deal with Superate at any stage?

MS DUNLOP: I hadn't planned to.

THE CHAIRMAN: Perhaps just something I ought to raise with you. I found it very difficult to pin down what happened to the Superate project. Can you sum it up in just a brief sentence?

A. I think there are two things here. One is Supernine and there is an S8 that was a development --

THE CHAIRMAN: Sorry, I have confused the two. It is the Factor IX product.

A. The Supernine was a Factor IX concentrate that was more highly purified, more potent, hence the name "Super", and it had a step that was deliberately introduced for removing viral contaminants and that got through to the point of some clinical trials and then, as far as I understand it, Mr Watt was talking to the licensing division, medicines division, and they wanted us to have only one Factor IX concentrate and we had a choice. We could either go with Supernine or we could keep the traditional product, which was called DEFIX. And at that time the haemophilia directors were more confident with DEFIX because they had a lot of experience with that, they knew it worked. So the choice was to stay with DEFIX. Supernine was discontinued. And this was at a time when heat treatment was being developed and it was thought that was going to be better anyway. It superseded it.

THE CHAIRMAN: That's fine. I had seen the relationship between DEFIX and Supernine in some correspondence but if that is the whole story, I'm quite content to park it at that. Anyone else who wishes to raise this can of

course do so, but I would be happy to leave it there.

MS DUNLOP: Dr Foster, in table 10 you have listed coagulation factor products. Earlier Factor IX products didn't give you just Factor IX but you had an omnibus of Factor II, VII, IX and X. I'm chancing my arm here but are these other factors which co-purify in some way with Factor IX?

A. That's absolutely correct and another term for this is the prothrombin complex. That would be the term that medical doctors might use because these proteins all exist in a very similar part in the human body, and they are all synthesised in the liver. There is a deficiency of these proteins in the liver that can cause the bleeding difficulties and a number of disorders. So this product would be used not only to treat haemophilia but also it might have been used for people who had disorders of the liver as well.

Q. Right. What does "PPSB" actually stand for?

A. You have got me there. It is a French term and I have to think back on the French words to get what they actually were.

Q. I don't think it matters.

A. I think it was to do with someone called Stuart factor and prothrombin complex. It got changed around in French.

Q. That's fine. We will just call it "PPSB".
A. In the preliminary report it is referred to as the method of Soulier.
Q. I suppose the thinking must be that for people with Haemophilia B, there was no particular downside in giving them something that is Factors II, VII and X in it as well?
A. It wasn't ideal but at that time there was no means for purifying Factor IX on its own. So this was the best that could be done, and as these types of products were used and began to go into wider use, there were side effects that emerged -- I think you have heard about that from Professor Ludlam -- to do with thrombogenic reactions. They were never fully explained I don't think, but they were partly to do with the degree of purification and maybe some of these other factors that are in there that weren't really necessary for the haemophilia patients, and so the purification of this product became important subsequently to deal with that issue.
Q. We have certainly seen references, and I think it is true around the time when heat-treated Factor IX comes in in 1985, references to the need for thrombogenesis studies in dogs?
A. Yes. This was seen as being quite a serious

complication, a potential complication of Factor IX treatment, that you would have these thrombogenic reactions. I think in the United States people died from these reactions. So it wasn't a trivial issue and in Edinburgh Professor Cash had pioneered quite a lot of work in this area in animal studies and because the mechanisms weren't known biochemically, the only way you could be certain that you hadn't actually caused a product to change and be thrombogenic was to do these studies in animals. So we did have a very substantial study that was done jointly with BPL, led by Professor Cash.

Q. Table 10 runs on to the following page and we can see a list up to 1996. Then in the next section, 6.3, you deal with commercial products, and moving on to the following page, you refer to approval by the Committee On the Safety of Medicines since 1973 and recommendations from haemophilia directors. We have seen a number of references ourselves. UKHCDO meetings, where no one voted for cryo if there was a choice between cryoprecipitate and Factor VIII concentrate. You have listed the principal commercial Factor VIII concentrates approved for use in the United Kingdom and I referred to this earlier on this morning. It's a table which gives different pieces of information

about these pharmaceutical products.

On to the next page, quite a complicated exercise keeping track of the companies in their different incarnations and different ownerships, Dr Foster.

A. Extremely complicated, yes.

Q. I think I noticed one of the things when I was looking at this table, that I had referred to Armour. I may have said in evidence about Armour becoming French. I think that's in the Douglas Starr book. But indeed you have taken that story on for us in footnote (f), and Armour is now part of Behring?

A. Rhone Poulenc was French. So you were correct in the reference to France but it is now CSL Behring.

Q. You have explained too, something which I hadn't picked up, the references to Speywood. That Speywood sold a Cutter product, presumably repackaged, remarketed as Humanate. That is note (k). And then you go on to talk about market shares in table 12. Quite interesting. Not least because it is not the same as another table that I have seen, which we can just look at. I don't think this matters in the slightest but can we look at [DHF0014517], please? Just slightly different figures, Dr Foster, and I suppose illustrating how difficult it is to get the definitive answer?

A. Yes, I would like to say, the difference might be

because this table here is given in units of Factor VIII, and I think much of the other table might be in sales, and depending on the pricing of the products between different companies, the sales might be different too.

Q. Yes. It was just that, looking at the Department of Health table, the DHSS table, for 1980, they are showing Armour as somewhere approaching 50 per cent of the UK market, which isn't quite what you have. On your table Armour is obviously a very big supplier in 1980. I just wondered why Armour -- was their product particularly good?

PROFESSOR JAMES: It's the same. This is the 1980 figure for Armour of 34 per cent is 34 per cent of the total UK market including the UK production.

MS DUNLOP: Right. Okay. Whereas the Department of Health one is excluding UK production.

PROFESSOR JAMES: Exactly.

MS DUNLOP: Yes, right.

PROFESSOR JAMES: So here on table 12 of Dr Foster's, it says:

"All 71 per cent share of UK supply."

So they have half of 71 per cent, which is 34 --

MS DUNLOP: I see that, thank you.

I just wondered, Dr Foster, do you have any

recollection of why Armour enjoyed such a large slice of the market?

A. I really can't answer that. I know they had a sales office in the UK, which I think may have explained it. They had a strong presence here. But that's really all I can suggest.

Q. Just going back to your paper. You mentioned the WHO policy and then Dr Galbraith's initiative in 1983 and indeed, steps taken by ASTMS, and I want come on to that because you have covered that in your statement as well. Then on to the following page you mention the correlation between HIV infection of people with haemophilia in the UK and the use of commercial concentrates. You refer to work by Melbye. Denmark and Glasgow. I don't remember where the Moffat work was based. I don't think that's work at which we have looked but conclusion to the same effect. Something in the Lancet in 1985 in which Dr Mortimer and Professor Bloom also took part. Then you go on to talk about the detection of antibodies to HIV.

The next paragraph in which you deal with antibody to Hepatitis C, I think, Dr Foster, we need to look at all of this in more detail when we come to look more specifically at Hepatitis C, but at first sight this seems slightly puzzling, what's in the paragraph

beginning:

"This much greater prevalence of Hepatitis C infection amongst USA paid plasma donors was reflected in the different levels of Hepatitis C antibody detected in plasma pools from which coagulation factor concentrates used in the UK were prepared. 89 per cent of plasma pools from commercial manufacturers were positive for antibody to Hepatitis C compared with none for UK donor plasma."

That's research that was done towards the end of the 1980s, presumably?

A. The author here is Phil Minor, who worked at NIBSC and because NIBSC were monitoring products, they were also looking at the plasma pools. So he had access to plasma pools from all of the manufacturers and he published this information in 1990, using what must have been the first generation antibody test, and using that test, he wasn't able to detect antibodies in the UK plasma donor, presumably because it was too diluted, not because it was absent. Whereas it was present in the pools from commercial plasma.

Q. Right.

THE CHAIRMAN: Is this raising the terrible topic of genotypes again?

MS DUNLOP: I suppose it might. Given that it's a slightly

surprising proposition at first blush, I think it's probably better that we defer it and look at it when we come to look at hepatitis in more detail. It may well be to do with the different genotypes, at least in part.

THE CHAIRMAN: We have heard some evidence of the ineffectiveness of the first generation Abbott test to pick up infection in the United Kingdom because it was largely based on experimental work with American blood, where the balance within the genotype spread is rather different.

A. I mean, this is not my area of expertise so I'll defer to other people on this one.

MS DUNLOP: Then you talk about commercial products free from the risk of hepatitis transmission. I think all of which we will defer.

Then finally in this section on the next page you tell us about SNBTS having imported some plasma after 1998, and then we move on to a section on yield, section 7, and I think we understand from earlier discussion about the importance of yield. The importance of yield in absolute terms and also as an assumption. You have given us another table, table 13, to show how the yield changed, indeed improved, and you go into this in more detail in section 7.2. You say:

"Normal plasma contains one international unit of

Factor VIII activity per millilitre by definition."

So that is how an international unit was first identified, is it? It's the activity of Factor VIII in 1 millilitre of plasma?

A. Of a normal person.

Q. Of a normal person. But that even begins to decline when anti-coagulant is put into the donation?

A. That's simply the dilution because the definition applies to circulating Factor VIII in the human body and of course, when you take a blood donation, you have to add an anticoagulant to prevent it clotting, and that adds a dilution. So once you get into the blood donation or the plasma, there is that dilution to take into account.

Q. So it's not a chemical effect, it's just a physical effect?

A. It actually turns out to be a chemical effect but at this point it's a physical effect.

Q. Then you go on to talk about other chemicals which are used in the early stages of the process, which is, I think, quite technical for us, Dr Foster. Collecting plasma in a reduced concentration of sodium citrate, but not pursued because of potential for thrombogenicity. Optimisation of process conditions. We can just perhaps note the thinking there. Then, 7.4, increased yield and

quality being improved by a continuous thawing. I think that's something that we saw earlier today as well, isn't it, about improving the yield of cryoprecipitate?

A. Yes, there are similarities. What was called a thaw siphon method in the blood bank has some similarities with what we were doing at PFC, which I have called continuous thawing, which is to have a much better control of this whole process to try and improve the yield because this is a point of major loss of yield.

Q. Perhaps we can move on to the next page, all of this dealing with really the thawing step, and then, 7.5, the addition of calcium. Again, rather technical, although you have set it out very fully for us. Thank you.

The addition of calcium, which is discussed if we go on to the next page. The addition of calcium, which reduced the degree of yield loss and the addition of sodium chloride, it looked as though these were both steps that that were really steps for which you at PFC deserve the credit. These were ideas at PFC, were they?

A. Well, you learn from other people as well but predominantly we took this forward, yes.

Q. You say that calcium addition has since become widely used and you also say that about the addition of sodium chloride.

Then section 8, you have supply of SNBTS products

for Haemophilia A. Can we move on to the next page? Two products, cryoprecipitate and Factor VIII concentrate. Both products being supplied to the NHS in Scotland free of charge.

Table 14, you have shown the amounts of cryoprecipitate produced as well as Factor VIII concentrate issued. We can see from 1975 to 1976 onwards, again a steady increase, in the column on the furthest right. A bit of fluctuation in the internal division perhaps but a steady increase in the amount of material issued.

On to the next page. The cryoprecipitate ceasing altogether in fact in the year 1990 to 1991.

A. Cryoprecipitate is used for other indications other than Haemophilia A. So, for example, that would be used to treat patients who need fibrinogen. So in earlier tables I had listed cryoprecipitate production, we couldn't say that all went to treat haemophilia.
I think by 1990 period, there were recommendations from the haemophilia doctors to cease using cryoprecipitate and I think it completely went out of use at that point. So I have not included it in the table after that.

Q. As we move on, you talk about -- going down the page a little bit, please -- the monitoring of Factor VIII use being undertaken by UKHCDO and you can use these

data to work out the amount of Factor VIII per head of population and compare this with the amounts supplied by SNBTS. You have done that in table 15 for cryoprecipitate and Factor VIII concentrate combined and for Factor VIII concentrate alone. Perhaps we can study table 15. If we take, for example, the year 1979 to 1980, this is a year in which, for the UK, the average use of Factor VIII in international units per head of population is 0.93 including cryoprecipitate; 0.77 excluding cryoprecipitate.

Looking to see from the other side of your table the extent to which the clinical use was matched by supply from SNBTS, if you take cryoprecipitate into account, you were producing -- you, as in SNBTS -- 107 per cent of what was being used, but if you exclude cryoprecipitate and look therefore only at concentrate, you were only producing 54 per cent of what was being used, if what was being used is measured as international units per head of population.

Is that right? So it makes a big difference whether you take cryoprecipitate into account or not?

A. Yes, and it goes back to the earlier figures where you saw that Scotland carried on using cryoprecipitate, or a greater proportion of cryoprecipitate, longer than England, and England took up commercial products to

a much greater extent.

Q. Yes. Then if we look at the following year, there is quite a change for the following year. Again, if you were to assume that the usage in the UK mirrored the usage in Scotland, then for 1980 to 1981, the usage excluding cryoprecipitate would be 0.91 international units per head of population, and of that use, SNBTS was able to provide 76 per cent and then a further increase 1981/1982. So we are back to the runner and the race. Certainly, in this period, maybe 1978 to 1979, up to 1981/1982, you look to be gaining on the runner although not yet pulling alongside. Excluding cryo.

A. Yes, I mean, this is all kind of looking back.

Q. Yes.

A. And at the time we didn't have these figures, so we were just doing as much as we possibly could. But looking back, we can now see, now the darkness has been lifted, we can see where we were.

Q. Yes. The really significant change obviously comes by the time you get to 1983 to 1984, where even excluding cryoprecipitate, SNBTS is producing 116 per cent of the average use, again average use being calculated on a UK-wide basis. That's a first. That has not been achieved at any earlier point in the table.

Although -- and you make this point in your paper,

Dr Foster -- the position is different if you take cryoprecipitate into account as well?

A. And the position is different if you look at Scotland on its own because this makes the assumption that clinical practice in Scotland is the same as the rest of the UK.

Q. Yes, and we go on to do that. So if we move on through the paper and look at the following page, table 16, where you have these figures for use, you explain has been appendix 1 of the preliminary report. I didn't completely understand this reference in the paragraph above the table, but you say:

"Data have been obtained from individual records of every batch of Factor VIII concentrate."

What did you do with that information? Why did you need that?

A. Column 1. In this table we are looking at calendar years. That's from January to December. All the other data from SNBTS is expressed in the financial year. Whereas the clinical data from the haemophilia centre directors' organisation is a calendar year, not a financial year. So to make a more precise comparison, we needed to go back and get data for the calendar year for PFC production, and the only way to do that was to go back to the raw data. So my colleague did look at the data files to allow me to assemble this table and

that's in column 1. That shows how much was produced each of these calendar years from PFC.

Q. And the reason you had to go to every batch is because there may have been differences in the number of units from batch to batch.

A. We definitely knew there were, yes. The only way you could get the information was to go back to the raw data, because the data that had been collected from management records had been done only on a management basis but it was on a financial year. So the only place where you could get the data was really to go back and look at each batch and add it up for each calendar year from the original orders.

Q. Was this quite a major exercise?

A. It took a few days.

Q. How many batches, roughly, would we be talking about?

A. 70 or 80 batches a year.

Q. Right. Okay. And then we have again, quite an illuminating exercise in the table. If we look at the two middle columns, so column 2 and column 3, this is the amount of SNBTS Factor VIII used clinically, and then the amount of commercial Factor VIII used, and that's totalled in the fourth column, and then we compare that with the amount that was produced.

So for 1979, the amount that was produced is greater

than the amount that was used. For 1980 the amount that was produced is less than the amount that was used, and the other interesting thing to note is that from 1979 to 1980 there has been a doubling in the total amount used, from 2.48 to 4.83, more or less.

Then we can follow on for ourselves how the figures go: 1981, more produced than used; 1982, more produced than used, and so on.

I think it's necessary to come back to this table but it's obviously an important table for our purposes. You say, reading the text from the bottom of the page, that:

"In order to maintain supplies of essential treatment at a time when demand was uncertain, the SNBTS supply chain comprised stocks of Factor VIII concentrate stored at the regional transfusion centres and a reserve stock held at the PFC, in addition to stocks held at the haemophilia centres and at the homes of individual patients."

There is quite a lot in that, Dr Foster. I suppose this is really logistics. If you think of the patient, the patient needs a stock in his fridge, the hospital from which he gets his supplies needs to have a stock, the regional transfusion centre from which the hospital gets its supplies needs to have a stock and PFC from

which the regional transfusion centre gets its stock also needs to have a stock. How did you do all that stock control?

A. I'm not the person to ask that question because really I wasn't involved with that at all. You might try asking Dr Perry or Dr Cuthbertson.

Q. I think we will ask Dr Perry, since he is coming, but even that very crude sketch, it does sounds as though there might have been a lot of forward planning involved.

A. I think there was a considerable lot of planning involved. Today we would call this the supply chain.

Q. Right. Then you say you have included stocks held at the regional transfusion centres in the amounts of concentrates supplied by SNBTS in table 15. But you haven't included the stock of Factor VIII concentrate in storage at PFC. Then you have listed that for us.

A. I should really make it absolutely clear that these figures are the stock taken at the end of each year shown here. These are not cumulative figures at all. It is just the blood in stock at that point in time.

Q. It's just a snapshot?

A. Exactly.

Q. And for all we know demand may fluctuate on a seasonal basis, I don't know.

A. I think one of the problems with haemophilia is demand fluctuates unpredictably. You can get patients who might have a severe bleed, who need emergency treatment. So you can have fluctuations, and I think that has been pointed out already in these hearings, that they would have to be accommodated.

Q. Yes. Just to take a for instance, if we look at what must be the end of March 1981, so that's in the year column, 1980 to 1981, because these are financial years, as I understand it, so the end of March 1981 at PFC there was 1.56 million international units of concentrate in stock, which is about a third of the usage for the last full calendar year. It should be 1980. I'm taking that by going back to table 16 and seeing that the total amount used in 1980 was 4.83 million international units.

So it would really be up to somebody who was experienced in stock control and so on to tell us whether that's a reasonable cushion to hold or not. I think we go on to read that the sorts of stocks that were built up in different places, at least in some areas, increased hugely. But just to get an idea of what that level of stock would correspond to, it's about four months' use. That's exactly what you say in the table.

THE CHAIRMAN: I imagine lots of different factors would enter into the determination of the appropriate level of stock, such as whether their phased refurbishment of PFC was expected, and you would have to cover a period of low production and so on.

A. That's quite right. I mean, the stock level is to cover emergencies and contingencies, and the contingencies could include stoppage of production for whatever reason in PFC and breakdown of equipment as well as medical emergencies.

MS DUNLOP: The next table is interesting too. That's table 18. Can we go on and look at that, please? This is really a similar exercise to that at which we looked a short time ago. You have tabulated the total SNBTS Factor VIII available in terms of million units per head of population, and to what extent that was matched or that matched the clinical use. Your conclusion, which is reproduced under table 18, is that:

"At any point in time, SNBTS had available sufficient Factor VIII to meet average UK clinical practice if cryoprecipitate was considered to be suitable to supplement Factor VIII. If it is excluded, [so if it is not considered to be suitable] then, with the exception of the two-year period, 1978/1979 to 1979/1980, the availability of Factor VIII concentrate

from SNBTS was sufficient to meet average UK clinical use throughout that period."

I think the chairman has just made this point: of course, that's not the end of the story because you have to have enough material produced at the right time and in the right place when it's needed. To say that on the ground a need was met, and that would be presumably impossible to assess in retrospect. I mean, do you think it's possible, even given these figures that you have worked out now, Dr Foster, that a clinician could have felt around about 1979/1980 that there wasn't a reliable enough supply coming through?

A. I'm really not sure how to answer that question. I don't know where the clinicians were with our stock situation, I don't know. They may have been well-informed or they may not. I just can't answer that.

Q. It is very difficult, Dr Foster, because it is such a long time ago and people, in some instances, are telling us things second or third hand, but Dr Pettigrew said, for example, that Dr Willoughby at the Hospital for Sick Children in Glasgow had felt he couldn't get a guarantee of reliable supply or a reliable guarantee of supply.

A. I think if you go back into the 1970s, when PFC was

really still getting going and usually doctors were moving forward with home therapy, there is clearly correspondence where SNBTS is really saying, "Look, we can't provide more at the moment, and the choice is for you", and they decide to buy commercial product because they want to do home therapy. So there is a period when clearly there is a discontinuity between the aspirations of the clinicians and what we can provide.

Q. I suppose particularly, if we look from the furthest right column, 1978/1979, 1979/1980, if Dr Willoughby reached that view around about that time, then it may be that there is some support for that in these figures, that the clinical use is ahead of the available Factor VIII at that time from SNBTS. That then pulls back again in 1980/1981, 1981/1982. So for somebody intent on using concentrate, as you say, it's very difficult to answer but one couldn't rule that out around about that time, that somebody intent on using concentrate might feel that there were difficulties of supply around about that time.

A. I would agree with that. I mean, we were quite clear that we were not able to provide enough concentrate. We couldn't meet the aspirations and we were always chasing this moving target.

Q. Yes. Can we look on to the next section, which is about

commercial products in Scotland. You have done your best to list those as well.

We can see it is really over quite a long period. One can do all sorts of exercises with these figures, Dr Foster, and trying to work out for the period of years, 1979 to 1982 inclusive, which is obviously a period that's of interest to us from the point of view of looking at what happened at Yorkhill, the first problem, if you are trying to do that from table 19, is that obviously these are financial years, not calendar years, but trying to approximate, therefore, for 1979 and 1982, by assuming that the usage is equal throughout the 12 months, which no doubt it's not, and get commercial usage for that four-year period and then go back and look at table 16, there did appear to be a slight discrepancy in that your figure from the information you held, or SNBTS held, about the use of commercial product seemed to be slightly higher than our figures in an appendix 1 of the preliminary report. Is that right?

A. Yes, and one possible explanation is that your figure is usage and our figure is purchase.

Q. Right. Okay. Another explanation, and I think Dr Hay said this, is that the data may be incomplete?

A. Yes, that may be another explanation. One other point

to bear in mind is that Factor VIII has a shelf life of two years, so if you purchase it in one year, it might not get used for the next year or even the year after that. So trying to match these figures equally across ussage and purchase, they may not end up in the same columns.

Q. Yes. Just for the record -- I'm not sure if I made this clear -- some of this is rather difficult material with which to work but your figures are slightly higher than UKHCDO, and you say one explanation may be that their figures are use and your figures are purchase?

A. I'm sure their figures are use and our figures are purchase.

Q. Yes. Then moving on to the next page, you have given a breakdown in table 20 on a regional basis of the purchase of commercial Factor VIII concentrate. Were these figures obtained at the time, Dr Foster?

A. They were obtained by Professor Cash and I would need to go back through the minutes of the various meetings just to see when he obtained them, and perhaps you could maybe put that question to him but they were close to the time, yes.

Q. I mean, I suppose opening up before us is another area in which there may be discrepancy, and that is that what was being said at meetings by way of information about

amounts purchased might not have been the same. You hear all sorts of reasons why people might have the wrong figure in their head; you might get a different figure from a regional transfusion director from a figure you would get from a hospital pharmacist.

A. I think this wasn't at all straightforward.

Q. No.

A. I think you have probably recognised that Professor Cash brought in Dr Stewart later on to try and get a better grip on this and made some progress. So it was a difficult area to try and get a handle on.

Q. Rather than worrying too much perhaps about mathematical accuracy and trying to get all the figures to balance, which is not easy, we can certainly understand the general picture, if we look at table 20, which is that there is commercial Factor VIII concentrate being bought in Glasgow in 1978 to 1979 and 1979 to 1980, and then at more or less the same level, 1980 to 1981, slightly dropping, 1981/1982.

Comfortingly that does seem to reflect the information we are given about use and which we reproduced in appendix 1 to the preliminary report. The figures no doubt are not the same but the pattern is similar. Yes. Then for Edinburgh, no commercial purchases 1978/1979 or 1979/1980, and that again fits

with what we have heard about Dr Davies and his policies. Then small amounts of commercial material from 1980/1981 onwards.

You no doubt know this: Dr Ludlam has given us a table detailing patient by patient those who received commercial concentrate and an explanation of why.

Then on to the next page, you have given us some percentages, that reference at the end of the first paragraph to imported Factor VIII concentrate being used at the Royal Hospital for Sick Children in Glasgow comes from the minutes of the meeting on 29 November 1984, which I think was attended by Dr Brenda Gibson, and she reported. In fact, what she said, I think, Dr Foster, was that imported concentrate had been used until recently. You have interpreted that as perhaps meaning 1984.

You go on to talk about the incidence of overt non-A non-B hepatitis and you say that:

"For the period 1980 to 1982, SNBTS Factor VIII concentrate was associated with the lowest degree of overt transmission of NANBH in the UK."

I thought we should just look at that. That's [SNF0010948]. Can we go on to page 8 of this document, please. Is this your source, Dr Foster?

A. That's correct.

Q. Can you just explain to us where you take the information from, please?
A. Well, the table shows the reach of a number of three years here, the number of patients treated with various products, various concentrates, both commercial and material from ourselves and from NHS in England, and if we look at the number of cases of non-A non-B hepatitis recorded here, which is kind of in the centre of the table, then in those three years there is only one case for the Edinburgh concentrate, and the other products, as far as I can see, with the exception of Speywood's humanate, which is only used in a small number of patients, have more cases of non-A non-B hepatitis associated with them.

Really, all I'm saying is that is all the information that was available at the time and this is the information that people would have been trying to make an informed decision on.

Q. Of course, as you say yourself in your paper, this is overt non-A non-B hepatitis?
A. That's correct.
Q. So this is people who actually got ill?
A. Yes, people turning yellow or whatever they do.
Q. If we go back to the paper, please, back to page 63, to the question of stock in fact, you say that when

Dr Perry looked into questions of stock, he found that in November 1982 the stock had stood at approximately 5 million international units and had risen to approximately 7 million international units by November 1983.

I think, just so that we can actually see that, we should look at [SNB0073984]. As far as he says, there has been a steady increase in stock over the past year, in a year which was not particularly outstandingly productive. So by this point, certainly as assessed by Dr Perry, there seems to be an excess annual output and understandably his concern is that you don't want to reach a point where batches are actually outdating or batches on the shelves passing their use-by date and having to be disposed of?

A. Yes. I should perhaps just like to say that we have already seen the stock position at PFC, where we had figures for the end of each year, what the stock was. Unfortunately, we don't have similar stock reports for each of the regional transfusion centres. So this memo is really the information that we have to give us some sense of what stockholdings did exist at this time.

Q. Well, yes, Dr Perry does refer to other documents and trying to find the other documents to which he refers. Some of them are charts about where within PFC

particular material was, you know, what stage it was at. But there is also a document [SNB0073985], so the next in sequence, that I think goes with this. You see, that looks like his writing. Is that Dr Perry's writing?

A. No, this is Mr Grant, who is our production manager. It is 1983.

Q. Yes, November 1983. Could we go on to the next page, please? Yes. Still Mr Grant?

A. Yes.

Q. Did you have this page when you were --

A. No.

Q. All right. I'm not quite sure how we -- I know how we have it but we seem to have it following immediately after Dr Perry's memo.

A. Presumably this is where he gets his 7 million.

Q. Yes. Quite a big stock in Glasgow.

A. I think that's in the memo. It talks about a large stock in Glasgow.

Q. Yes. I don't think he gives any actual figures, though. That may be wrong.

A. I think it's in the memo. It says 4.5 million, I think.

Q. I think the 4.5 million maybe comes next. Can we go back to the memo? That's [SNB0073984]. It is quite interesting. If we hold in our heads the Glasgow figure, which is 900,000 international units, and go

back to the memo at 3984, this is November 1983. I think that's a one-page memo, is it? So then if we go back to your paper --

THE CHAIRMAN: Could you just pause on it until I read it?

MS DUNLOP: Yes. Sorry, we need to go back to the memo. [SNB0073984].

THE CHAIRMAN: Yes, he is presuming that the increase in stock levels reflects an excess of production over demand but, of course, present demand can mean a variety of things and if Glasgow, for example, were holding SNBTS material in stock but using commercial material at this time, one would get a divergence of this kind. It wouldn't just reflect in excess productive capacity.

A. That's true, yes.

THE CHAIRMAN: So it needs quite a bit of drilling into the material to find out precisely what the explanation was.

A. Yes.

THE CHAIRMAN: I really would like to see the histograms and so on, if I could, because there clearly are stories here that are not coming through in particular clarity. I don't know how far we have to go, Ms Dunlop.

MS DUNLOP: I was only looking at this, sir, because Dr Foster had made the point about what was available in Glasgow in his paper and I looked for the surrounding documentation and I found the list in handwriting which

shows what the stock in Glasgow was in November 1983 and it's therefore remarkable, as Dr Foster goes on to say in his paper, in May 1984 a stock of 4.5 million international units is reported in Glasgow.

THE CHAIRMAN: Yes.

MS DUNLOP: That's really the point.

THE CHAIRMAN: Yes.

MS DUNLOP: I do not understand that. It's a very big rise.

THE CHAIRMAN: Well, it would suggest to me immediately that the reporting of data was not particularly reliable. That's the first thing one would consider because otherwise the explanation has to be pouring something like 3.6 million units from SNBTS into Glasgow during a relatively short period.

MS DUNLOP: Yes.

THE CHAIRMAN: And I think that might have been noticed.

MS DUNLOP: Well, indeed.

A. I think if you could go to the letter of Hopkins, it is possible it's somewhere where Hopkins does say that they have looked again and revised their figures.

MS DUNLOP: I don't have the number for that at the moment. We have looked at it already. It is a very memorable letter because of the terms in which it is expressed.

THE CHAIRMAN: This is sitting on a great big bundle.

MS DUNLOP: Yes. Certainly, I think so. Maybe we could

find it. It is a letter of 3 May 1984, please.

I should say, sir, the histograms are not very illuminating. For a start they are rather faint and they do just tend to show where in the facility various bits of stock are, rather than where in Scotland, which is perhaps more interesting for our purposes.

THE CHAIRMAN: I keep hoping for an easy way to communicate some of this information, Dr Foster, but I have been frustrated so far.

MS DUNLOP: Here we are.

THE CHAIRMAN: [SNB0074655].

MS DUNLOP: It's my mistake, sir. It's a different letter. It's the one that refers to using the A74 or the A1. Which is memorable too, but not as memorable as the letter about the Picts.

THE CHAIRMAN: Oh, yes, the A1 letter is earlier. The A1 is suggesting that it might just be put on a truck and sent down, yes. You don't want the December 1984 letter?

MS DUNLOP: Well, it was just that I think because Dr Foster has referred to this letter of Dr Hopkins, Dr Foster wanted to see it to see the reference to the 4.5 million, and there it is and it's coming from Law.

A. I think there is another correspondence somewhere here where Dr Hopkins comes back and says, "We have looked again and we have actually discovered we have got more

Factor VIII". That might explain why some of the figures don't seem to change rapidly over a period of time, that he didn't have quite a good accurate figure of what was in the stock when he was communicating to Dr Perry. Dr Perry was dealing with this himself. I had nothing to do with it. So again, this is a topic you might want to discuss with him if you want to understand it better.

MS DUNLOP: Perhaps the only thing we can take from it Dr Foster is that around about this time there does seem to have been a large stock in the West of Scotland and I think that's about as far as we can get, possibly, which had risen greatly over a six-month period or possibly there have been errors at some point, and the rise is not as great as it might at first appear.

But you go on to narrate in your paper that the stock at this point was so high that 2.1 million international units were transferred to BPL. Thank you.

Then 1983/1984 to 1987/1988 which I don't particularly think we need to go into at the moment, and likewise the next section, 1988/1989 and 1989/1990 and so on. I wonder if we could just move forward to section 10, which deals with other countries. This is page 66.

Some description of what happened in England and

Wales. Go on to the following page, please. Table 22 is your comparison between fresh-frozen plasma collected in Scotland and what was collected in England and Wales, and we can see quite a difference there. Then the paragraph at the bottom, you cover what you have already described, which is that decision to build at BPL rather than use PFC to fractionate English plasma.

Then on to the following page. You illustrate what happened in one part of England, the West Midlands Regional Health Authority. Is that because Dr Perry used to be there and had easy access to the material?

A. No, this is Professor Franklin's papers from the time he was a haemophilia doctor in Birmingham.

Q. You tell us what to take from the table. Maximum contribution from BPL to West Midlands of a little over 50 per cent in 1983 and 1984, when in Scotland, SNBTS was supplying 94 per cent and over 99 per cent. A marked increase in the use of Factor VIII concentrate in 1986 following the introduction of heat-treated products, and then a very high proportion of commercial Factor VIII in 1985, 1986 and 1987.

You say:

"Supply from BPL was at its lowest during 1985 to 1987. Falling as low as 14 per cent and 15 per cent in the West Midlands region in 1985 and 1987 respectively."

On to the next page, please:

"Commercial Factor VIII concentrate that was safe from the transmission of Hepatitis C was not approved for use in the UK until December 1989."

So significantly beyond the time when the NHS in England and in Scotland had achieved that.

Other countries. Interesting to note the relative rates of blood donation. The most blood donations per thousand population appear to have been collected, at least in 1986, in Denmark, 79 blood donations for every thousand people; second Belgium, third Luxembourg, fourth France and fifth Scotland at 59 donations per thousand people.

I suppose everybody who worked for SNBTS was a blood donor, were they?

A. I don't know.

Q. Did you only give plasma or were you a blood donor as well?

A. I gave blood and plasma but then I stopped going because I had an illness and I didn't want to go back.

Q. I'm only thinking, because Professor Leikola told us when he was here that he gave blood, I suppose as much to test the systems as anything else.

Can we then move on to the next page, please? We revert to something that we saw this morning. If we

look at the third paragraph, countries reporting being self-sufficient according to WHO criteria, and this is reverting to the definition that we looked at this morning:

"The United Kingdom reported being self-sufficient according to its own definition."

We can see that definition again. We looked at that this morning. You say:

"According to the WHO definition, England and Wales never achieved self-sufficiency at any time."

Belgium and Switzerland both depended predominantly on freeze-dried cryoprecipitate, and you go on to tell us that continued use of unheated freeze-dried cryoprecipitate in Switzerland was associated with HIV infection in 67 people with haemophilia. The population of Switzerland being about, I gather, 7.7 million. In Denmark -- we can read that.

And conclusions --

THE CHAIRMAN: I want to understand the definition of self-sufficiency. Does it mean that if I plant one courgette plant this year, I can claim to be self-sufficient, provided I can get the other needs from Savacentre down the road.

A. That's what the UK Government definition seems to imply from 1990. As long as you prefer the Savacentre.

THE CHAIRMAN: Yes. And most times of the year that would be so since my plant would either be immature or dead.

MS DUNLOP: Most importantly for the purposes of the Inquiry, Dr Foster, the two paragraphs in your conclusions that begin with an "if", firstly:

"If cryoprecipitate is accepted as having been suitable for the treatment of Haemophilia A when there was a shortfall of Factor VIII concentrate, sufficient Factor VIII was supplied by the SNBTS to provide treatment at the average UK level throughout the period from 1975/1976 to 1989/1990, except for 1982/1983, but if cryoprecipitate is considered to have been unsuitable, then you say:

"Supply from the SNBTS did not fully match the level used in the UK until 1983/1984."

THE CHAIRMAN: Ms Dunlop, I think it's time for a short break.

MS DUNLOP: Yes, absolutely. I think we don't really need to take any more from this paper, sir. We have reached the conclusion. Perhaps we can just look at it briefly when we resume and then go back to the statement.

THE CHAIRMAN: What format does your data stand in? Is it Word or by any chance could it be put into a different format and converted into tables and diagrams and so on?

A. It's in Word at the moment and I can't claim to be adept

at formatting anything, so I would rather somebody else did that but I don't see why not.

THE CHAIRMAN: If you can make it available, I think we can find the resources to manage it.

(3.21 pm)

(Short break)

(3.40 pm)

THE CHAIRMAN: Dr Foster, could we look at table 16, please, for a moment?

In that you have set out the Factor VIII production.

PROFESSOR JAMES: 1182.

THE CHAIRMAN: Sorry, thank you. At SNBTS from 1979 to 1985, and these are figures, as I understand it, that are available to you within SNBTS.

A. That's correct, yes.

THE CHAIRMAN: If we look at the second column, we have the amount of SNBTS Factor VIII used clinically year by year and we compare the two, and making allowance for 1980, when the use exceeded production by a small margin, it appears that SNBTS production was about 9.5 million units more than use over that period. Where did it go?

A. Well, 2 million units went to England. 2 million units went to England.

Q. To England, right?

A. Yes. Then when we introduced heat treatment, there was

a yield penalty because we heated the stock of material we had.

THE CHAIRMAN: That I remember. You drew it all back in.

A. That's correct. Then when we made a transition to the product that was heated at 80 degrees, we actually stopped production for about six months or longer before we introduced that product and the stocks there were left over from this allowed us to do that.

THE CHAIRMAN: So they were all recycled, were they?

A. They were all used one way or another, yes.

THE CHAIRMAN: I can understand that up to a point. The difficulty was that heat treatment was 1984 onwards and predominantly it was the first half of 1985 that the stocks were drawn back for reprocessing, as I understand it.

A. That's correct, yes.

THE CHAIRMAN: So that might deal with the very end of the history, as it were, but quite a lot of that surplus has built up in the middle section of this table, if one looks at it. We have got in 1981 an excess of 2.1 million units of production; 1982, an excess of nearly 2 million units of production; 1983, an excess of over 4 million units of production; and I rather recollect that again it was in 1984 that the major export, if I can call it an export, of material to

England took place.

If that impression is correct, there is still a very considerable excess of production over use in the middle part of this table and it does still raise the question: where was it? Where did it go?

A. We would have to try and go back and look at that in more detail, if that is what you would like us to do, but my feeling is that when we heat-treated the Factor VIII, we would have a yield penalty of about 20 per cent. Then we increased the heat treatment, so we had an even higher yield penalty, and it's conceivable that there were some batches that didn't withstand heat treatment that didn't get used, and then we had a period where we stopped production for about six months or so while we developed the heat-treated product at 80 degrees.

So all of that taken together I had assumed would accommodate that but I can't say for sure that was the case.

THE CHAIRMAN: I would be happy if that were the explanation but my difficulty is timing because I think it was November 1984 that the experiment with heat treating material was carried out, following the information obtained at the conference on the continent, and you discovered in PFC that you could heat treat the

intermediate Factor VIII without significant loss of activity and in the event that met the criteria for AIDS inactivation. Then there was the development, largely in England, of the extra heat-treated process, the dry method, that was adopted in Scotland. But that was well into 1986, was it not?

A. That's correct, yes.

THE CHAIRMAN: So that can't explain this build-up of data.

A. My -- and this is very, very rough -- memory is that we had about 1 month's supply of Factor VIII that we called from stock and we heated at the end of 1984/early 1985 and, because of the yield penalty and possibly increased usage, I'm not sure, that lasted us almost through 1985, before we then moved on to the next stage, which was the product heated for 24 hours at 68.

THE CHAIRMAN: Could you look at it again? Because my current impression is that these factors you point to would be a very good explanation of what happened in 1985 and 1986 and 1987, but it leaves rather a gap in one's understanding of what appears to be significant excess production as against use in the middle parts of your table. If there is a good explanation for it, I would be delighted to hear it.

A. Yes. The other point I should perhaps mention, that has just occurred to me, is that we did have a three months'

shutdown at the end of 1984, when we stopped production altogether. So again, as we talked about earlier, there were periods when we stopped production to make changes to PFC, and there was quite a significant period of shutdown at the end of 1984.

THE CHAIRMAN: Just as there had been in 1983?

A. Exactly.

THE CHAIRMAN: But in 1983 you were still able to produce more overall than the demand for that year.

A. Yes.

THE CHAIRMAN: So at the moment I have got a concern and it is that there may have been an unproductive production, if I can put it that way, in the sense that PFC was maintaining a high level of production but the Factor VIII product was not finding its way into patients. That could be for a number of reasons: product selection could have been one of them by the clinicians; another could have been the failure to use the product before it became dated; all sorts of theoretical possibilities that seem to emerge out of the raw data, and I would really like that to be looked at.

A. Yes. I have to say I'm not aware there was ever any surplus Factor VIII that never got used and that was disposed of. That's not something I have ever heard of but we could look into that.

THE CHAIRMAN: I would like an answer to it since one can't just look at the raw data here and immediately assume that there wasn't a problem. You might, of course, not have had any returns since -- as you know, I have got some concerns about the data that was returned, centrally, before Dr Stewart came along.

Now, Ms Dunlop.

MS DUNLOP: Yes, thank you, sir. I suppose the other possibility, Dr Foster, is that the UKHCDO data might be incomplete, their figures for how much was used.

A. Yes,I have taken these figures from your preliminary report, so it goes back to those data.

Q. Yes, and as we understand Dr Hay's evidence, they ask for usage to be reported to them but I suppose it's conceivable that there could have been some usage that, for whatever reason, someone omitted to report to UKHCDO. That would be another contributing factor.

THE CHAIRMAN: Yes, that just leads us eventually to conclude that the data is so unreliable that no one can form any views on the basis of it at all. I'm sure Mr Anderson would be delighted to have a finding like that.

MS DUNLOP: Dr Foster, we have your conclusions. Just so that we understand them, if we look at page 71 again, it was the second paragraph that begins "if", where you say

that if cryoprecipitate was considered to be unsuitable, supply from the SNBTS did not fully match the level used in the UK until 1983/1984. Despite this apparent shortfall in supply of Factor VIII concentrate, production of Factor VIII concentrate at PFC exceeded that amount of concentrate used throughout during 1979 to 1985, except for 1980, when the amount use doubled, I think that is, in one year. That is table 16, is it?

A. Yes.

Q. Just so that we understand that. We can read the rest for ourselves. We know that most commercial Factor VIII purchased in Scotland in the early 1980s was obtained by haemophilia centres in Glasgow. It was comparable in quantity to the unused stock of SNBTS Factor VIII concentrate that had accumulated at the Glasgow regional transfusion centre?

THE CHAIRMAN: Is that 4.5 million units or what?

MS DUNLOP: Well, if you added up the commercial purchases from Glasgow in the early 1980s, they would be a lot less than the 4.5 million in fact, but the 4.5 million is 1984 and the commercial purchases are around about 0.9 and 0.8, I think, Dr Foster, if I recollect correctly, page 62 --

THE CHAIRMAN: Does that include The Royal, Ms Dunlop?

MS DUNLOP: I don't know, sir, this is Dr Foster's table.

Commercial Factor VIII concentrate, purchase of commercial Factor VIII concentrate by region. I imagine it would be both the Royal and Yorkhill.

PROFESSOR JAMES: Table 16 specifically excludes Koate from the Royal.

MS DUNLOP: Well, this is based on SNBTS information about purchases, sir, so it is actually a different source of information altogether. Table 20 is based on information held by SNBTS prior to the publication of the preliminary report. So the total purchases in Glasgow from 1978 to 1983, as it were, 3.96 -- I think that's the comparison you are making, is it, Dr Foster?

A. Yes, I may really have made a mistake here and it's possible that I should have said "use" rather than "purchase" and was referring to table 16. Presumably it was purchased before it was used. So in that sense it was purchased, but it is not in our data of purchases.

Q. Yes.

THE CHAIRMAN: Dr Foster, it should be no surprise that I don't expect any of these tables or any sources of information always to be right the first time round. If you want to revise any of it --

A. I'm not sure I do.

THE CHAIRMAN: If you just let us know.

A. I'm meaning table 16 when I say "purchase", assuming

that the material wasn't provided free of charge before it was clinically used, then it was purchased.

THE CHAIRMAN: I repeat, I'm perfectly content for you to correct anything that you think needs to be corrected.

A. Thank you.

THE CHAIRMAN: But not to speculate. I wouldn't want you to change something just on an off chance.

A. Thank you.

MS DUNLOP: It was the last sentence on page 71, Dr Foster:

"Most commercial Factor VIII purchased in Scotland in the early 1980s was obtained by haemophilia centres in Glasgow."

Is that not table 20? It certainly seems to be vouched by table 20 on page 62.

A. Yes, okay, I'll defer to that. Yes, table 20.

Q. No, you tell me. It's just that table 20 seems to make that point. Glasgow is quite a long way in front. Is that right?

A. Yes, I would accept it's table 20, yes.

Q. Right. Then we have looked at such information as we seem to have about what was sitting in Glasgow in November 1983 and May 1984 but with the health warning that that's rather hard to understand. Then you say:

"Supplies were sufficiently strong thereafter to

avoid commercial Factor VIII concentrate being purchased in Scotland until 1988 to 1989."

You have given us six bullets to show how SNBTS achieved what they achieved even without plasmapheresis.

THE CHAIRMAN: Just contemplating the range of problems that there might be, Ms Dunlop. But, of course, where we have data with different reference periods, calendar years on the one hand, financial years on the other and data for purchases at some level and data for use at others, and really at the moment irreconcilable stock figures, it all becomes extremely difficult to rationalise and present a comprehensive picture, Dr Foster.

A. I quite accept that and I obviously have had activity putting those figures together in the first place because -- it is a long time ago and a lot of the raw data are not available.

THE CHAIRMAN: I'm sure I'm extremely grateful for the work you have done because I do know how difficult it has been for us to try to put figures together, but let's see if we can get even better in time.

MS DUNLOP: Certainly, sir, some bits of it -- and I accept at a high level -- some bits fit with the narrative that we have heard from other witnesses about the patterns of usage in different parts of the country.

THE CHAIRMAN: I'm not absolutely sure. If we look at table 20 and take a per capita approach into account, Edinburgh's use of commercial products in 1980/1981 onwards, doesn't look as small, as it were, given that Glasgow's population is several times that of Edinburgh; lots of factors that might have to come into the assessment of the significance of the data.

It certainly doesn't look as if there was a predominant use of PFC to the exclusion of commercial products in Edinburgh.

MS DUNLOP: I suppose, sir, the relevance for the Inquiry would be in looking at Professor Ludlam's data about how many patients were infected by commercial material, which, if my recollection is correct, is, one. So as between Glasgow and Edinburgh, we are looking at a much higher rate of infection from commercial product in Glasgow than in Edinburgh.

THE CHAIRMAN: I know, which may be explained on the specifics of the commercial product, I don't know.

MS DUNLOP: Yes. Sir, we have finished Dr Foster's paper and I obviously have to go back to his statement and cover some other matters that he raises there, but I think it would be better done tomorrow when we might be fresher.

THE CHAIRMAN: You might be right.

MS DUNLOP: If I can put it like that.
THE CHAIRMAN: Ms Dunlop always knows when I'm becoming less than fresh.
MS DUNLOP: I think I was referring to myself, sir.
THE CHAIRMAN: I take it as a general comment that probably applies to everyone.

I do like figures. I'm an accountant after all, but yes, they get a bit much after a time.

Tomorrow morning.

(3.59 pm)

(The Inquiry adjourned until 9.30 am the following day)