Wednesday, 23 March 2022

(9.59 am)

Presentation to the Inquiry on domestic production of blood products in Scotland and for Northern Ireland by MR BOUKRAA

SIR BRIAN LANGSTAFF: Yes?

MR BOUKRAA: Good morning, sir. We are turning now to demand estimates. For those who are following in the written note that I referred to yesterday, we should be in section 4. We are going to start by going back in time, compared with the documents that we were looking at yesterday afternoon, to the early 1970s.

The focus is going to be on Factor VIII because that was understood to pose the greatest challenge. Before I move the chronology, sir, I should say we've used the word "demand" in the written note and I'll be using it during this part of the presentation because that reflects the terminology in the documents from the time.

I think this may have been picked up last week during England and Wales but "demand" is a word that might need a bit of unpacking. It brings with it some questions, whose demand? What information was that demand based on? All sorts of other questions no doubt, but we've used it because it was in some of the

documents. When we get to look at some of the annexes that accompany the written note, in which we've set out the use of Factor VIII and IX, we've used the word "consumption" rather than the word "demand" but I just thought I'd flag that at the start to explain why I'll be using that word in this portion in this presentation.

SIR BRIAN LANGSTAFF: The two are, I suppose, different in that consumption is what is used, demand is what is asked in order to be used.

MR BOUKRAA: Yes. Yes. That's right, sir. They can sometimes be used almost interchangeably. We can sometimes see when demand has been estimated, what it seems to refer to is how much Factor VIII is going to be used, but it's quite right, sir, they are two different words. We've tried to use them in different ways in the presentation.

SIR BRIAN LANGSTAFF: Thank you.

MR BOUKRAA: So last week with the England and Wales presentation you looked at the meeting and the report which came about in March 1973 with the Expert Group on the Treatment of Haemophilia. I'm not going to go back to that. A couple of points I would note about it relate to attendees. It's worth just noting, sir, that Dr Maycock was a member of that group. Mr Watt,

his counterpart in Scotland, was not.

The meeting and that group was attended, I believe, by Dr McDonald on behalf of the Scottish Home and Health Department but not Mr Watt. It's just something to bear in mind when we look at some estimates that were being made in Scotland.

We turn now to a document which was prepared by Mr Watt around that same time as that expert group was considering demand for Factor VIII and, Sully, it's PRSE0003153.

So you can see from the date of this document at the bottom, 12 June 1973, prepared by Mr Watt, title "Plasma Fractionation in the United Kingdom. A Personal Appraisal". You'll see in the top right-hand corner, this is said to be a draft. We haven't been able to find an updated or more finalised version. Compared to the other document from Mr Watt that we looked at yesterday, this one is easier to follow. It seems to be more of a finalised document.

In terms of its timing and what it was prepared for, it's not completely clear from the chronology. It comes about eight days before that 20 June meeting of the joint steering committee that we looked at yesterday.

If we go over to page 3, and I'm just going to

highlight a few passages in this document, but it is quite an important one. If you start with the introduction, you can see that Mr Watt introduces this paper by referring to communications that he has had with a number of different people, including counterparts in Europe, America, Australasia. If we look at the second paragraph in this introductory passage, Mr Watt says:

"The population in the United Kingdom is estimated at 60 million. Of this, for purposes of discussion, the Scottish population is estimated at 5 million."

The estimated number of haemophiliac patients, ie patients with haemophilia A, is 3,000.

Now, I know that figures for population of the UK came up last week. My understanding is that, in fact, the population of the UK around this time was closer to 56 million, I think about 50 million in England and Wales, 5 million in Scotland, about 1.5 million in Northern Ireland. It may be that population estimates were not quite as clear at the time. It may be that when different figures are talking about UK population, they've got different numbers in mind. It's not always clear from all the documents but at least Mr Watt here sets out what he

understands the UK population to be at this time.

If we could have the whole page or rather the second half of the page, this is really just to note, sir, because we'll come back to it later, the third paragraph in this page refers to a policy on the use of cellular components, which I understand to be a reference to the use of red cell concentrates. We'll come back to that when we look at supply from PFC a little later.

At the bottom of this page, Mr Watt gets on to AHG, and he says:

"The official estimate of the need for fresh frozen plasma for AHG preparation is given as 10 donations [per] 1000 population."

Now, it's not totally clear to me which official estimate Mr Watt is referring to there. It's worth noting nonetheless. Then we're going to continue with the rest of this passage. It says:

"On this basis the Scottish plasma availability is correct. It is my personal belief that this figure [ie 10 donations per 1,000] is probably 30% too low since it presupposes an overall process yield of 40%. These calculations do not allow for:

"Increased use in domestic therapy."

I pause there, sir, to draw a contrast perhaps

with some of the work from Dr Biggs that was referred to last week and we'll come back to, which suggested that domestic therapy was not likely to lead to increased use.

Next:

"The need for a proportion of the production as low yielding, high purity fractions.

"A probable drop in yield, of Intermediate concentrate, to 30% when made on a realistic scale", ie when you start making more of the product, when you scale it up, it is likely that yield is going to drop from what it is when you're making smaller amounts.

He then says:

"Allowing that this argument is correct, Scottish need for [fresh frozen plasma] becomes 15,000 donations [per] million rather than the 10,000 donations now becoming available. This would provide (at 30% yield) about 4.8 million plasma units of AHG per annum for the country's need; approximately one million [units per] million population or 20,000 [units per haemophiliac per annum].

"It is my belief that a production of 15,000 litres of fresh frozen plasma is well within the capacity of the Scottish [RTCs] without [needing to use] plasmapheresis."

Now, there are number of figures that are set out there that will be worth noting and bearing in mind. It is also worth picking up from this passage, and this is something we will come back to as we look at the other documents. Demand estimates were quite often expressed using number of different metrics at this time, they are sometimes expressed in terms of the number of donations that are needed, they are sometimes expressed as the amount of Factor VIII in terms of units, that's all kinds of Factor VIII per head of population. They're sometimes expressed as the amount of Factor VIII that's needed per haemophiliac patient.

I've, at least, found it easy to not always be totally clear which is being referred to. I point that out because it's something that we'll see also in some later documents.

If we go on to the next page, please, Sully, page 5.

SIR BRIAN LANGSTAFF: The unit is used in the second -- in the paragraph in the middle of the page --

MR BOUKRAA: Yes.

SIR BRIAN LANGSTAFF: -- here is 1 million pu per million population. That's "plasma units", presumably?

MR BOUKRAA: Yes.

SIR BRIAN LANGSTAFF: What is a plasma unit?

MR BOUKRAA: My understanding is that it is a unit of Factor VIII. That seems to me to make the most sense, and that equates to about a unit of Factor VIII.

SIR BRIAN LANGSTAFF: I'm not sure that can be right, can it? Oh, I see. Plasma units of AHG. Right. I now see it. Yes. He defines it himself, doesn't he, in the second-last line.

MR BOUKRAA: I think that's right.

SIR BRIAN LANGSTAFF: So a "pu" there is a plasma unit of antihaemophilic globulin.

MR BOUKRAA: Exactly, yes, and he refers to that both in terms of million population.

SIR BRIAN LANGSTAFF: Yes.

MR BOUKRAA: So that's one per million, ie one per person, because the Scottish population at this time was around 5 million, that leads to 4.8 million units for the whole of Scotland.

SIR BRIAN LANGSTAFF: Yes.

MR BOUKRAA: If we go over the page to the top, he refers here to, at the top passage, to the number of litres of plasma that he thinks are going to be necessary, suggesting that the figures may have to increase to reflect his estimate of need AHG.

If we go down to the middle of the page, we have

it here actually, "Estimate of English Need", Mr Watt moves away from just looking at Scotland to apply his estimates to England, I presume that means England and Wales, perhaps also Northern Ireland, and he says this:

"Since there should be little difference between the community need of England and Scotland on a proportional basis it would appear that the Scottish figures should be applicable to England; especially since these figures are in close agreement with those established in other countries."

That leads him to a figure for England, or probably England and Wales at least, of 48 million plasma units of AHG, 48 million units of Factor VIII, split probably across all different types of Factor VIII.

He then applies that -- if we can go down, please, Sully, to the last part of the page -- to UK figures and his estimate is that the total UK requirement for the two plasma factions, one of which is an albumin product and the second one is AHG, is 53 million plasma units. At the bottom of the page, he suggests how many litres of plasma per annum are going to be necessary to obtain in order to meet those requirements.

If we could go over the page, please, Sully to page 6, and then about the middle of the page, 5.20, "Summary of Need for Plasma". Now these two paragraphs aren't -- might not be thought to be all that clear. They're worth looking at alongside each other, particularly the first sentence. He says:

"The amount of plasma (200,000 litres or 1 million donations) required for AHG preparation is of no account in consideration of overall need."

I think that that sentence can be understood in light of the next paragraph, where he says:

"The critical figure of 400,000 litres required for PPS [ie albumin production] should ... be available from when existing [productions] ..."

Sir, maybe you can assist on this more than I can. I think what he's saying is that as long as you are getting enough to meet the albumin requirement, you should also be getting enough to meet the Factor VIII requirement. That's my understanding of these two passages read together.

And if we go down, then, to the paragraph we can see at the bottom here, Mr Watt then starts applying these figures to fractionation capacity, both within Scotland and also England and Wales. And he says, and this links back to what we were looking at yesterday:

"BPL and PFC are each specified for 70-80,000 litres of plasma per year. It is my opinion that BPL production could be increased to about 150,000 litres, but further increase would appear impossible on the present site and could hardly be justified."

He then refers to a difference of more than 250,000 litres that need to be accounted for.

At the bottom of this page, he says:

"Assuming that Scotland's resources will not be misused to subsidise England, a dual standard of clinical availability could come to exist."

If we go over the page, he sets out another comment:

"In my opinion, this intolerable situation could not be maintained, enough plasma to meet real need will be collected in England and, unless prompt action is taken, UK fractionation and finishing capacity will be inadequate to meet demand."

Before we go on to the next passages, worth just remembering the timing and context of this document. It's June 1973, so it's when the planning for the PFC that we looked at yesterday has already taken place in the late 1960s, and the facility is in the process of being built. It's getting towards the end of its

construction. He appears to be, Mr Watt, considering the possibility that there might still need to be a change of plans which might include further expansion to PFC.

He starts by ruling out, in paragraph 6.10, a third centre in the UK. He then says in 6.20, that:

"The PFC at Liberton has process potential to handle up to 300,000 litres of plasma per year but is unable to finish PPS at equivalent rates. However, the construction of premises equal to this task on the Liberton site would appear to be the most economic and most rapid means of achieving adequate fractionation capacity in the UK."

If we go down, please, Sully, to the bottom of the page. I'm moving a bit beyond demand estimates, sir, but I think these passages are worth looking at together. He says this:

"If, as seems certain, the additional facilities should be available as soon as the specified capacity of Liberton is exceeded (ie by the end of 1974). Planning would be required to start immediately, despite the fact that some technical questions remain unresolved. Obviously, this timescale is impossible, but it would seem feasible that, provided planning detail started at once, the increased facilities could

be available on the Liberton site by the end of 1975. Such a programme could be costly since it would involve persuading existing contractors to accept a new contract ..."

But he thinks that should be possible.

And if we then just get -- I'll just pick up the last part of the last sentence here:

"However, in comparison with the global sums involved, this additional expenditure could be recouped in a period of months since each month 'saved' has a current financial implication of approximately £1 million."

I think what he's referring to there is the cost of having to buy commercial concentrates if you're not able to produce enough of them in the UK. So what we seem to have from this document, sir, is Mr Watt coming at his own estimate for how much Factor VIII is likely to be needed both in Scotland and in the whole of the UK, and suggesting that, despite the fact that PFC is coming close to the end of its construction period, the PFC and the English facilities are not going to be enough to meet demand, and he has some suggestions for what might be done in response.

So, soon after this meeting, the joint steering committee on blood products production met on 20 June.

We've already looked at the minutes of that meeting last week -- I think you were also taken to it yesterday, sorry, and you were also taken it to last week, so I'm not going to return. The meeting referred to Dr Biggs' estimate at that time of a need for 400 to 700,000 donations.

We then enter into a period, sir, towards the end of 1973 and into 1974 where there appears to be some disagreement between the Scottish Home and Health Department and their counterparts in England and Wales, the DHSS, about how to approach estimating need for blood products. We've got a number of documents which are summarised in the written note. It's important to be aware that the meetings that took place and the correspondence that happened between the two Departments often related to blood products other than factor concentrates, in particular to albumin products. Nonetheless, some of them do provide some insight into how the different departments were approaching these questions.

There's a document that I'm not going to bring up on the screen, sir. I'm just going to give you the reference for it because you may wish to return to it. It's the 14 November 1973 letter from the SHHD to the DHSS. The reference for it is SCGV0000074_033. The

context of the letter is that the official is concerned that another meeting of this joint steering committee that had last taken place in June 1973 was being postponed, and it seemed because there was a divergence of view between Scotland and DHSS about how to estimate needs, in particular for albumin. But the official sets out some views that are more generally applicable which illustrate the different approaches. One of the things she says, and this is covered also in the written note, she says this:

"The situation has been changed fundamentally within the past year by the commencement of importing blood products, beginning with Factor VIII."

She then outlines two alternative approaches. The first is for the Blood Transfusion Service to attempt to meet the reasonable demands of clinicians. The second is:

"... to accept that we must depend upon a significant level of imports over which we will have no direct control because purchases will be made at hospital level."

Alongside these meetings and this correspondence -- so you'll be aware that Dr Biggs and her colleagues were undertaking further work on demand estimates for Factor VIII. You were taken last week

to the paper which was presented at a January 1974 meeting of Haemophilia Centre Directors. I'm not going to return to that paper, sir. It recorded a suggestion that 500 to 700,000 donations annually were going to be necessary.

I will pick things up in Scotland in the mid-1970s by reference to a meeting of SNBTS and Haemophilia Centre Directors which took place on 11 June 1975. We are going to look at a paper which was prepared for that meeting.

Sully, it is at SCGV0000065_117. Now, this was a paper which I believe was prepared by Professor Cash who at that time was the director of the Edinburgh and Southeast Regional Transfusion Centre. It was an annex to a paper prepared by Major General Jeffrey, who was National Medical Director of the SNBTS, Professor Cash's predecessor in that role.

And if we can just have the passage at the top of the page, Professor Cash sets out suggested figures for donations for fresh plasma. So you can see the title is "Fresh plasma processing for Factor VIII". He says:

"In order to facilitate the detailed planning, at Regional Transfusion Centre ... of targets for the production of fresh plasma destined for the management

of haemophilia A, it is suggested that we should aim at a basic maintenance figure of 12,000 donations per [million] population per annum."

He says that this figure is the upper limit of the MRC estimate and is close to the current usage in some regions.

I won't take you to the minutes of the meeting, sir, but the SNBTS Directors and Haemophilia Centre Directors who were present at that meeting in June 1975 appeared to accept this figure as an appropriate target for donations for fresh frozen plasma.

There is a document that was prepared in 1976 by Major General Jeffrey, National Medical Director of the SNBTS, which is referred to in the written note, sir. I'm not going to take you to it. The title is "Problems of supply and demand". The reference is RCPE0000314_002. It covers a whole range of different blood products. It does provide some useful insight into issues such as the use of red cell concentrates at the time.

It suggests a planning figure for Factor VIII and, by that, I mean all types of Factor VIII, so concentrate as well as cryoprecipitate. Then Major General Jeffrey suggests a figure of 10,000 units of

Factor VIII per patient per year, and we'll contrast that figure with some of the others that we're about to look at.

And I'm going to start with a paper prepared at a similar time in September 1976 by Professor Cash and a colleague. If we can turn to that. It's PRSE0003425.

I'm not going to go into the detail of this because there's quite a lot of detail. I pick it up partly because it was prepared by Professor Cash within just a few years by 1979, who becomes director. So his views on these issues are particularly noteworthy.

If we look at the summary box in the introduction, you can see that the estimates that are in this paper are based on use in south-east Scotland in the 1961 to 1975 period. There's then, in fact, a more helpful summary, I think, of the figures that are suggested two pages ahead on page 3.

If we can then have in the left-hand column, about halfway down, the passage that begins "Hence". That's it, thank you.

Conclusions here are set out, sir:

"Hence we have concluded that the blood transfusion services should consider a production

target of an average of 15 000 units of factor VIII/patient/year with a total UK annual requirement of around 50 million units. Regionally [Regional Transfusion Centres] should aim to process at least 12 000 fresh donations/million people/year."

He then refers to the differences that might exist between regions and he picks up an important point -- or I should say they, because this paper was prepared with Mary Spencely, I presume Dr Spencely.

"These calculations are based on the assumption that 70% of the concentrate used is cryoprecipitate, which is by most standards a high yielding product. Any movement towards completely replacing cryoprecipitate by AHF [ie concentrate], unless counterbalanced by reducing the dose of factor VIII at treatment, will, because of diminishing yields, necessitate a substantial increase in donations. A more appropriate figure in these circumstances would be 20 000 donations/million population/year. This figure would rise further if the volume of fresh plasma obtained from each donation was reduced ..."

That's something that's already happening with the use of red cell concentrates.

Then the conclusion and comment:

"It is difficult not to conclude that

a programme designed to switch completely from cryoprecipitate to AHF will prove to be too costly and wasteful of raw material for the next decade. Consideration should instead be given to striking a balance between both products and perhaps even rethinking the cost-effectiveness of freeze-dried cryoprecipitate."

So we can immediately see, in terms of the number of Factor VIII units that are suggested per patient per year, 15,000, compared to the 10,000, in the Major General Jeffrey paper I referred to, contrasted with the 20,000 figure in Mr Watt's paper, and also the suggestion that, if we're going to be providing more concentrate than cryoprecipitate, the number of donations that will be necessary is going to go up.

That's it for that document, thank you, Sully.

One of the elements in these estimates of demand that you can see in some of the documents we have from the time is about the purpose of haemophilia treatment. There's one document which we referred to in the written note, which I won't take you to, which sets out an apparent view of the purpose of haemophilia treatment. It's a letter written by Mr Watt in February 1977 to a colleague at the York

Hill Children's Hospital.

For your note, sir, it's PRSE0000659 and Mr Watt's suggests that the number of units required for both Factor VIII and Factor IX could only be calculated by the number of units required to maintain the patient in a reasonable state of health and he suggests there was general agreement that this could be defined as health that would allow the patient to maintain a normal sedentary existence.

We get to the end of 1977, the Working Group on Trends in Demand for Blood Products, which was a UK working group, which you were taken to last week during the England and Wales presentation, publishes its findings. I'm not going to go back to that document or repeat all of them. I'd ask you, again, sir, to note the membership, Dr Maycock was a member of that working group. Dr Cash was as well, and Dr McIntyre of the Scottish Home and Health Department. Mr Watt wasn't a member.

The estimate of the need for Factor VIII that's reached by that working group at the end of 1977 is 1,000 units per thousand population, in other words 10,000 units, using the metric we've been using so far.

I'll pick things up now at the end of December

or rather the end of 1979, December 1979. I believe, by this point, Professor Cash has taken over as director of the SNBTS. We can see a changing and, again, increasing estimate of how much Factor VIII is thought to be needed.

Sully, the document is SBTS0000089_120.

You can just see the description of the meeting; attendees, Mr Watt, Dr Cash was in the chair -- I presume he has taken over as director by then.

Then if we just go through to page 4, at the top of the page, section 5(ii):

"Dr Cash confirmed that the Directors should, in their calculations, now assume a target of 1,800 units of factor VIII per thousand population per annum."

So that figure has increased again. The figures that we've seen so far have tended to be 1,000 to 1,500, 1,800, there was also Mr Watt's earlier higher figure. So that's the position as of December 1979, at least in Scotland.

You'll recall, sir, from what we looked at yesterday, by the time we get to the late 1970s, the position as regards UK production, things had started to diverge. So we'd moved from a strong focus on UK planning at the start of the 1970s to, by the end of the 1970s, things had diverged to some significant

extent.

The next document is an important one from January 1981, it's a report prepared by Professor Cash and it's at CBLA0001252. So we can see that it's Professor Cash's document, partly from the initials in the bottom right-hand corner. You can see the date, January 1981. This is note or report prepared for a meeting of Haemophilia Centre Directors and Transfusion Directors.

If we go through to page 3, I'm going to pick up a few different parts of this report, sir, because it's an important one.

The introductory passage is worth just noting. Professor Cash there sets out what he considers the role of the SNBTS to be:

"... to eliminate the necessity for the purchase of factor VIII concentrates for commercial concerns."

He says that there's a need for close collaboration with Haemophilia Centre Directors.

If we could go over the page, please, Sully to page 4, and the passage that begins "Future Developments in Demand", and if we could go down a bit, thank you. This is Professor Cash introducing the section of this report in which he is estimating the future demands. He says:

"This is a particularly difficult problem at the present time, primarily because the practice of Home Therapy is still evolving, the appropriate method of managing patients with inhibitors is unresolved and the unequivocal evidence that haemophilia patients are living longer, thus increasing the overall population and becoming subject to similar disease processes of older age-groups in the non-haemophilia population which are amenable to surgical intervention.

"Despite these difficulties efforts are now required which will enable the SNBTS to formulate long term plans which can, if necessary, be adjusted at a later date."

He then makes reference to conversations that he has had with colleagues within the UK and internationally and, if we go down, please, to the rest of this page, he starts to set out the basis of his reasoning for the figure that he gets to, and he starts with home therapy or severe haemophilia A patients, which forms the bulk of the estimate for demand.

You'll see, sir, that Professor Cash sets out use figures from the time, from different settings, a figure from Oxford, from Newcastle, the USA, Treloar's, and West Germany. We'll come on to see

that he suggests that the figure for Newcastle is an -- forms an appropriate basis for planning demand for home therapy patients, and we can see that, if we go to page 6, please. At the top of the page, there's a summary. Professor Cash says:

"I believe it would be appropriate, for planning purposes, to accept the figures from Newcastle for the single largest contributor (Home Therapy).

"It is probable that this figure has a sufficient margin of clinical flexibility to make it realistic for the next 10 years."

We'll come back later in the paper to the time period in which the demand has been estimated, but he suggests it would be realistic for the next 10 years, and he sets out the different elements of the figure for demand that he believes is appropriate with home therapy as the biggest element in setting out the others, as we can see on that page there.

That gives Professor Cash a figure of 2.75, and that's per million population. If we translate that into the metric we've been seeing in other documents, 2,750, as opposed to 1,800. That was the figure in 1979.

If we go through to page 9, please, we can see in the second half on the page heading "Specific

Proposals for Discussion". We can see the time period that Professor Cash is proposing. He suggests that there's discussion that a target for 2.75 per million population for units of Factor VIII per year be considered as the one to which the SNBTS should aim for the next 5 years, ie until 1986, "with an increment thereafter" of 1,000 units per year.

While we're on this document I would just note very briefly on page 11, there is reference to Factor IX. If we could have the passage just at the top of the page, it links back to a comment I made at the start. Professor Cash says:

"Fortunately, because of the much smaller number of haemophilia B patients than A, the supply of these products is always more than adequate", with an exception that, I think, links to that table.

That helps to explain why the focus of these documents is on Factor VIII more than it is on Factor IX.

Now, this paper was discussed at a meeting of Haemophilia Directors and SNBTS Directors at the end of January 1981. The minute records that the figure of 2.75 million per million population was accepted as a suitable basis for further consideration. It seems that it is then accepted and becomes the accepted

target.

There's one more document I wanted to come to in this section. It's another report from Professor Cash, it's from the following year there he revisits these figures and provides a little bit of comment that allows us to compare them with the figures for England and Wales.

Sully, it's SBTS0000613_003.

SIR BRIAN LANGSTAFF: Can I just pause there for a moment.

MR BOUKRAA: Yes.

SIR BRIAN LANGSTAFF: Can I just understand how the figures play out and see if I am understanding what you've been telling me. You say that the paper which Cash produced was discussed at the end of January 1981, and a figure of 2.75 million, that's million units per million population.

MR BOUKRAA: Yes.

SIR BRIAN LANGSTAFF: If that's so, then what does that translate into, in terms of the targets that were made for the production at BPL in England, which was in the region of 100-120 long term. This would suggest rather more than that.

MR BOUKRAA: It was, sir, and, in fact, I hope the document we're about to look at will help on that front because it compares the two figures.

Professor Cash suggests that his figures, 2.75 and the figure of the NBTS is 2, so if we take a population of say 50 million, that gives you 100 million.

SIR BRIAN LANGSTAFF: Yes. 2.75 gives you 137,500.

MR BOUKRAA: Yes, so a higher --

SIR BRIAN LANGSTAFF: Yes, higher than any other estimate which was ever produced, south of the border.

MR BOUKRAA: Certainly as far as I'm aware, sir, and as far as I've seen, I'm sure that's right.

SIR BRIAN LANGSTAFF: Yes, I see. So I had understood it correctly?

MR BOUKRAA: You had sir, yes.

SIR BRIAN LANGSTAFF: So this was -- this particular meeting in 1981, signing up to a target which was half as much again, roughly, as the target which England thought was the maximum that they might need.

MR BOUKRAA: That's right, sir. It's a big figure. In fact, in the document that we're about to look at, Professor Cash himself describes it as a dramatic increase on his previous figure.

SIR BRIAN LANGSTAFF: Yes.

MR BOUKRAA: There is no doubt, it seems, that it was a higher target than the one that was produced in England and Wales.

SIR BRIAN LANGSTAFF: Yes, it certainly was. Thank you.

MR BOUKRAA: Thank you.

Sully, could we pan out to get the whole of this page. We can see the date in the bottom left-hand corner, 1 February 1982, this is again a figure, a document prepared by JDC, Professor Cash. It's titled "A proposal to Increase the Production of Factor VIII Concentrate in order to Achieve Self-Sufficiency in Scotland for the Next Decade".

Now, we don't need all of this document for present purposes. If we could go to page 3, and the second half of the page that starts "The Need".

Sir, I'll read this out and you'll see that it picks up, I believe, some of the comments that you've just made and reflects them:

"Less than 5 years ago a Committee, created by the DHSS, advised that the basic needs of the haemophilia A population in the UK would be met by the production of [1 million units of Factor VIII per million population per year]."

I believe that's a reference to the December 1977 working group that I mentioned earlier:

"SNBTS representation on the Committee was of the opinion that the figure advised was more closely related to what was believed to be possible with regard to plasma procurement and the fractionation

facilities of the NBTS, rather than a true estimate of what was required."

Now, the reference there to SNBTS representation on the Committee, that may be a reference to the fact that Professor Cash himself was a member, of that working group:

"In any event, it should be stressed that this Committee referred itself to basic needs and did not take into consideration the extensive production of Home Therapy and in particular, the concept of prophylaxis.

"Studies carried out in the last 6 months in Scotland, in association with the Scottish Haemophilia Centre Directors under the aegis of the SHHD, have revealed, when examining world-wide trends, that it would be more appropriate to plan towards the production of [2.75 million units of Factor VIII per million population per year]. This dramatic increase takes cognisance [if we go over the page, please, Sully to the top of the next one] of the introduction of prophylactic therapy, the increased life expectancy of the haemophilia A population with the concomitant increase in surgery for cardiovascular disease, orthopaedic surgery of the elderly and surgery required to manage malignant disease. In addition it

is believed that the proposed target may go some way to meeting the potential needs for bleeding associated with chronic liver disease, which is likely to appear in this patient group within the next 10 years.

"It is significant that the use in Scotland in the year ending 31st March, 1981 was of the order of [1.5 million units per total population] and that is likely to have risen further to 1.7 for the year ending 31st March, 1982."

Now, sir, I may have mistakenly told you that it's in this document that Professor Cash contrasts his figure with the one for NBTS, and my apologies for that. I will get to you --

SIR BRIAN LANGSTAFF: I think he has done, hasn't he? If we just go back over the page, to talk about the DHSS figure.

MR BOUKRAA: Yes, well, he's talking about the DHSS figure --

SIR BRIAN LANGSTAFF: 5 years before?

MR BOUKRAA: -- 5 years before.

SIR BRIAN LANGSTAFF: So the contrast is there.

MR BOUKRAA: The contrast is there, sir. He does also contrast the figure with a more up-to-date one. I will make sure I get you the reference, sir, in that document. I'm sure that it's there.

SIR BRIAN LANGSTAFF: Just before you pass from this, the -- it's not part of the presentation, really, on self-sufficiency, but it may be worth noting that Professor Cash says, in just the last sentence before he turns to paragraph 2.03:

"... the potential needs for bleeding associated with chronic liver disease, which is likely to appear in this patient group within the next 10 years."

So he in February, 1 February 1982, foresaw a significant impact of chronic liver disease arising in that patient group, and that might, probably be because of the treatment they were having.

MR BOUKRAA: That certainly seems to be an inference which is available from that passage.

SIR BRIAN LANGSTAFF: And --

MR BOUKRAA: It would be difficult to explain otherwise what Professor Cash was referring to there.

SIR BRIAN LANGSTAFF: Well, the question would be why would that patient group itself, of those with severe haemophilia A, or (inaudible) ^ haemophilia A, why would they, rather than other people as group, suffer from chronic liver disease?

MR BOUKRAA: That's right, sir.

SIR BRIAN LANGSTAFF: Yes, and he's stating it as though it wasn't at all controversial.

MR BOUKRAA: That's certainly one reading of this document, sir.
SIR BRIAN LANGSTAFF: That's how he's stating it.
MR BOUKRAA: That is how --
SIR BRIAN LANGSTAFF: It may be controversial but he's certainly setting it forward as an assumption without trying to justify it. Yes, thank you.
MR BOUKRAA: Sir, those are all the documents I wanted to take you to for this part of the presentation. I will get that contrast that Professor Cash made with the NBTS figure.

In the written note we have, towards the end of this section, set out some comments that were made later on by a number of figures including, in particular, Professor Cash looking back at these estimates, in particular the estimate that he made in early 1981 and commenting on whether or not it proved to be a successful estimate of what was going to be needed. There's more detail on that in the written note.

So that deals with this section. We're now going to be moving on to the section dealing with production of concentrates at PFC, the question of self-sufficiency, whether it was reached and, if so, what that meant.

Now, in the written note we've divided up this part of the presentation into three sub-areas and three parts of the chronology. The first one deals with the position in the 1970s up to the end of 1984, when heat treatment, at least for Factor VIII concentrates, is introduced in Scotland and for Northern Ireland.

We then divided it into heat treatment and the impact of heat treatment on self-sufficiency. That broadly covers the years '85, '86 to '87, and then we've looked more briefly at the period at the end of the 1980s to see whether or not self-sufficiency was maintained in Scotland, assuming it was reached before.

Now, as I go through this part of the oral presentation, I'm likely to spend some time, a good deal of time, on the first of those subheadings. I'm likely to spend less time on heat treatment. Now, heat treatment is obviously a very important topic but we are going to be hearing very shortly from Dr Foster and then from Dr Perry who were directly involved in a number of the issues. So I'm intending to set out an overview of some of the key dates, look at some important documents, but perhaps not go into as much detail about documents which were authored by

Dr Foster or authored by Dr Perry in advance of their oral evidence.

So we're going back in time, again, from the 1980s to the early 1970s, sir. There are a couple of documents, which are set out in the written note, from 1973, 1974, 1975, which I won't take you to. There's one from December 1973 prepared by Mr Watt, which is a report on the development of Factor VIII concentrates at that time. The reference for it is PRSE0000678. We don't need it up.

It's a useful document to look at to get a sense of what sort of concentrates were being developed by the PFC at that time, while it was still at the RIE, so before it moved to the Liberton site. What Mr Watt considered production capacity might be, and what sort of concentrates PFC should be focusing on. Similarly, there's a quarterly report for the end of September 1974, which gives some insight into the development of concentrates at that time.

There's a letter, sir, which it may be useful for you to turn to -- I won't go to it now -- later on, from January 1975. It's by Major General Jeffrey, he's writing to administrative medical officers in health boards. He sets out some of the recent history of the development of PFC and the impact of its move

to Liberton on the production of blood products.

The reference for that, if you want to look at it, sir, later is SCGV0000127_062. We don't need it up.

One of the points that's made in that letter, which is January 1975, is about the impact of the move from the RIE site to the new Liberton site, and what the letter seems to suggest is that it was not going to be possible to overlap production at those two sites, as I understand it, because, in this new system, there was a computer which had to be moved from the old site to the new site and you couldn't have production at the two happening at the same time.

That was thought likely to have an impact on the supply of certain blood products but it was not thought likely to have an impact on the supply of factor concentrates, including Factor VIII, at the levels that they were being produced at the time, because a stock had been built up.

I highlight that point, partly because it's an interesting one on the question of building up stocks that we'll come back to as we look through these documents, through the later 1970s and into the 1980s.

Now when we move into the second half of the

1970s and the PFC is trying to increase its production of Factor VIII in particular, one of the themes, as with England and Wales, that comes up, is about plasma supply. Getting enough fresh plasma.

In this respect, it appears that, from this period, Scotland had something of an advantage over England and Wales, which is its use or the use in Regional Transfusion Centres, and perhaps hospitals, of red cell concentrates, rather than whole blood, was already at a more advanced stage. Now, those who were here last week and attending some other hearings will know what that means.

Effectively, what it means is that when a unit or a donation of blood is collected, rather than using that whole blood for a blood transfusion, it is separated out into different components, including red cell concentrates, which are used for the transfusion, including plasma which can be sent off to be fractionated. So what that means is you've got the same number of donations but if you divide them up into these different components, including red cell concentrates, you can get more plasma out of the same number of donations.

There's a meeting of SNBTS directors, sir, in June 1975 where this issue was picked up, some targets

are mentioned, and it suggests that good progress has been made on continuing to increase the use of red cell concentrates in Scotland. I will give you the reference. Again, sir, I won't go to it. It's PRSE0003812.

It was noted at that meeting that targets of a 40 per cent minimum use of concentrated red cells by September 1975 and 50 per cent by March 1976, the following year, were in some cases already being reached or exceeded.

Now, the use of red cell concentrates varied regionally but what that meeting suggests is that good progress was being made in a number of regions.

Notwithstanding that, the greater use of red cell concentrates, plasma supply was still a concern from the perspective of the fractionators, who were trying to produce more concentrates. We can see that in a paper prepared by Major General Jeffrey for 11 June 1975 meeting of SNBTS directors. Again, sir, just for your note, the reference is SBTS0000098_031.

In that paper Major General Jeffrey said the main concern was the supply of fresh frozen plasma for Factor VIII, so that a stockpile can be built up before a changeover from cryoprecipitate to intermediate factor can be planned.

Now, we're going to turn to a document in which some of these supply issues were discussed in a good deal of detail. It's a meeting, again, of SNBTS directors and Haemophilia Directors, it took place in November 1975. The reference is PRSE0002823. If we start with the attendees at the meeting, we see number of individuals we've been looking at already: Professor Cash, Mr Watt, Major General Jeffrey. So this is 1975, at that time Cash is still at the Edinburgh Transfusion Centre.

Now, this meeting covered a number of different issues related to supply and we're going to look at those, starting over the page. Towards the bottom of this page, the last passage, section headed "Supplies of Factor VIII", and I'm going to pick out a few sentences in these various paragraphs that start here. So it's recorded that:

"At the May meeting of Directors it had been agreed to look again at the possibility of releasing material to Haemophilia Centres before the stock target of 1,000,000 units had been reached and as a result, Major General Jeffrey had agreed with Mr Watt that reserves could be held in Blood Transfusion Centres rather than the Protein Fractionation Centre."

I've highlighted on that -- I've alighted,

rather, on that, sir, because it points to what becomes and appears to be already an important part of the supply policy of the SNBTS, which is to build up a stockpile of Factor VIII, which is held partly at the PFC, partly in Regional Transfusion Centres.

SIR BRIAN LANGSTAFF: Now, was the reason for that the move to Liberton, what you were telling me earlier about the need to build up stock to cover the drop-off in production there would be before Liberton became fully operational? But Liberton began to be operational in '74, didn't it?

MR BOUKRAA: It began to be operational from the point of view of producing blood products, I believe, in 1975, and really only gets going more in 1976.

SIR BRIAN LANGSTAFF: So the computer system, which was necessary to operate the system of continuous production which had been developed by Watt and was in operation at the Royal Infirmary in Edinburgh, there being only one computer that was able to control the process, that was moved. When it was moved you couldn't get any more continuous production in the Royal Infirmary, so whatever production there was, was in a different method and obviously would produce much less, so they wanted to build up the stocks in advance of that, so they could distribute it.

So this is dealing with that problem, is it? In other words, is this stockpile a stockpile for all time as a form of strategic reserve, as it were, or is it to cover particular period?

MR BOUKRAA: I believe that the two are probably linked, sir. It seems to me, from some of the documents that we'll look at, that this is at least part of a more entrenched policy of building up a strategic reserve, but I'm sure you're quite right that this policy may well have originated in this period when there was a move from RIE to the Liberton site.

So, before the move took place, it was understood to be important to build up stockpile, so there wouldn't be a gap in supply during the transitional period, but once the move has taken place, we see, from number of documents starting around this time, a repeated emphasis on the importance of building up a stockpile in case there are future gaps in production.

SIR BRIAN LANGSTAFF: So the reason for having the stockpile is to smooth peaks and troughs in production?

MR BOUKRAA: That's my understanding, sir. Well, I'm sure it would have had a number of elements. One of them, I am sure, would be smoothing peaks and troughs. One

of them, I suppose, related to that is, if at some point there's a shutdown --

SIR BRIAN LANGSTAFF: Well, that's a trough.

MR BOUKRAA: That's a trough. Yes. A big trough. I was thinking of perhaps smaller peaks and troughs that might happen as plasma supply goes up and down month to month. But you're quite right, sir; that's another type of trough.

SIR BRIAN LANGSTAFF: It would have been, I suppose, standard manufacturing practice at the time to have stocks always available. The just-in-time process of manufacturing is fairly recent, isn't it?

MR BOUKRAA: I'm sure that's right, sir, but we do see this policy and this approach being picked up on a number of times in the documents. The size of the stockpile being seen to be important. The period of time that the stockpile covers also being seen to be important. We get to the later period, in to 1980s, and I believe it's understood that there's a need for about 12 months' supply of stock. We'll also see in some of the documents that when the SNBTS and the fractionators are assessing whether or not self-sufficiency has been achieved, self-sufficiency seems to be understood as: not only is Factor VIII being provided to meet demand, whatever that might be,

to provide to patients, but also that there's a stockpile which exists of a certain size, and it seems that there are points at which Factor VIII is not been sent on to Regional Transfusion Centres and Haemophilia Centres in order to build the stockpile back up. So I --

SIR BRIAN LANGSTAFF: So this is, what, a robbing Peter to pay Paul type policy? It's not providing the Factor VIII which a Centre might wish to have manufactured by the NHS at any rate because there may be a future occasion when there is even less to provide to the -- to that centre.

MR BOUKRAA: There would certainly --

SIR BRIAN LANGSTAFF: And we want to use what we've got to build up the stock, rather than give it to you?

MR BOUKRAA: There would certainly seem to be a period in time when those dynamics start to come to the fore, and there's a sense that --

SIR BRIAN LANGSTAFF: What period of time, roughly --

MR BOUKRAA: Certainly the early 1980s. It comes up in the documents at least then. It may well have been implicit in the policy the whole time, that we're not going to provide you with the concentrates that you say you want in order to build up the stockpile. But certainly from what's in the documents, that tension

starts to become clear at least in the material that we've got during that time period. I believe it's early 1980s, but I'll come on to it.

SIR BRIAN LANGSTAFF: So that particular reason for having a stockpile didn't apply in '75, or at least there's no evidence of it applying. Or is there?

MR BOUKRAA: Well, not that immediately comes to mind, sir. I'll come back to you if there is. In this period, it's also important to note that patients are being treated with cryoprecipitate as well as concentrate, and we'll come to the graphs later on which show what kinds of products were being used. I believe some -- a small amount of commercial concentrate was still being used. So it could be that this dynamic was in place also in the second half of the 1970s. I don't believe it's quite as clear from the documents as it becomes later on.

SIR BRIAN LANGSTAFF: Thank you.

MR BOUKRAA: If we move on now to a document in March 1976. We'll pick up on this question of plasma supply again. Sully, it's SCGV0000114_023. Sir, you might consider this to be an interesting document because it links back to some of the issues in England and Wales as well as looking at Scotland. We can see from the top that it is a note of a meeting I believe

prepared by a DHSS official that was called to consider Factor VIII production, 11 March 1976, attended by figures including Dr Maycock, Mr Watt, General Jeffrey.

If we look at the heading "Production capacity at present", in just the first sentence there it says:

"In both England and Wales and Scotland, the main factor is the availability of fresh plasma."

I understand that to mean the main factor holding back the production of more factor concentrates is the availability of fresh plasma.

The end of that first paragraph refers to production in England and Wales at that time. And we considered yesterday this figure of 17.5 million, 15 million, when it might have been achieved, whether it reflected capacity or actual production. This is another piece of the jigsaw perhaps.

At the present time, production in England and Wales is at 30,000 containers of 250 units a year. The target is 55,000 containers by June 1977, the equivalent to 14.5 million units a year. Yesterday we looked at a document which was based on -- well, which referred to a date in August 1977, appeared to suggest a figure of 17.5 million, though that related both to BPL and PFL. As I say, it might just be another piece

of the jigsaw, sir, when trying to disentangle those different figures.

If we look at the second passage on this page, just the first sentence:

"The amount of Factor VIII concentrate required in Scotland, based on the same 1973 expert committee report, is 4.5 million units. That's 10 to 12,000 units per year for each haemophilia A patient."

And then I'm just going to highlight the final sentence that we can see on the screen at the moment:

"The target in Scotland of 4.5 million units a year can easily be met, given sufficient fresh frozen plasma. There's ample manufacturing capacity."

So a suggestion in that meeting in 1976 that production manufacturing capacity at PFC should be ample to meet Scotland's needs, provided enough fresh frozen plasma is available.

I'm now going to look at a document which sets out a number of points relevant to the supply position in Scotland in the mid-1970s. It's, in fact, one I believe Mr Hill took you to last week, but we're going to look at some different passages.

It's PRSE0002133. Now it's an SNBTS annual report, covering 1975 to '76. Again, at this time, Major General Jeffrey was the director for the SNBTS.

This was a document which referred to there being an emotive response to the issue of Factor VIII supply in the UK. I believe Mr Hill took you to those passages. I won't go to them again, but this is a document in which those passages appear.

If we could go to page 11, please. In fact, if we could go back a page, we'll just see the heading. At 14, you can see this is about the use of coagulation factors including subparagraph (b), Factor VIII, and this was a passage that I was mentioning an emotive response.

If we go over the page to the bottom, subparagraph 4. So this is 1975 to 1976:

"Requirements of Factor VIII are at present based on an estimated average use of 10,000 units per patient annually ... some 4 million units for the known haemophilia population in Scotland."

If we go over the page, please, Sully, to page 12, looking at the second half, the section that is subparagraph or paragraph 6, "Present supply and demand situation". I'm not going to read all of that out. I bring to your attention, sir, the final third of that paragraph which is about plasma supply:

"The crucial point which should be a main target in the future of the directors is that by increasing

issues of concentrated red cells instead of whole blood and by releasing plasma which would be used for cryoprecipitate production to the PFC as concentrated Factor VIII becomes available in increasing quantities (which depends on these two major factors) [it says] at least half of the plasma sent to the PFC is in the form of fresh frozen plasma."

There's then some comments on self-sufficiency and what self-sufficiency might mean, which points to its different uses at different points of time by different individuals. The report says this:

"As regards self-sufficiency, Factor VIII is available to treat adequately the known haemophilia population in Scotland. The form in which it is available does not as yet meet the major demand for home therapy. Present policy is to issue intermediate factor to centres, with only a very small national reserve at the PFC; Directors of haemophilia and Regional Transfusion Centres are expected to maintain their own reserves, and patients should be introduced to home therapy only when an adequate reserve -- three months' anticipated use -- is available for each individual in case the PFC meets manufacturing difficulties."

Now, there we're looking at the different

aspects of reserves and stockpiles and the reasons why they might be necessary. We've looked at some of the big picture strategic ones: if there's a drop in production, it's important to have stockpile.

I believe the three months period there is referring to patients who will be on home therapy who will be using concentrate in order to avoid the possibility that they'll have to come off that programme. You want to have at least three months available for each patient who you've put on home therapy.

If we can just pick up briefly on page 18 and the bottom of this page, "Summary concerning the state of self-sufficiency". Now, this table is not laid out perhaps in the most immediately clear way, but it's useful looking at it to see at the top what the symbols mean:

"(+ = attained; - = not yet achieved; NA = not applicable ...)"

The table then deals with different products and, if we go over the page, we'll see Factor VIII as well as Factor IX. Thank you.

So towards the bottom of the table at the top, you can see I-Factor VIII -- I believe that's a reference to intermediate Factor VIII which is a product -- the target, and then two aspects to

self-sufficiency on the right-hand side: day-to-day, and one year's reserve and, for Factor VIII, the target was achieved at this time for neither. Neither was there enough day-to-day Factor VIII concentrates, nor was there a year's reserve.

And what I mentioned earlier, sir, this question of how self-sufficiency was defined by different people, this is one of the ways in which it's approached by the SNBTS, at least in the mid-1970s, and we can see that there are two forms of concentrate containing Factor IX. I believe the relevant one for our purposes is the top one, Factor II, IX and X. There, there is enough being produced for day-to-day self-sufficiency but not enough to meet the requirement for a year's reserve.

Then, finally, over the page, a couple of last points to pick out. Actually, it should be the previous, page 19, please. Sorry, it was the same page. The second half of this page, "Targets for 1977-78", I just draw your attention, sir, to subparagraph (a) there, there's a target for red cell concentrates, "CRC" is concentrated red cells. A suggestion that they need to get to 60 per cent use of concentrated red cells.

Then subparagraph (b), again, this is a target,

it's envisaged that at least 90 per cent of cryoprecipitate is replaced by concentrated Factor VIII.

That's all I wanted to take you to in that document. I'm going to be moving on now into the 1980s. I note the time. I wonder if this would be a convenient moment.

SIR BRIAN LANGSTAFF: Yes, well, let's take a break then until 11.45. 11.45.

(11.13 am)

(A short break)

(11.45 am)

SIR BRIAN LANGSTAFF: Yes?

MR BOUKRAA: Sir, before we move on to the 1980s, I wonder if we might very briefly return to the table we were just looking at, a representative for one of the Core Participant groups has helpfully pointed out couple of features of that table I think I should draw to your attention.

Sir, we are back at the table, at the bottom of the page, the first point to note is that cryoprecipitate is included in the list of products. You may have already picked up on this, sir, 10 per cent present use. More importantly, over the page, and we look again at those entries for Factor VIII and

Factor IX, I wanted to highlight the asterisk that appears next to the minus symbol.

SIR BRIAN LANGSTAFF: Yes.

MR BOUKRAA: So for Factor VIII, no asterisk appears. For Factor IX, an asterisk appears next to the "One year's reserve", and if we look below in parenthesis, it says that the asterisk means "capable of achievement with present PFC stocks". Now, it's not entirely clear to me what those two symbols mean together. On the one hand, there's one year's reserve is not achieved, on the other hand, a year's reserve can be achieved with present stocks.

There's a little more explanation in the passage which follows, sir, but I thought I'd highlight that for anyone who is watching and perhaps for you to note this is another feature of that table.

SIR BRIAN LANGSTAFF: Yes, it's -- as a matter of literal reading, it's inconsistent but that's probably not what it means.

MR BOUKRAA: That's right, sir. Yes. I agree. It must mean something. It's not altogether clear what it does mean. Thank you.

So we move into the 1980s. It's important to note that when we get to the 1980s, and I'm not going to take you, sir, to any documents about this -- that

there has been, in the late 1970s to about 1980, 1981, significant changes in developments in manufacturing processes at the PFC. We pointed to, in the written notes, some documents which set some of those out. They cover things like continuous thawing.

Dr Foster in his statement suggests that, between 1976 and 1981, Factor VIII yields increased by about 50 per cent. Now I'm not going to go into any more detail about that issue but it's an important part of the picture as we move into the late 1970s and early 1980s, that we trying to understand changes to supply of concentrates.

SIR BRIAN LANGSTAFF: It increased by about 50 per cent?

MR BOUKRAA: That's the suggestion, I believe, in Dr Foster's statement, sir, between '76 and '81 -- 50 per cent by '81.

I am going to take you to a couple of documents from 1980, which go to this issue of PFC's distribution arrangements. They seem to relate to the introduction of a pro rata arrangement some time in the early 1980s but they also link back to this stockpile question.

The first one is PRSE0004005. This is letter from Mr Watt to Dr Boulton in Edinburgh and Southeast Transfusion Centre. We don't need to go to all of it,

I think the context of this letter is that Professor Ludlam is trying to obtain more Factor VIII for his patients in Edinburgh, I believe, in order to place more patients on the home treatment programme.

If I can just highlight the second paragraph here, where Mr Watt summarises what the distribution arrangements are at that time for PFC product, and he says:

"The present situation regarding the distribution of Factor VIII to regional centres from the [PFC] is that each pool comes to be ready for issue we place 10% in the national stockpile to be available for emergency purposes and the remainder is distributed to regional centres in a proportion which has been agreed by the Directors. This is roughly according to the distribution of population in the various regions but with a slight bias in favour of Inverness where the geography of the region makes a more widespread utilisation of home therapy a rather necessary fact of life."

That's the position as of February 1980. We can pick things up later in the year, December 1980, with PRSE0004005. This is another letter from Mr Watt, this time to Professor Cash.

SIR BRIAN LANGSTAFF: It probably is.

MR BOUKRAA: I hope it is.

SIR BRIAN LANGSTAFF: This is not looking at the right one.

MR BOUKRAA: I might have given the wrong reference.

SIR BRIAN LANGSTAFF: You gave the same reference as you had before.

MR BOUKRAA: I've got the right one here. PRSE0002207. Thank you.

Sir, this is December 1980, later on in the same year. Again, Mr Watt, a letter to Professor Cash. I'm going to look at the introductory passages of the letter. Mr Watt says:

"After our discussion ... I made the following arrangements for the distribution of Factor VIII concentrates, to be effective from 1 January 1981.

"Each month when we prepare the total issue from production we shall allocate as follows:

"The first 15% of the total product will be placed in the National Reserve."

That contrasts with the 10 per cent figure that we just looked at. There is a special arrangement for Inverness as there was in the previous letter. Then there is a summary of the proportions that will be provided to the remaining regions in Scotland.

At the bottom of this page, Mr Watt outlines

some ways in which the proportions might be adjusted, month to month, and refers to a league table which exists at PFC.

That's the position at the end of 1980. As we get into 1981, one of the issues that becomes significant at PFC is a Medicines Inspectorate report. I'm not going to go to the detail of that report, sir, some of it is set out in the written note. I believe it is also covered by Dr Foster in his statement, but it's an important part of the chronology and trying to understand what's happening around this time.

I believe the visits start from the inspectors in 1979. They produce some initial comments. There's an updated report that they produce in October 1981, and that timing, what's set out in that October 1981 report, is relevant both for what's going to happen at PFC in the years that follow. It's also relevant to those discussions we were looking at yesterday between Scotland and England. This figure of £6 to £7 million appears, which is linked to changes that are going to be necessary to be made at PFC.

SIR BRIAN LANGSTAFF: Well, half of them, I think, we decided or roughly?

MR BOUKRAA: That's the suggestion in one of the letters. I believe -- I don't have the reference immediately to

hand -- that that number is divided up differently in different documents.

SIR BRIAN LANGSTAFF: I think you mentioned that yesterday.

MR BOUKRAA: Yes.

SIR BRIAN LANGSTAFF: So it's somewhere between nought and six or seven, but it's probably around about half.

MR BOUKRAA: It might be around about half. It's certainly a proportion of that figure.

I'm going to turn now, sir, to a document from December 1981. It's PRSE0003364. It's one which relates both to where PFC had got to in terms of its supply but also this question of stockpile. I'm also going to pick up in this document a reference to that contrast between the NBTS and the SNBTS that I couldn't find earlier. It appears a bit later in time. This is when it appears.

So this is an 8 December 1981 meeting of SNBTS directors. If we could go through, please, to page 3, and the passage in section 4, "National Stocks of Blood Products".

In the first paragraph there there's a reference to a table, PFC products which had been issued. Then in the second paragraph there's a reference to what self-sufficiency was understood to mean by SNBTS

directors at the time. So:

"It was agreed that the concept of self-sufficiency implied uninterrupted supply and that, generally, the national stock should consist of 12 months' usage of products, labelled and ready for issue."

It was also mentioned that there would be an evaluation of a pro rata distribution of product, which I think ties in with that document from late 1980 that we just looked at.

If we go to page 5, please, and the second paragraph that appears on that page, you can see the contrast between the Scottish figures and those England and Wales:

"There had also been discussion on the current target of 2.75 million [units of] Factor VIII [per] million [per] population per annum, in view of the fact that the current NBTS target was 2.0 million [units per] million population per annum."

So it has been decided and was decided then to retain the target of 2.75. So a significantly higher target for the production of Factor VIII in Scotland than in England and Wales at that time.

Now, as we're moving through 1981, sir, we can see from the documents that are set out in the written

note that plasma supply is increasing very significantly to PFC. A problem that begins to emerge relates to the amount of plasma that's been sent and whether or not PFC could fractionate it all quickly enough.

There's a memo which is in the note, 20 August 1981, where reference is made to an estimated 25 per cent growth in supply of fresh frozen plasma in six months.

We can see some of those issues reflected in a document we'll go to now, another letter from Mr Watt. It's PRSE0002316. This is a letter which gives us some insight into that particular difficulty that I was just describing but also more generally into PFC's production capacity around this time.

So it's dated February 1982, it's from Mr Watt to Mr Cash. If we go down to the first couple of paragraphs, Mr Watt said that:

"By the time of the March issue of Factor VIII under the 'Pro Rata' scheme the PFC will be substantially in debt to the regions."

He then refers to a "slowly gathering difficulty because of freeze-dryer limitation at PFC. At present we are getting 700 [kilos] of fresh plasma weekly and can process up to 720 [kilos] in a full capacity week.

If a lot is missed, for whatever reason, the net effect is to increase plasma stock, which cannot be cleared."

He also makes reference to the shift-working trial we looked at yesterday and its effect on stocks of plasma.

If we go down, actually, we've still got it up here but if we look towards the bottom of the screen, Mr Watt says:

"In summary, with the new shelf in the dryer [which he outlines elsewhere in the letter] and a reduction of cycle time by correction of the dryer tray fault we expect to increase plasma process capacity for [fresh frozen plasma] to about 2000 [kilos] per full two week period ..."

In other words about 1,000 kilos a week. It is suggested:

"... this will help to make in road in the stockpile and also keep up with input."

SIR BRIAN LANGSTAFF: So the new shelf in the dryer, is that something which occurred because there's just the dryer, it has to be utilised? There's a little bit of space in it, but the bottles are too tall, and so the size of the bottles is reduced or they get smaller bottles; is that the -- is there is the -- where they

found space for the new shelf in the dryer? Do you remember?

MR BOUKRAA: It's a good question, sir. I'm not sure is the answer. I don't know if it relates to the size of the bottles. It may well.

SIR BRIAN LANGSTAFF: I think it may be Dr Foster who talks about that but I can't remember where I recently read that, but I'm just wondering if this was the extra shelf.

MR BOUKRAA: You could well be right, sir. I'm sorry I can't assist by confirming that particular point. It could well be that we could check it by checking Dr Foster's statement or confirming with him when he's giving evidence. That sounds right. That sounds right. That sounds like what a new shelf in a dryer would help to achieve.

SIR BRIAN LANGSTAFF: There's a lesson in it for people packing their fridges, really.

MR BOUKRAA: Yes, exactly.

I'm going to pick things up, sir, later in 1982, 30 September 1982, and I'm going to go to a letter sent from Mr Watt to the Glasgow and West of Scotland RTC because it picks up on that issue that you were -- we were discussing earlier about the national stockpile and the effect that that might have on

products being sent to particular RTCs. It's PRSE0000408, a letter from Mr Watt to the Glasgow and the West of Scotland RTC.

In the first paragraph, Mr Watt referred to the perilous state of Factor VIII supply. He then, actually still in that first paragraph -- I'm sorry, in the first sentence he refers to an arrangement between the Glasgow RTC and the PFC, and he thanks Dr Hopkins for the:

"... generous decision to return 2 000 vials of Factor VIII Concentrate to the national stock."

What that appears to be referring to is a request from Mr Watt at the PFC to an RTC to get some Factor VIII concentrate back in order to build up the national stock, rather than it remaining at the RTC and then being sent to patients.

Now, the implications of this sort of arrangement aren't immediately clear from this letter or from some of the other documents we have. From a patient's perspective, it's not entirely clear what the effects might be because it's not clear from these documents whether returning or keeping back more PFC concentrate in the national stock would mean for a patient that they're treated with cryoprecipitate or treated with commercial concentrates. So we can't get

that part, that effect of the arrangement, from these documents but it does provide some further insight into how this policy of having a significant national stock, national reserve at PFC could play out during these years in the early 1980s.

At this point in the written note, sir, we've got a few documents summarised and a few paragraphs relating to freeze-dried cryoprecipitate. I'm not intending to take you through any of those. It's an important issue at this time.

The broad brush headline picture is that there were proposals to investigate the production of freeze-dried cryoprecipitate, particularly in the West of Scotland. There was a trial that was agreed. This all takes place between about 1980 and 1983. The PFC's input, so far as we can see, were a number of letters from Mr Watt, in which Mr Watt sets out his pretty firmly expressed opposition to any sort of move to producing freeze-dried cryoprecipitate.

He has some opinions expressed both on freeze-dried cryoprecipitate as a product, and also suggests that, if there's going to be any move towards making it, it could not be produced at PFC or at least he would strongly oppose it being produced at the PFC.

Now, that's gets us, sir, to 1983 to 1984.

I will pick matters up with a meeting of SNBTS directors and I think Haemophilia Directors in January 1983. That's PRSE0001736. Now, this -- as we can see, it's a meeting of SNBTS and Haemophilia Directors. It's got a few passages that I'll take you to, sir, which provide both a summary of what's been happening in recent years and also set out the position as it was at that time.

If we could go over the page, please, the second half of that page (a), "Trends in supply and demand". I won't read all this out, but what you'll see and what will be apparent from this summary of the five-year period from 1978 to 1982 is that there have been very significant increases in PFC's production of Factor VIII concentrate. Alongside that, a decrease in the amount of cryoprecipitate had been issued from RTCs.

If we go over the next page, please, page 3, and there's a discussion starting at paragraph two about continued purchases of commercial products in Scotland at this time in, 1983:

"Concern again was expressed about the amount of commercially produced Factor VIII which was still being purchased and members went on to discuss the regional breakdown of usage of cryoprecipitate, PFC

concentrate, and commercially produced Factor VIII. It was noted that while purchases of commercial [Factor] VIII had declined in Glasgow, purchases in Edinburgh had increased. Dr Ludlam explained that the reasons for the use of commercial material in Edinburgh were partially clinical and partially a policy of conserving a cushion of an NHS Factor VIII against an anticipated shortage when production at the PFC would be suspended to carry out alterations required by the Medicines Inspectorate."

So that's a link back to that report produced by the inspectorate, suggestion that there's going to be a need to undertake some works and a slowdown in production.

In the second paragraph, if we can -- I'll just highlight the second part of that. This is in response to fears of future shortage of Factor VIII supply. It said that:

"Fears of a shortage were remote, and he [Mr Watt] was confident that in co-operation between regions, difficulties could be overcome. Dr Cash emphasised that the pro rata scheme was not intended to be applied inflexibly ... products could be transferred between regions in the event of a local shortage."

And in the next paragraph, I'm just going to note a sentence in the middle of that:

"Dr Ludlam also expressed some misgiving that Edinburgh perhaps did not receive as much PFC factor VIII concentrate as it should pro rata."

The reason for highlighting that is that I'm going to briefly describe an arrangement that came to be agreed between Dr Ludlam in Edinburgh and Dr Mayne in Northern Ireland around this time, there to be an exchange of commercial and PFC concentrate between the two centres.

If we go to page 5, this is really just briefly to note the position on Factor IX, subparagraph (f). All it's said is:

"The supply position of DEFIX over the last five years had remained strong ... demand reasonably stable."

So no issues it seems with the supply of Factor IX.

And just finally on page 7, this is not so much on the supply issue, sir, but this is more to note that this issue was discussed at this meeting. In the middle of the page, there's a reference to AIDS.

So this is 21 January 1983:

"Dr Cash drew members' attention to recent

articles in the United States and also in the Observer and The Lancet about this problem. An MMWI extract (CDC Atlanta) had been circulated with his paper. Dr Ludlam informed members that in the UK a letter and questionnaire had been sent out to Haemophilia Directors."

Now, the arrangements between Edinburgh and Northern Ireland is one that I'll summarise briefly. It's set out with as much detail as we've been able to provide in the written note, although there's not much in the way of documentation about it. The arrangement appears to have been that around the start of 1983, Dr Ludlam agreed with Dr Mayne that Scotland would send commercial product to Northern Ireland, and in exchange, Dr Mayne would return some of the PFC product that had been sent to Northern Ireland to Edinburgh and Scotland.

We have got a letter that I'll briefly take you to about that arrangement from the end of December 1983. It's LOTH0000005_071. Thank you. So this a letter from Dr Brian McClelland to Dr Ludlam, end of December 1983, by which point, as we'll see, the arrangement has been in existence for some time.

This is essentially Dr McClelland asking Dr Ludlam whether this arrangement was intended to

continue. He says it has just been pointed out to him:

"... that we are continuing to receive substantial deliveries of PFC Factor VIII from Belfast. I was indeed aware that you had on one occasion made an exchange with Dr Mayne for some commercial Factor VIII which you had previously purchased, but I did not know that the process was continuing."

The next paragraph, sir, I don't know if I'm misreading it, or perhaps if a word is missing, it reads:

"So far as I know, our stock level is low, and indeed the total stock situation within the SNBTS is at present very healthy, and I wonder if there is some specific reason why the exchange ... [is] still necessary ..."

I don't know if that should read: "As far as I know, our stock level is not low and indeed the stock level in the SNBTS is very healthy." In other words: "We've got lots of stock. Why do you need to keep receiving it from Belfast?"

And I'll take you very briefly to the response from Dr Ludlam. That's LOTH0000005_085. Have I taken you to the wrong ... there you are. Thank you.

Sir, this is January 1984. Dr Ludlam responding to Dr McClelland:

"Thank you for your letter ... about exchanges of commercial factor VIII with Belfast. The exchange was agreed early in 1983 because at that time SNBTS factor VIII was in very short supply. The first part of the exchange arrived shortly after the negotiations, and at the time, SNBTS material markedly improved. The material that has arrived recently just completes the exchange. As I understand it, we are now quits with Belfast."

So it seems to be an exchange that lasts effectively for a year, 1983, early 1983 to the start of 1984.

I won't take you to it, sir, but in the written note it's worth being aware that Professor Cash doesn't seem to have been aware of this arrangement. He writes a letter in January 1984 to Dr Mayne saying that he's just been made aware that there was this arrangement for this exchange, asking to be filled in effectively with the details, highlights some concerns. I'll just read out what he says in his final paragraph. He says:

"Am I right that this arrangement exists? If so, could you illuminate. On the face of it, this

development looks a little worrying, AIDS, etc, and I'm anxious to help as much as possible."

Now, that gets us to later in 1983 and into 1984 and it appears, when we get to this period, that Scotland is at least on one measure, depending on how you define it, getting close to self-sufficiency in Factor VIII. A number of claims begin to be made that Scotland is now self-sufficient in Factor VIII. I won't take you to it, but there's a letter from July 1983 from Mr Watt in which he is informing Professor Cash of his resignation from the PFC, so he announces the resignation in 1983. He stays on for a few more months before Dr Perry takes over.

In that letter, Mr Watt says that Scotland has become the first country in the world to be truly self-sufficient in plasma fractions. Now, I'm not going to comment any further on that claim, sir, aside from highlighting two points. The first is the suggestion that Scotland itself was self-sufficient at this point, July 1983, will have to be considered in the light of some of the figures that we're about to look at from 1983, and indeed 1984, on product usage in Scotland. They seem to suggest that in 198 -- both in 1983 and in 1984, commercial products, commercial Factor VIII were still being used.

The second point about the international context, I'm afraid I'm not able to assist the Inquiry much further with that at this stage, suffice to say it may be that it's necessary to investigate that claim further before accepting that it's accurate.

Towards the end of November -- towards the end of 1983, November 1983, the supply situation at PFC is getting to a point where there's concern that so much Factor VIII is being produced and added to the national stockpile that some of it is in danger of becoming out of date. Factor VIII obviously has a limited shelf life.

You can see that in the November 1983 memo from Dr Perry, an internal PFC memo. He notes that the previous year, the stockpile was 5 million units. It's grown to 7 million units. He starts to question whether some steps should be taken to reduce that stockpile.

There's a series of statements and claims that are made from September 1983 to quite a bit later in -- for example, from the DHSS, the Scottish office, suggesting that by this point Scotland had become either self-sufficient or virtually self-sufficient in blood products, as set out in the note that we're picking up from a chronological perspective.

The next document I'm going to turn to, which examines this issue of self-sufficiency, is a paper prepared by Professor Cash. It's at PRSE0001556. Sorry, I think this is actually the minutes of the meeting, rather than Professor Cash's paper.

So Professor Cash prepared a paper in advance of this meeting. It's another meeting of Haemophilia Directors and SNBTS directors, February 1984. If we turn over the page and we focus on the section 5, "Review paper from SNBTS", this section of the minutes is -- reflects a discussion of a paper produced by Professor Cash.

The first point, sir, is worth noting:

"Details of the amount of fresh plasma [produced] for Factor VIII concentrates and the issues of concentrates indicated that the production level was about right. However, trends over the last five years indicated that the SNBTS production of Factor VIII concentrates may be exceeding clinical demand, and the current stocks at RTCs appear to be increasing."

I'll pick up subparagraph (ii), there's a discussion about the continuing use of cryoprecipitate at this time, February 1984:

"Members discussed the suggestion that the

production of cryoprecipitate could now be reduced. Dr Ludlam said that cryoprecipitate was preferred in the treatment of children at present, because of the new danger of AIDS. Dr Hann concurred. A policy seemed to be emerging however to use less cryo for haemophilia A patients. It was agreed that a certain minimal amount of cryo was required and Dr Cash pointed out that [Transfusion Directors] could produce it in emergencies."

If we go down the page, point (iv), I won't go into the detail of this now but it's just worth noting that Dr Cash, during the course of this meeting, suggests that the time might be right to introduce a batch dedication system. The reason for that is to reduce the number of batch exposures per patient per year, so this is early 1984. I'll come on a bit later to when batch dedication was introduced by the PFC but it appears to be the case that it wasn't introduced until sometime later, end of 1984, early 1985.

I'll then pick up point (v):

"Dr Cash asked members to consider whether, given the present SNBTS production level of factor VIII concentrates, it was necessary to purchase commercially unless exceptionally a superior product was available."

I take the reference to a "superior product" being available to mean, as an example, a higher purity product for certain kinds of patients.

If we go over the page, we can see recorded a discussion involving the Haemophilia Directors about their preferences and approach to commercial versus PFC concentrates, so it's the top of the page:

"Dr McDonald said that the adult centre in the West was totally satisfied with the NHS product and that it was no longer necessary to purchase commercially. Dr Hann however found himself in the position of having inherited 30,000 [units] of commercial factor VIII which was rapidly going out of date and which he was prepared to dispose of.

"Dr Ludlam said that he required to have a small stock of high purity commercial material ...

"Dr Bell [who is there on behalf of the Scottish Home and Health Department] emphasised that the aim of the SNBTS and the national policy was for Scotland to be self sufficient, and although the Department would not wish to intervene in what clinicians prescribed, it was not sensible to purchase imported material when suitable NHS product was available."

In May 1984, sir, a document was prepared by Professor Cash and a blood transfusion subcommittee

meeting took place. I won't take you to those documents. What they concerned was a proposal for Scotland, in view of its supply position, to send more of its Factor VIII products to Northern Ireland and to England and Wales. There's a paper by Professor Cash from May 1984, the title of it is "Proposal for the Decanting of Excess Factor VIII Concentrate to Northern Ireland and England and Wales".

He sets out in some detail the background to that proposal in the paper. He makes a number of proposals at the end of it. He suggested the first priority in the disposal exercise should be Northern Ireland, and that's disposal of Factor VIII concentrates which are surplus to Scottish needs, and suggests that the residual surplus be offered to the CBLA, ie England and Wales. He also suggests that some consideration should be given to charging for the arrangement.

There's a meeting which Professor Cash's proposals are accepted. That takes place on 23 May 1984.

We can then see what I believe is that proposal and agreement reflected in a letter between Dr Morris McClelland in Northern Ireland and Dr Mayne, and we'll just go to that document. It's NIBS0001718.

It's not very easy to read because of the quality of the copy. You can see the date at the top, 21 May 1984, and if we go down, please -- thank you -- I'll pick up the first paragraph where the issue is introduced.

"Some changes have recently taken place in the arrangements for the supply of blood products from Scotland and I thought it would be appropriate to update you."

Thank you. "Factor VIII concentrate", Dr Morris McClelland says:

"This has been produced in considerable excess of demand in Scotland during the past year or two with the result that the present pro-rata arrangement for supplies (in proportion to input of fresh frozen plasma from Transfusion Centres), this has been abandoned at least for the present.

"On a pro-rata basis we would now be entitled to receive Factor VIII at the rate of about 1.8 million units per year. (The increase has resulted partly from increased plasma supply and partly from increased yields during fractionation). With this new, more flexible arrangement we could certainly obtain more than this -- at least 2.5 million units per year."

Then the next paragraph:

"I am aware from conversations with you that you are not at present planning to use this amount but you may find this information useful for future planning."

Now, it's not clear from the documents we've looked at, in the context at least of this presentation, why Dr Mayne might not have been proposing to use that amount of NHS product. We'll go on to look in a moment at some tables showing consumption figures in Northern Ireland, as well as Scotland, which show that a significant amount of commercial product is still in use at that time. But this is a reflection, at least, I believe, of Professor Cash's proposals to change arrangement -- those arrangements with Northern Ireland.

As for England and Wales, in October 1984, Dr Perry, who by this point had become acting director at PFC, wrote to Dr Lane at BPL to offer around 2,000 vials of Factor VIII, equating to about 460,000 units. In the letter, Dr Perry said that these vials of Factor VIII had failed to meet certain product specifications, things like solubility time, in other words these products were taking longer to dissolve, certain other technical specials.

Dr Perry says in the letter that, if there was any shortfall in Scotland of PFC product, then they

would be sending this product to RTCs. Because their supply position is strong, they don't need it, they're therefore offering it to England and Wales.

We can go to Dr Lane's response to that proposal just very quickly, CBLA0001912. I should say that in Dr Perry's letter making the offer, he made reference to tentative evidence in relation to the AIDS infectivity of commercial products. In other words, question marks around AIDS infectivity of commercial products, so would you therefore like to have this Scottish product? Dr Lane's response that we have here, November 1984, says:

"Thank you for your letter about those batches of factor VIII which are outside your defined finished product specifications. Whilst I entirely take the point you are making, I do not feel that it is in order to step outside normal regulatory practices, even in our current complicated situation with AIDS. In the same way that we would not release material which failed our quality control, regardless, I do not think that we would wish to circulate material in a similar category."

That's Dr Lane there refusing that offer to take product from Scotland.

Now, that addresses Factor VIII during this

period. I made some references already to Factor IX. For completeness, I'm going to pick up just a few other parts of the chronology briefly. The written note during this section separates out Factor VIII and Factor IX. That is because the stories become different in important respects. The chronology of products that are introduced at different times become different, and that's the reason why we've separated them out.

I'll highlight just a few points, sir. On the early history of product used to treat haemophilia B patients in Scotland, we've referred in the note to a 1973 article, journal article, which sets out some of that history. It suggests that, until 1967, fresh frozen plasma was the only product available to treat haemophilia B patients.

In 1967, the PFC, which was then known as the BPU, began producing a concentrate which contained Factor IX, known as PPSB. But then in 1971, and the article was concerned with the development of this product, a new concentrate is developed, which also contains Factor IX, and this is the product which becomes known as DEFIX, and it seems to be introduced routinely from around 1971.

Most of the documents I've covered in relation

to Factor VIII for the 1970s and 1980s suggest that the supply position in relation to a Factor IX concentrate DEFIX was strong. There generally weren't issues with supplying and producing enough of it.

I've already picked up in Professor Cash's January 1981 paper the comment where he says:

"Because of the much smaller number of haemophilia B patients than A, the supply of these products [ie Factor IX concentrates] is always more than adequate."

He makes reference to an exception, I believe, that's one year, in 1979, where the supply drop.

In January 1983 Professor Cash suggested that the supply position with regards to DEFIX remains strong. The issue from PFC to RTCs is reasonably stable. At a January 1983 meeting of SNBTS and Haemophilia Directors, it was noted that the supply position of DEFIX over the last five years, so five years to 1983, have remained strong and the demand reasonably stable.

There's a reference in the documents to a supply difficulty that seems to arise around the middle of 1983. It appears to be related to the use of DEFIX for haemophilia A patients with inhibitors. So, around this time, clinicians start to try to treat

haemophilia A patients with inhibitors with DEFIX, that has a knock-on effect on the supply of DEFIX, and there are difficulties with keeping up with demand.

We set out in the note how that issue plays out. It continues into February 1985.

Now, sir, that completes the chronological part of this section of the presentation. At this point, I was intending to turn to some of the annexes and figures that the Inquiry has produced. We've got a bit of time still, I believe before the lunch break, so I don't know if you want to break now or if I can continue on. I've got some time left.

SIR BRIAN LANGSTAFF: Let's use the time, shall we?

MR BOUKRAA: Thank you.

So if we can get that the annexes up, Sully, you should have them at INQY0000344, thank you.

Now, before we go in to the detail of the figures in the tables, there are a few points I should explain. This is a set -- a document which contains all the annexes accompanying the presentation. Annex A, which we have the first page of here, sets out consumption of Factor VIII and then Factor IX concentrates in Scotland and Annex B does the same for Northern Ireland. Both Annex A and Annex B and both the Factor VIII and Factor IX figures are based on

annual returns from haemophilia centres.

You can see at this page, we can set out the annual returns that apply to Scotland with the URNs in footnotes at the bottom. So as we go through the figures in the tables if any Core Participants, legal representatives at any point want to interrogate any of the figures, check whether we've got them right, if they want to look into particular issues, all of the sources for the data should be set out in those footnotes.

One effect of using the returns as the source of data means that the narrative and the figures only start in 1976. That's the earliest date for which we have returns.

Those returns are probably the most accurate guide to the consumption of these different factor concentrates during this time period that we have. But there are also, in some of them, gaps, issues with how the data is recorded, and it's important to be aware of them. What we've done in the tables is tried to flag any of those issues so that readers can be aware of them as they're looking at the tables and at the figures.

Lastly, sir, I've already said that we'd use the word "consumption" here rather than "demand" for this

table.

In fact, that wasn't quite lastly. One more introductory point to note, these are consumption figures, rather than production figures. That may be an obvious distinction but it is an important one to bear in mind because, in some of the documents, there's reference to production, ie how much the PFC was producing each year. Figures for consumption are, of course, different.

So we can turn, please, to page 2. So this is the table setting out -- actually, can we have -- yeah, that's fine. That'll do for now. Thank you.

These are the figures recording in Scotland consumption of Factor VIII products, going from 1976 to 1990. You'll be able to see that there are footnotes which appear next to some of the entries, for example 1981, 1982. In fact, also, at the heading at the top, next to "Cryoprecipitate", there are footnotes.

If we pan back out, please, Sully, and go into the footnotes -- I wouldn't ordinarily go to footnotes, sir, but we've highlighted them here and I think they're important to bear in mind -- they suggest some caveats.

One of the caveats relates to figures for

cryoprecipitate. In some of the annual returns, as we've seen during the Haemophilia Centre presentations and hearings, cryoprecipitate was sometimes recorded in a number of bags or packs. Generally speaking, we've translated that into 70 units per pack, which correlates with some explanations which are sometimes given in the returns. Obviously, all cryoprecipitate figures are estimates, even when there's a number recorded in the return. That's based on an estimate of units per pack, and of course a point to bear in mind.

When we've set out the figures for cryoprecipitate consumption, that also -- they include the figures for patients with von Willebrand's. For much of this period patients with von Willebrand's were treated with cryoprecipitate. Now, what that means is that the comparison, at least for some of the period, between cryoprecipitate and factor concentrates becomes less direct because von Willebrand's patients generally weren't treated with factor concentrates, so far as I understand it. But we thought that these were an important part of the overall picture, in terms of cryoprecipitate consumption at the time, so we've included that.

In terms of data for individual returns, gaps in

the data, some of them make more difference than others. There's one I wanted to pick up here because it does make a material difference to the tables we're going to go on to look or the figures -- the charts we're going to look at. It's the Edinburgh data for 1981.

Now, the annual return for Edinburgh in 1981 is only very faintly legible. We can just about make out the figures for cryoprecipitate. Unfortunately, it's not possible to make out what the figures were for NHS or commercial concentrates. That's an important caveat to bear in mind when we go on to look at the tables.

Now, the data here has been used to create, first of all, a graph and then a set of bar charts. So if we can go on to the next page, I'm going to spend less time on this one. We can see how the figures have translated. The blue line is NHS PFC Factor VIII concentrate. The orange line is cryoprecipitate. The red line is commercial concentrate.

We can see that commercial concentrate is at a low level in the early period, increases a little up to about 1980, starts to decrease again to reach very low periods in 1984, and low figures in 1984 and, in

fact, when we get to 1984 onwards, we'll see just how far the figures drop.

Cryoprecipitate, relatively steady until 1980, and then starts to decrease. The use of PFC concentrate increases slowly in the 1976 to 1979 period. There's a significant jump in 1980. I haven't interrogated, sir, the exact reasons for that jump. It may be related to Professor Ludlam's arrival in Edinburgh. As I understand it, he changed the treatment policies in Edinburgh to have more of a focus on the use of concentrate, rather than cryo.

I should say the dots represent years. On the blue line, after 1980, here there's a suggestion of a drop in 1981. That is likely to be a somewhat artificial figure because, in 1981, we don't have the return data for Edinburgh for its use of concentrate. Then we can see the figures increasing from '82 up to '84, dropping down and then increasing again as we move through the second half of the 1980s.

If we go on to the next page, please, Sully, again this is the same data that's recorded in the tables, this time translated into a bar chart. This might be a helpful chart for trying to assess whether or not self-sufficiency was achieved, when it was achieved. Now, I'm not going to go into all the

different definitions of that term, sir, but one way of defining the term might be: were patients treated with domestic product only or were they also treated with imported product?

We can see that Scottish patients are treated with some commercial concentrate, which is the red block, relatively small amounts at the end of the 1970s, a larger amount in 1980. There's the figures for 1981, although they come with that same health warning because of the Edinburgh gap. Relatively small amounts of commercial concentrate, there's still some being used in '82, '83, a very small amount in '84 and then no commercial concentrate recorded used in '85, '86, '87, which coincides with the introduction of heat treated Factor VIII in Scotland.

If we look at the figures for cryo, we can see, starting in 1976, relatively steady levels, small increase in 1981, then the figures start to drop off. Then PFC Factor VIII, reasonably steady levels in the second half of the 1970s, a significant increase in use in 1980. I'll ignore 1981 for the reason I've given before. Then from '82 onwards, we can see that PFC Factor VIII becomes, by some distance, the greatest -- represents the greatest proportion in use of these products from '82, '83, '84 onwards.

I haven't yet covered heat treatment. I'll do that very briefly, but we can see that when we get to '88, by which time all factor concentrates, at least, are heat treated, commercial products make a reappearance, '88, '89, '90.

So, sir, that's the picture for Factor VIII in Scotland that we've been able to establish from the data. I'll look more briefly at Factor IX. If we go over the page, please, Sully. So we started again with a table of figures. I won't go through it in as much detail. A few caveats to note in -- a few caveats to note in footnotes that people can come back to. It's a bit easier to see from this table what the position is, because we can see, in the right-hand column, "Commercial Factor IX". Most years, no use of commercial Factor IX recorded, other than 1980, 1981.

If we go on to the -- in fact, can we go straight to the chart, so I think it'll be the bar chart two pages on -- you can see these figures translated into this bar chart. They are mostly blue, so it's mostly NHS Factor IX concentrate that's being used. Small amounts of commercial Factor IX in 1980 and 1981.

In contrast to Factor VIII, commercial Factor IX makes a reappearance in 1985. I'll come on to explain

very briefly the reasons why that happened. In short, it's related to the introduction of a PFC heat treated Factor IX, during the course of 1985, being later than the commercial heat treated Factor IX product then available.

In other words, clinicians got to 1985, PFC wasn't yet able to provide heat treated Factor IX, so they started buying some commercial heat treated Factor IX.

We'll turn briefly to Northern Ireland. If we go to the next page, please. So this is the introduction to Annex B, which covers Northern Ireland. Again, similar points and caveats are summarised at the top. We'll start with Factor VIII on the next page, please.

A similar table is set out. We'll see this when we go on to the graphs and the charts but, as we've covered during the course of this presentation, it's important to be aware that there was a change in the arrangements for Northern Ireland, BPL -- or BPL/PFL generally providing Factor VIII concentrates up to 1982, PFC taking over in 1982.

In fact, if we just look at this table for a moment, and if you see the column for NHS Factor VIII, and we move down the figures from the late 1970s to

the early 1980s, we'll get to 1981, 122,000 units, then we see a very significant drop to 12,000 units in 1982. That's the changeover year.

I took you, sir, yesterday afternoon, to the Northern Ireland return for 1982, which records that NHS Factor VIII was only available in November and December of that year.

If we can go over the page, please, Sully. We can see here a different picture in Northern Ireland than in Scotland. So, again, the red line is commercial concentrate, the blue line is NHS Factor VIII. Up to 1982, that comes from BPL, and then comes from PFC. The orange line is cryoprecipitate.

If we go on to the bar chart, please, on the next page. Thank you. We can again see a different picture emerging from the one we just looked at in Scotland. In short, much more red, which means much more in the way of commercial concentrates, particularly in the period up to 1982. Still significant amount of -- amounts of commercial concentrate being used in '83 and '84. Still commercial concentrate being used in 1985, though by that stage it may have been heat treated. One of the reasons for explaining why the figures for NHS PFC

concentrate don't increase immediately, my understanding is that because the Northern Ireland arrangement was a pro rata one in PFC, it took some time for Northern Ireland to increase the amount of fresh frozen plasma that it was collecting and was able to supply to PFC, so it took some time to increase the amount of PFC Factor VIII that it was receiving in return.

And the last -- the next page, please, Sully.

Factor IX. I'm not going to go through the figures in this table. If we could go through two pages on to the bar chart for Northern Ireland. So this is the position for Factor IX in Northern Ireland, and we can see some commercial Factor IX had been used in 1976/77, almost as much commercial Factor IX used as NHS Factor IX in 1978, and then no commercial Factor IX used again before 1990, by which time it will have been heat treated.

Sir, that takes me to the end of this section of the presentation. I was intending next to turn much more briefly to the arrival of heat treatment in Scotland and in Northern Ireland. I will finish that portion of the presentation and the presentation overall in time for Mr Hill to take over to cover pool sizes. I wonder if it might be a convenient moment to

break for lunch now. I then anticipate that I'll be able to try and finish things in the early part of the afternoon.

SIR BRIAN LANGSTAFF: Yes. Well, shall we break then now until 1.50? 1.50.

(12.52 pm)

(The Luncheon Adjournment)

(1.49pm)

SIR BRIAN LANGSTAFF: Yes?

MR BOUKRAA: Sir, I'm going to continue much more briefly now with an overview of the introduction of heat treatment of PFC products. I'm going to start by returning to the annex that we looked at earlier, a different part of it.

Sully, it's that document INQY. If you could go through, please, to page 15. Now, this is a table of products, PFC concentrates, that we've prepared in the Inquiry team. This table contains PFC concentrates -- products that were routinely issued. It doesn't contain all of the various products that were being developed, were sometimes issued for trial but were not issued routinely.

It provides a helpful route map and an overview of where we're going to go. As you can see, it's divided into Factor VIII and Factor IX and I'll just

pick up a few dates in the middle column for Factor VIII. We can see the very early introduction of Factor VIII concentrate, Cohn Fraction I in 1956, then the next date, 1974, that's PFC's standard intermediate Factor VIII concentrate, sometimes known as NY and the NY prefix refers to a link between PFC and colleagues at New York University.

Then, you can see, we go from 1974 to December 1984, when PFC's first heat-treated product is introduced. There's then a series of other heat-treated products. The first one that's introduced is dry heat treated for two hours at 68 degrees. The next one is introduced around September/October 1985. It's a similar product again, 8Y, with some stabilisers added. Dry heat treated at the same temperature, 68 degrees, but this time for 24 hours. Then the next date, it's half cut off at the bottom, it's April to May 1987. It's a product which becomes known as Z8, April/May 1987.

If you go on to the next page, Sully, you'll just be able to see -- that's perfect, thank you.

That's a product which is dry heat treated again for 72 hours, initially at 75 degrees and, eventually, for 80 degrees.

We can contrast -- I won't pick up the 1991

product which changes approach. We can contrast that Factor VIII timeline with the Factor IX timeline, which is in the right-hand column. So the story starts in 1967, I've covered already, PPSB, 1971, the haemophilia B patients, that's replaced by DEFIX. We can then see that the next key date for Factor IX is August 1985 when a heat treated Factor IX product, DEFIX, was introduced.

Two points to note about that introduction. First of all, as you can see from this table, it's later than the heat-treated Factor VIII product. The second point is that it is heat treated for longer at a higher temperature from the first iteration, and that remains the same product through the rest of the time period that we're looking at.

Sir, that's just to provide an overview of where we'll be going with some of these heat-treated products and I'm going to turn to a very brief chronology that goes back in time to the early 1980s, and I'm really just going to pick out a few key dates, focusing on Factor VIII first.

So far as the Inquiry has been able to identify, PFC and the wider SNBTS first begin to look into the possibility of heat treating Factor VIII concentrates in late 1980. That seems to follow a conference that

took place in Germany, in Bonn, in October 1980 that was attended by Professor Cash. During that conference the German company, Behringwerke -- I'm sure I pronounced that wrong -- report that they have been able to heat treat a Factor VIII product using pasteurisation, pasteurisation as opposed to dry heat treatment. Pasteurisation, I think, like Mr Hill said, is more like a water bath, dry heat treatment is more like an oven.

You can get a sense of the reaction to that claim from a letter that Professor Cash wrote to Mr Watt on 27 October 1980. He briefly described what was -- what the company was saying, this German company was saying and he ends with:

"Sounds unbelievable. Thought you might be interested."

As we're looking at heat treatment in this very early period, the focus is on trying to inactivate hepatitis, hepatitis B, and then also non-A, non-B hepatitis in Factor VIII concentrates.

I'll pick matters up in late 1981, the following year, when the SNBTS, through Professor Cash, establishes the Factor VIII study group. Now, the Factor VIII study group looks at a whole series of different issues and problems relating to Factor VIII.

It establishes a subgroup, the Safety Action Group, which focuses on viral inactivation.

Now, that group meets in January 1982, prepares a first report around March 1982. At least in that early period, it's made up of a Dr Cuthbertson from the PFC, two other members, Drs Pepper and Sommerville, so includes non-PFC members as well from the wider SNBTS. A report is prepared by that Safety Action Group on possible viral inactivation of Factor VIII, considering different methods, considering the possibility of inactivating hepatitis.

By the time of a March 1982 meeting of the Factor VIII study group there was a discussion of the proposals. At that time, the suggestion of the Safety Action Group was that proposals to achieve a hepatitis reduced Factor VIII product -- and that was how it was phrased at the time, "hepatitis reduced product" -- would take time and considerable investment. It was thought that this could not be achieved in less than two years. So in March 1982, the suggestion to produce a hepatitis reduced product, Factor VIII product, would be around two years.

The group continues investigating viral inactivation through the remainder of 1982, there are various important parts of the chronology that are

picked up here in the written note, including meetings internationally that Dr Foster attends, and various other meetings and reports that are prepared, but I won't go into the detail of those now.

By the time we get to October 1982, the Factor VIII Study Group is suggesting that it's first option, preferred option for viral inactivation, is heat treatment. Now, the context for that is that, in this early period, various other possible viral inactivation methods have been considered: irradiation, for example; treatment with detergents; there's more of a focus at this point in heat treatment. The kind of heat treatment that the group is focusing on is pasteurisation.

Alongside that focus on pasteurisation, what we can see in these documents from this early period is a belief that part of the key to producing a successfully virally inactivated Factor VIII is to have a higher purity concentrate, so there investigation into producing high purity concentrates, alongside investigations into pasteurisation.

That gets us to around January 1983. This work is ongoing. There's some discussion on the relationship between this work on heat treatment and self-sufficiency. There's a meeting of SNBTS and

Haemophilia Directors on 21 January 1983, during which Mr Watt explains or sets out, rather, this link explicitly. I'll just read out a couple of -- part of the passage that's recorded in the minutes. It's said that:

"Mr Watt explained the problems which had to be overcome in preserving acceptable yields and providing a product which was not too expensive, considerations that were of less importance with the commercial product."

Around this time, early 1983, commercial producers of early factor concentrates were also trying to market virally inactivated products. He said:

"During the meeting, Directors were made aware of fierce competition facing the PFC from commercial concerns and were asked to bear in mind the state of policy for the Scottish Health Service to be self-supporting in blood products. The PFC would have limited amounts of heat-treated Factor VIII available for trials in the near future, and the Haemophilia Directors agreed to support the PFC as much as possible in the development and clinical trials of the NHS product."

So that gets us to early 1983. In the first few

months of 1983, reference begins to be made to AIDS. In the first references that we can see that are set out in the written note, there's not always a direct link between AIDS and PFC's heat treatment strategy, but a direct link is made soon thereafter in May 1983 and it's a document I'm going to bring up.

Sully, it's PRSE0001111. I'll just check I've got the right --

Sir, all I'm going to do with this document is highlight the context and read out some of the passages. It's an important document. As you'll see, it's drafted by Dr Foster, so I'm not going to suggest any inferences or meaning that might be drawn from it beyond what's set out in the document. Before we go to that, it might just be worth noting the date, 3 May 1983. Now, the direct reliance of this document, for present purposes, is to try to work out what the impact was for reports of AIDS on PFC's heat treatment strategy. It also has a place in the Inquiry's wider investigation into knowledge and understanding of the risk of AIDS and how that was communicated to patients.

I've mentioned the date, 3 May 1983, because it is almost exactly of the same date as the message which went out from Professor Bloom through

The Haemophilia Society to patients about AIDS and what the reaction should be to AIDS. Now, I'm not suggesting there's any direct link between Dr Foster, the PFC and Professor Bloom, but when we're looking at how the AIDS risk is set out in this document and how the AIDS risk was set out in that Professor Bloom communication to patients, it's worth just noting that timing.

SIR BRIAN LANGSTAFF: Well, the two days before was 1 May, it was a Sunday, and that's when the Sunday papers carried articles concerning the risk of AIDS. So talk of "killer blood". So that may well have something in the mind of anyone who was concerned with producing something which might transmit the cause of AIDS.

MR BOUKRAA: It may well have been, sir. I'll obviously leave that Dr Foster, who is giving evidence.

SIR BRIAN LANGSTAFF: Yes.

MR BOUKRAA: But you're quite right, sir: those articles appeared and, in fact, they prompted the message from Professor Bloom. A request went out to him from The Haemophilia Society in response to those articles, saying "Please can you prepare a message for patients as a result of what's been said". I think he drafts it around 3 May, it goes out the following day.

If we can scroll down, please, Sully, just to

get the first few passages.

We can see at the top -- actually, sorry, can we get the top half of that, that's great -- "Until very recently" -- and this summarises the background to PFC's heat treatment programme at the time. Dr Foster says:

"Until very recently the objective of our heat treatment programme was to cope with the hepatitis problem in haemophiliacs.

"Because severe haemophiliacs have already been heavily exposed to untreated products then only mild and moderate haemophiliacs could benefit from a treated product (in the foreseeable future). It was estimated that the mild/moderate group could use up to 30% of the total [Factor VIII]. This estimate, plus the fact that these patients are presently likely to be treated with single donor cryoprecipitate have determined our present strategy ie that we will.

"Plan for 4-6 pilot-scale lots during 1983.

"Design a full-scale plant to handle 30% production for 1984/85 at the earliest.

"Mild and moderate haemophiliacs can continue to receive single donor cryo meanwhile."

He then goes on to say -- and if we can scroll down, Sully, I'll pick up the impact of AIDS:

"The possibility that another more serious infectious agent (AIDS) is now involved suggests that we may need to review this strategy. In the new scenario:-

"i) The haemophiliacs most at risk are the severes rather than the mild and moderates.

"ii) There is already evidence of a panic recourse to cryoprecipitate.

"In the absence of any hard data, heat treatment (of everything) looks at the moment to be the most likely possibility that we have to face up to. If this is so, then we will have to plan to pasteurise all of the Factor VIII (rather than 30%) and we may also want to review the timescales noted above."

If we could go down a bit further, please:

"Timing may become crucial for a number of reasons:-

"i) The publicised view that FVIII is infectious and that there may be a long incubation period (ie 3 years). We may argue that this has not been proven but hard data (one way or the other) could take years to achieve. Meanwhile, decisions will probably be taken according to the 'worst case' hypothesis."

SIR BRIAN LANGSTAFF: Just pause there for a moment. Yes,

that's Mr Watt, the last sentence, expressing a view that people will err on the safe side.

MR BOUKRAA: It looks like that, sir. I should clarify this is Dr Foster --

SIR BRIAN LANGSTAFF: The word "err" is simply adopting a colloquial expression. It's not a suggestion that they will be in error to do so.

MR BOUKRAA: No, sir. Just for the transcript rather than you, sir, this is a Dr Foster memo rather than Mr Watt's.

SIR BRIAN LANGSTAFF: I'm sorry. He can explain what he had in mind.

MR BOUKRAA: Yes, quite.

SIR BRIAN LANGSTAFF: Thank you.

MR BOUKRAA: I'm not going to comment too much on what all of this might mean. Dr Foster is meant to be here --

SIR BRIAN LANGSTAFF: Ultimately, it's for me having listened to submissions.

MR BOUKRAA: Yes. Then the final passage on this page:

"ii) There are some who would find a move back to cryo attractive, and if this gathers momentum (it would only need one suspected case from NHS Factor VIII), we can see our fresh frozen plasma disappear overnight."

If we go over to the next page, please, at the

top, Dr Foster says:

"There may therefore be a case for accelerating our heat treatment programme. While I do not disagree with point (2) above [I believe point (2) is about plans for building a full-scale plant], it may be possible to introduce an intermediate stage still using the pasteurisation cabinets. We probably have most of the equipment to allow us to do this already."

He then sets out some detail of the technical process that would be involved in the rest of this memo.

Sir, that's all I wanted to take from this document for now.

In the written note, we've recorded that it appears that a change of approach was agreed at the PFC as following this memo in a meeting which may have followed it. I believe that that involved scaling up the pasteurisation product, but I'll allow Dr Foster and Dr Perry perhaps to explain that further.

The Safety Action Group was still continuing its work during this period. It met again on 15 June 1983, and I just want to take you to a record of its meeting very briefly. It's PRSE0003460.

I just want to highlight two passages. If we can have the top of this page where we can see the

date and those who were present. These are the members of the Safety Action Group, so there's Dr Cuthbertson of the PFC, and then there's two other members, reflecting -- who are not from the PFC, reflecting that this is part of a wider SNBTS initiative.

If we go down to the bottom of this page, there's a summary there of the approach of PFC to heat treatment at this time. It says:

"Considerable progress had been made at PFC in producing heat treated Factor VIII, and clinical trials should start towards the end of the summer in Glasgow and Edinburgh. No infectious model for non-A, non-B has been produced yet. The putative 'AIDS' virus must be considered as a potential hazard in Factor VIII concentrates."

A lot of this document involves technical issues relating to viral inactivation. There's one more passage I wanted to draw out that links into the wider context, and that's at page 5, please, under the heading "AIDS". It's just the first two or three sentences:

"Although not proven to be a virus, this apparently infectious agent had been found in haemophiliacs in the UK. It would seem wise to try

somehow to encompass AIDS inactivation along with hepatitis B and non-A, non-B inactivation schemes."

There's then a discussion of the impact of that on viral inactivation methods.

June 1983, sir, we've previously had a presentation on the first patient, of which the Inquiry is aware, in the UK with haemophilia, to exhibit symptoms of AIDS, one of Professor Bloom's patients.

SIR BRIAN LANGSTAFF: Well, he probably, it was said. That's how it was reported to the NIBSC, that he probably had AIDS.

MR BOUKRAA: That's right, sir. There was a report on 6 May 1983 to the CDSC about this patient. It may be that that's the patient who was being referred to here. There was another patient in Bristol, I'm not quite so familiar with the chronology of that patient but my understanding is that it may not have become common knowledge until later in 1983 that there was a Bristol patient with AIDS too.

I'm going to move forward to the beginning of 1984. Now, Drs Foster and Perry will be able to correct me if I'm wrong, but my understanding is that the trials of PFC's first heat-treated Factor VIII products didn't take place, as it was thought they

might, during 1983, during the summer or later 1983, that they in fact started towards the start of 1984, January to March.

An important date in the chronology to note is January 1984, Professor Ludlam reports an adverse reaction in one of his patients who has been treated with this pasteurised trial Factor VIII. He reports symptoms like chest pain, retching.

Dr Forbes provides some -- a report of these early observations of the product in March 1984, with no adverse reactions. Now, during the remainder of the first half of 1984 and the beginning of the second, it appears that the focus of the PFC continues to be on producing a pasteurised Factor VIII product, and that's not to say that there weren't some -- wasn't some consideration given to dry heat treatment, I believe starting during 1983. I won't go into the details of that but, in terms of the overall focus, it seems that continued to be pasteurisation until later in 1984.

There's then a major shift that occurs in PFC's strategy. It appears to be linked to two events around the same time. The first is the discovery in October 1984 that a cohort of patients in Edinburgh who had been treated with PFC Factor VIII had

developed antibodies to HIV -- HTLV-III, as it was then.

Now, the Inquiry has explored the timing related to that discovery and other evidence, no doubt it can be picked up with the witnesses we'll be hearing from so I won't go into it any further. Alongside that discovery, on the 1 to 2 November 1984, a plasma fractionation conference took place in the Netherlands, somewhere called Groningen. It was attended by Dr Foster, Dr Perry, and Dr McIntosh as well, of the PFC. During that conference it was reported that dry heat treatment appeared to successfully inactivate HIV.

Those attendees come back from the conference, there is a major change in the PFC's approach during the course of November and December 1983 to dry heating the existing PFC Factor VIII concentrate. What appears to have taken place is that the stocks which existed of PFC NY, normal intermediate unheated product were heat treated from December -- a point in December 1984. That product begins to be sent out to RTCs in Scotland and also Haemophilia Centres, and the PFC and the wider SNBTS introduce or appear to introduce a policy of seeking to re-call unheated products that was at RTCs and was also in blood banks

and possibly stocks of home treated product as well, although it may be that there's more to explore on those details.

So we get into 1985 and this first heat-treated product is being introduced. The type of treatment, as I said, was dry heat treatment, it was heated at 68 degrees for two hours.

Now, that gets us into 1985. I'm going to say very little about what happened with Factor IX during the period we've just looked at, the '83 to '84 period, other than to say that there was some early investigation into heat treating Factor IX during that period. Heat-treated products, Factor IX, is not introduced as we've seen also in December 1984. It comes a little later.

So we're into 1985. PFC is continuing to explore further the heat treatment of its Factor VIII product and, in particular, to explore different heat treatment viral inactivation regimes being applied to its product, not just 68 degrees for two hours. We've set out the detail of some of those attempts in the written note. What appears to take place is that, from around January to September 1985, the first heat-treated product, the first generation product, the 68 degrees for two hours is issued. From around

September 1985, it's replaced by a second generation product which is heated at 68 degrees for 24 hours.

Now, as part of that policy of introducing the second generation of product, there appears to have been a PFC policy of exhausting existing stocks of heat-treated product before bringing in the second -- the new generation one. So, in other words, it may be that a product treated for 24 hours at 68 degrees was available earlier but, before it was introduced to RTCs and the patients, they would exhaust the first generation product, all of that would be used up.

The new product would be introduced through a batch dedication scheme that had, by then, been introduced at the PFC. I mentioned this briefly earlier. I'm going to go into very little detail about it, sir, save to note that, in the written presentation, we've picked up a suggestion from Professor Cash in 1983, November 1983, that the SNBTS and PFC might need to be considering some sort of batch dedication arrangement.

He raises it again, Professor Cash, at the 2 February 1984 meeting that we looked at earlier. There's then a period between February 1984 and early 1985 where it's not quite clear, at least from the documents, what happens to this proposal to introduce

a batch dedication system.

It then comes in around March 1985, and I'm just going to go to a document which briefly explains it. It's PRSE0004101.

This is, we can see from the title, a PFC report that was prepared for a meeting in March 1985.

If we go through to page 5, please, there are other parts of this document that are certainly worth considering. It has an update on heat treatment. If we go down to the second half of the page, there's an explanation of the approach to batch dedication. It says:

"The ability to prospectively dedicate whole batches of product to individual patients or groups of patients depends, for success, on substantial reserves of product. Such reserves are now available and it is now possible to implement a system of limited batch exposure.

"Briefly, such a system would operate by dividing patients into groups (on a regional basis) with each group receiving product from a designate batch held at the RTC. RTCs would also carry reserve batches for replacement of 'active' batches where these became exhausted."

Then it sets out how groups of patients might be

divided up and then, at the bottom of this section of the report, it says:

"Present estimates indicate that such a system can be in place by the end of March 1985 with existing product which will sustain supply until Autumn 1985."

Now, it appears that a batch dedication system was introduced around this time, and that it remains in place until at least some time in 1987. The exact end date isn't completely clear from the documents.

So we're now into -- late in 1985, PFC's second generation heat treated Factor VIII, heated for 24 hours, is being issued. Research is being undertaken into a third generation of product and, so far as it appears from the documents, that appears to be because it was understood, at the time, that heat treating -- dry heat treating at 68 degrees for 24 hours should be successful in inactivating HIV/HTLV-III but was thought unlikely to inactivate non-A, non-B hepatitis. In other words, this 68 degrees, 24-hour product could still transmit non-A, non-B hepatitis.

We're done with that document now, thanks, Sully.

So there then begins focused or more research, rather, on this new product which becomes to be known

as Z8.

There's -- it seems that there's a change of direction which happens towards the end of December 1985, with the focus on this Z8 product, which will involve heating for 72 hours at 80 degrees, ie the same amount of time, the same temperature, as the BPL 8Y product, which we heard about last week during the hearings on England and Wales.

I'm not going to go into all of the detail around the development of Z8. What would appear to happen is that the product has been developed. Around August 1986, there is some difficulties encountered in manufacturing it at a large scale, scaling it up from the initial small test batches. There's a reference in a 29 August 1986 letter from Dr Perry to an 11th hour problem with freeze drying.

We get to late 1986, around December 1986, and it appears that Z8, this new product, which it is hoped will be effective against non-A, non-B hepatitis as well as HIV, is ready for clinical trial.

Now, while this product development was taking place, there had been a number of letters and some discussions around what's termed in the documents "compensation arrangements for patients". Now, what this relates to is the arrangements for compensating

patients who participate in clinical trials in the case of an adverse reaction. Dr Ludlam had raised this issue some time earlier. It had not been resolved. Resolving it required the involvement of the Scottish Home and Health Department and others.

We get to the beginning of 1987. Dr Ludlam raises his concern again, and effectively appears to say, "I'm not prepared to enter my patients into the clinical trials of Z8 until this issue has been resolved."

There's some evidence that Haemophilia Centre Directors in other parts of Scotland adopt a similar position. There's correspondence back and forth with a number of individuals, including at the Scottish Home and Health Department. It appears around February 1987 some form of compensation arrangement is agreed, at least with the clinical trial aspect. Trials appear to begin around February 1987 for Z8.

We then get to April, and it seems that the SNBTS and PFC, following those clinical trials, are ready to start issuing Z8 on more of a routine basis. It seems, generally speaking, to be fed into that batch dedication system that we discussed and to reflect the policy of exhausting stocks. At least from the documents, there's a suggestion that those

existing policies might be subject to a caveat for certain patients, in particular patients who had been -- not been treated previously with factor concentrates, or treated very little with factor concentrates, on the basis that they were understood to be the highest priority for a new product which was hoped to be effective against non-A, non-B hepatitis as well as other viruses.

Now, that's a brief overview of the position on heat treatment of Factor VIII products.

Factor IX we've covered in a reasonable amount of detail in the written note.

As we get into 1985, with a heat treated Factor VIII product in existence but no heat treated Factor IX, Haemophilia Centre Directors start to ask PFC what might be happening and when they might expect a heat-treated Factor IX. Around that time, and in fact even before from some years previously, there's an explanation that in order to introduce a Factor IX heat-treated product, there might be additional complexities because of the need to ensure that the product is not going to result in -- I always pronounce this wrong -- thrombo --

SIR BRIAN LANGSTAFF: Thrombogenicity.

MR BOUKRAA: Thrombogenicity. Sir, thank you.

I understand that to be -- might cause blood clots in patients. That required an additional amount of testing involving animal studies. That is one of the explanations provided for why heat treated Factor IX was going to be introduced later.

In the meantime, during the course of 1985, some Haemophilia Centre Directors appeared to decide that while they're waiting for the PFC to introduce its product, they'll start buying some commercial heat treated Factor IX, and that will explain why, in the graphs that we looked at earlier, there is an appearance of commercial Factor IX concentrate in 1985 when there hadn't been before that.

The reasons why the Factor IX heat-treated product that is introduced around August 1985 by the PFC is immediately at the higher end of the heat treatment regimes that we've been considering -- 80 degrees for 72 hours -- is related to the nature of the Factor IX molecule as against a Factor VIII molecule. I won't try to provide any more explanation for that issue.

That gets us, sir, to the end of 1987 and more or less to the end of this presentation. In the written note we've covered the 1988 period to 1991. I don't propose to go through any of the details now.

For those who'd like to review that portion of the written note again, what will become apparent is that, in the later 1980s, Scottish Haemophilia Centre Directors start to purchase heat-treated product, including heat-treated Factor VIII products, again, rather than just relying on Z8. The reasons for that are set out in the written note. There is also, during this period, another arrangement between Professor Ludlam and Dr Mayne in Northern Ireland to exchange PFC products for commercial products, and we set out the chronology of that agreement and some correspondence which points to the reasoning and the rationale behind it.

Sir, that was all I was intending to say in the oral presentation for Scotland and Northern Ireland. As I've said many times, there's more detail in the written note. I'm going to be handing over now to Mr Hill, who is going to be dealing with pool sizes, sir, but I wonder if before that, it might be appropriate to take a short break.

SIR BRIAN LANGSTAFF: Well, let's take an early break in that case, and come back at 2.50.

2.50.

(2.32 pm)

(A short break)

(2.49 pm)

Presentation to the Inquiry on the size of pools of plasma used in domestic production of blood products by MR HILL

SIR BRIAN LANGSTAFF: Yes, Mr Hill?

MR HILL: Sir, we are turning now to two presentations on pool sizes used in fractionation, firstly in England and Wales and then in Scotland.

All of the qualifications that usually apply to presentations given by counsel to the Inquiry apply to these as well, and I won't repeat those here. The focus is going to be on Factor VIII, in terms of the pool sizes. We have some data for Factor IX but it is much less satisfactory, unfortunately.

I'll start with the England and Wales presentation. There is a written presentation that goes alongside this, and similarly for the Scottish presentation as well. It may be that people find it easier to read the written presentation than to reflect back on the transcript today because there are a lot of figures which are going to be given and I'm afraid it might be quite hard to follow at points but we'll do our best.

In England and Wales, the focus of the presentation is on BPL. There are various sources that we will look at. I'm afraid it's the same story

of different data sets, different figures, some correlation, more correlation perhaps here than in other cases. But there is, I'm afraid, a little bit of leaping from one set of material to another.

I will go through what those sources show in terms of figures and present that in tables and in some graphs. Then we will go back and look at some of the underlying documents to see what they can tell us about the reasons behind the increases, and about the processes involved, although, as a spoiler warning, there is only a limited amount of material that the Inquiry legal team has been able to discover on that.

I'm also conscious that you will hear evidence in the coming days from Dr Snape, for England and Wales, and Drs Perry and Foster covering Scotland. As ever, we do not seek to pre-empt that evidence. They may be able to shed some more light on this.

Before turning to what is covered in the presentation, there is, as ever, a pre-history to the growth of plasma pools in the 1970s. We don't have a great deal of evidence about plasma pool sizes in the '60s and '70s at the moment but more work can be done on that area in due course.

What we do have, are little fragments, which may help to set the scene before we pick up the story

again in the mid-'70s, from where we have much more data, not least because that is the area which the HIV Litigation focused on.

If we could go first, please, Sully, to HCDO0000581, page 1, please. This is an article that has been introduced before the Inquiry and I'm certainly not going to go through it in any detail. It is an article from the British Journal of Haematology in 1974, Volume 26, page 313 by Dr Rosemary Biggs, entitled "Jaundice and Antibodies Directed Against Factors VIII and IX in Patients Treated for Haemophilia or Christmas Disease in the United Kingdom."

As I say, I'm not going to go into the substance of that article. What I am going to take you to at page 6, please, Sully, is a table that Dr Biggs gives us that shows the material given to haemophiliac patients in Oxford from 1969 to 1971, to quote the words which she used in the article.

We can see three years are given, 1969, 1970, and 1971. The table includes information about the number of patients treated and then gives figures for the different types of material that those patients were treated with, plasma, cryoprecipitate and Factor VIII concentrate. If we look at the last of

those for each of the years, Factor VIII concentrate, in the final column we can see the mean pool size given in terms of the number of donations that went into the pool. For 1969, that mean pool size is 160 donations. In 1970 it is 192 donations. In 1971 it is, again, 192 donations.

That is from the PFL in Oxford. We can see from the preceding column that for those years the number of pools fractionated were 83 in 1969, 72 in 1970 and 80 in 1971.

In the presentation, the general way of translating donations into the size of a pool or vice versa is to adopt an assumption that, at this time, about 180 millilitres of plasma was given per donation. Some sources have it at a little higher, some have it a little lower, but we've adopted 180 millilitres.

Using that figure, the pool sizes would be about 30 litres to 35 litres, expressed as volume, rather then donations, according to this table.

When comparing this to the later figures I'm going to give you, it is important to emphasise that these come from the PFL in Oxford and not BPL, which is where the later figures come from. Second, as Dr Lane put it, this was at the cottage industry stage

of plasma fractionation. Later, we're going to move on to the factory stage or the industrial stage, where far more factor concentrates are being produced. But that is a figure that we have for 1969 to 1971 in Oxford.

The next document we're going to take you to in terms of history is CBLA 0000253.

This is a memorandum from Dr Bidwell of the PFL to Dr Maycock, then director of BPL, dated 22 January 1975.

It is entitled "Number of donations in a batch of factor IX", and I'm going to come back to this document when we're talking about Factor IX specifically. But for now, I'm just going to take you to the first sentence. Dr Bidwell wrote, and I quote:

"When we talked about labels at Elstree in November we agreed to have printed on the label for factor VIII that it was derived from 'not more than 500 donations' and that we would cease putting on the precise number of donors whose plasma had gone to make up the pool."

That is where I will stop for now. What this appears to be saying is that, before this discussion in November 1974, the label on a bottle of BPL Factor VIII would have the exact number of the amount

of donors whose plasma had gone into that bottle.

The agreement that was reached in November 1974 was that, instead of doing it that way, the label would carry the words "Not more than 500 donations". We'll come on and look at some labels shortly.

SIR BRIAN LANGSTAFF: So it might mean -- well, it obviously means less, the 500 donations or less. It could be 500 donors at most, but it may be less if, for instance the donors had given more than one --

MR HILL: Yes.

SIR BRIAN LANGSTAFF: -- donation.

MR HILL: Again, in the presentation, we have assumed that one donation equals one donor. We're on safer ground doing that in England and Wales, and indeed in Scotland, than we are with commercial concentrates because plasmapheresis isn't generally being used. So a donor will be giving, at most, two donations a year. So it's unlikely they will end up in the same pool. The exception is the plasmapheresis donors, but they are a relatively small number in the UK at this time.

If we could take that down, please, Sully. The third document I will take you to is BPLL0003721. This is a memorandum from Dr Maycock to Dr Bidwell from 8 December 1975, so approximately 11 months later than the one that we have just looked at, and it is

not in reply to the previous memorandum, but it does refer to donor pool numbers.

Dr Maycock wrote:

"Thank you for your memorandum of 3rd December, 1975.

"As we increase preparation of Factor VIII concentrate we propose to increase the size of pool as far as labelling is concerned in two steps during 1976 and 1977:

"Present 150 [litres] 830 donations

"1976 270 [litres] 1500 donations

"1977 360 [litres] 2000 donations

"[Numbers] of donations are based upon 180 [millilitres] of plasma per donation)

"The large pool size can be defended on the ground that starting plasma and concentrate are tested by RIA.

"I think PF Lab and BPL should keep in step.

"Therefore I would like you to introduce steps of 1500 and 2000 donations in the size of plasma pools for Factor IX concentrate.

"I think the number of donations should be shown on the Factor IX label as well as on the Factor VIII label."

We'll come back, again, to the question of

Factor IX. For present purposes what I draw your attention to is this: firstly, as of 3 December 1975, the present pool, as expressed at least in terms of labelling, was 830 donations, being a plasma pool of about 150 litres, and you'll see that Dr Maycock uses that 180 millilitres figure as a way of translating from donations to litres.

You'll see that there is a plan to increase the size of the pool from 150 litres to 360 litres between December 1975 and December 1977, and that will be an increase from 830 donations to 2,000 donations.

I had brought you to that document because that is the first one that appears in the tables in the written presentation that I'm going to show you shortly. But, as we can see from the documents that proceed it, there has already been a growth in pool size by that time.

SIR BRIAN LANGSTAFF: Well, we've moved from Biggs's 160 average number of donations in a pool through to 180 -- to CBLA, not more than 500 donations, to 830, 1,500, 2,000.

MR HILL: Yes, we had switched centre, at that time, as well, from Oxford to BPL, but yes.

SIR BRIAN LANGSTAFF: But if the -- yes, it's no longer the cottage industry we're looking at; it's the

production facility.

MR HILL: Yes. Yes. It's also relevant to note that in this memorandum, Dr Maycock says:

"I think PF lab and BPL should keep in step."

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Now, the qualification to that is that the memorandum as a whole is talking about labelling, but whether or not that translates to actual donation sizes is not wholly clear, but he does say:

"I would like you to introduce steps of 1,500 and 2,000 donations in the size of plasma pools for Factor IX concentrate."

I'm going to turn now to the two sets of contemporaneous documents that we have that help to set out the maximum limits on pool sizes in the 1970s and the 1980s at BPL. These are primary sources, in the sense that they come from the time that they are describing. It is important to note that they are about the maximum limits and, in terms of labels that are placed on bottles and correspondence about what the maximum limit could be, it doesn't necessarily follow that the maximum was being used at the time, but we will see in due course we have some other data on that which correlates relatively closely.

The first set of documents that we're going to

look at are some BPL product labels from the 1970s and the 1980s. I note that I'm not going to be going to product labels from Scotland because Ms Richards is going to be looking at those in due course with witnesses, so I won't pre-empt that.

If we could turn, please, Sully, to CBLA0009269. This is a label from a BPL Factor VIII bottle, which is dated, according to the date at the bottom of the document, March 1976. We don't have any reason to doubt that date, even though the label itself is not filled in.

If we look at the left-hand side, we can see that it says, the label says, "Prepared by Blood Products Laboratory, Lister Institute, Elstree, Herts."

That is BPL.

The label is entitled "Human anti-haemophilic fraction", and we can see the bottle contents are said to contain Factor VIII, and there is a gap left for saying how many international units are contained in the bottle. There are instructions about how to reconstitute the concentrate.

Then on the right-hand side, we can see on the label:

"Less than 1,500 plasma donations used in the

production of this batch."

We're having a little difficulty spinning it around, but I hope people can see that on the right-hand side of the label, written bottom to top, as it were. Thank you, Sully.

SIR BRIAN LANGSTAFF: Ah, there we are.

MR HILL: So 1,500 donations -- that's it. Thank you -- or less than 1,500 donations 1,500 plasma donations, used in the production of this batch. That is March 1976.

If we could now go, Sully, please, to BPLL0001692_008. If we could go to the second of those labels, please. This is a label -- sorry, if we could just pull out for a second, Sully. Thank you.

This is a label that comes from a bottle that was fractionated, according to this sheet, on 11 September 1980, and the Factor VIII assay date is 3 October 1980. So we're in the autumn of 1980.

If we can now please expand it, please, Sully.

We can see again that this has been prepared by BPL in Elstree. It is said to contain Factor VIII, 250 international units. It is an intermediate purity product. If we look on the left-hand side, first of all, we can see that less than 5,000 plasma donations were used in the preparation of this batch.

If we could turn it back around, Sully, to its original orientation, and expand the central part of the label.

This label contains the warning:

"The preparation is of human origin and cannot be assumed to be free of hepatitis virus."

That is a warning that was not on the previous label from 1976.

Thank you, Sully.

The next label we will look at comes from 7 January 1983. It is BPLL001692_009.

BPL0001692_009. Apologies, Sully.

The top label is, if we could just pull out a little, please, Sully, we can see a date at the top, "Date effective", 7 January 1983. Then if we could zoom in on the label, please. Again, the warning is there:

"The preparation is of human origin and cannot be assumed to be free of hepatitis virus."

We can see that the batch number is HL and then the batch number is given. HL is the intermediate purity product that was produced by BPL.

On the left-hand side, we have the words "Less than 7500 plasma donations were used in the production of this batch."

SIR BRIAN LANGSTAFF: I think that may be so small you can hardly see it, but it's --

MR HILL: I have read it on the computer. I am confident it's --

SIR BRIAN LANGSTAFF: I can read it but I'm just thinking about those who are watching it at a distance or maybe on a home screen.

MR HILL: Yes.

SIR BRIAN LANGSTAFF: So I think they can be assured that it is there. If they need further assurance, they can go into the actual document itself, those who are Core Participants, and can do so into the Relativity or catch it online.

MR HILL: All of these figures are set out at paragraph 12 of the written presentation. I'm going to bring up that table in a second, and the references to the underlying documents are there as well. So they can be checked in that way.

SIR BRIAN LANGSTAFF: Thank you.

MR HILL: I'm now going to go to a document which contains --

SIR BRIAN LANGSTAFF: Can we just go back to that page, the original page?

MR HILL: BPLL0001692_009.

SIR BRIAN LANGSTAFF: I'm looking to see if -- because the

second label is about a year later, isn't it?

MR HILL: The second label is March '85 and concerns 8Y. There's a document which helpfully sets out a number of different labels including labels for 8Y and gives dates for them.

SIR BRIAN LANGSTAFF: Well, this one does actually have a figure in it. If you look underneath "Dried Factor VIII Fraction", and look at the wording underneath that, underneath the warning:

"... the preparation is of human origin (less than 10,000 plasma donations used per batch)."

MR HILL: Yes.

SIR BRIAN LANGSTAFF: So albeit that it's 8Y, it's heat treated, we have moved from less than 7,500 in January '83 to 10,000 or less -- sorry, less than 10,000 in 1985.

MR HILL: Yes, that's right. We can see that helpfully on the document BPLL0002039. We have three labels set out and before we go to any of them you can see on the right-hand side, added to those labels, written next to them by whoever has prepared this document, are the words "Pre-June 1985", "June 1985 -- February 1987" and "February 1987 onward".

Now, we don't go who put these dates there, we can't say that we have found evidence that absolutely

confirms those dates but we can say that we haven't found evidence which disproves those dates given.

The first one, pre-June 1985, if we could expand that, please, Sully. This is stated to be for an intermediate purity product with no heat treatment and that fits with what is on the label and fits with those labels we have just seen.

On the left-hand side, a little bit more clearly this time, you can see that it says, "Less than 7,500 plasma donations were used in the preparation of this batch."

So that is in keeping with what we have just been looking at. The warning there, "The preparation is of human origin and cannot be assumed to be free of hepatitis virus", is also consistent with the labels we have just seen.

If we could go to the second of those labels, please. This is stated to be from June 1985 to February 1987. It is for a high purity HT3 product, which is 8Y. We can confirm that it's 8Y because, in the bottom right-hand corner of that label, you can see the code "8Y1".

As with the label that you just went to, sir, it says:

"Warning: the preparation is of human origin

(less than 10,000 plasma donations used per batch). It has been subjected to heat treatment, in the vial, to reduce the risk of infection by viral agents (including hepatitis and AIDS viruses) but cannot be assumed to be free from risk of infection."

If we could then expand and go to the final of these three labels, it's stated to be from February 1987 onward and for FHC1. I have to say I'm not entirely sure what FHC1 stands for there. It is also stated to be barcoded, and we can indeed see a barcode in the bottom right-hand corner. It is also stated that there is no donation limit. That is confirmed by looking at the section on the warning, which now reads, and I quote:

"... the preparation is of human origin. It has been heat treated, in the vial, to reduce the risk of infection by viral agents (including hepatitis and AIDS viruses) but it cannot be assumed to be free of the risk of transmission of viral infections."

So the same warning as the previous label but with the reference to the product being derived from less than 10,000 donations removed. It is stated to be a dried Factor VIII fraction, high purity heat treated.

If we could just go to one further document,

which helps to bear out what I have said about the fact that we can't establish, from our own research, that those dates are correct, the material that we have seen is consistent with them. To make that point, could we go to BPLL0016009_161.

If we could look at the top left-hand corner there is a date given for "Date effective", which is 15 February 1988. The batch number is FHC. The label below, which is stated to be a sample label, is headed "Dried Factor VIII Fraction, High Purity: Heat Treated". We can see on the left-hand side that "8Y" is stamped on it. A barcode in the bottom right-hand corner, and the warning is this:

"... the preparation is of human origin. It has been heat treated, in the vial, to reduce the risk of infection by viral agents (including hepatitis and AIDS viruses) but it cannot be assumed to be free of the risk of transmission of viral infections."

Again, no reference to the number of donors.

Thank you, Sully. If we could take that from the screen and if we could, instead, put up, please, INQ0000375, the tables on page 5 and 6, please.

Sorry, INQY0000375. The tables on pages 5 and 6. It's the presentation itself.

Just give me a moment, sir.

I have given you a duff reference. It's INQY0000345, not 375. Sorry, my mistake. This is the written presentation. The labels I've just taken you to and some others are included in this table, and we can see how the maximum pool size on those labels increases from 1,500 donations in the March 1976 label; up to 5,000 donations on the September 1980 label; then 7,500 donations on the January 1983 label; 10,000 donations on the March 1985 label; and then from June 1985, according to the document we saw.

Then no stated limit from February 1987 onwards, according to the document that we saw and according to our own research, as we've found that on a label from June 1988. It is important to note that we cannot say that the label changed on 11 September 1980 just that we have a label from that date which shows 5,000 donations, whereas the previous label we'd found from 1976 has 1,500.

The second source that we have from the time itself which helps us to understand the maximum limits on BPL pool sizes are references that are contained in correspondence, and particularly correspondence between people at BPL and people at PFL, about what the maximum pool sizes are. I'm not going to take you to the documents, but I will take you to the table

which is at the same reference, Sully, at page 7.

We can see table 2 at paragraph 16 contains four references. The documents are given their unique IDs in the right-hand column. The information that we have obtained from those documents give maximum pool sizes of 5,000 donations in October 1980, 7,500 in January 1982, 10,000 in June 1985, and then 25,000 in June 1986. We will come back and look at that document a little later.

That correlates closely with the labels that we have looked at, the additional piece of information coming from the June 1986 data suggesting 25,000 donations at a time when there was no limit stated on the labels on the bottles themselves.

We also have some secondary sources which help us to check and to test the information that we have received from the primary sources.

The first is a series of estimates about pool size given by Dr Terry Snape during the course of the HIV Haemophilia Litigation. Dr Snape is going to be coming to give evidence next week, so this may be something that we pick up with him then. But for now, I will show you the table that is in the written presentation at paragraph 27 which records Dr Snape's estimates. These were given in response to a request

from Dr Lane for information on the pool sizes used to manufacture Factor VIII at BPL from 1975 onwards.

If we could go, please, to page 11. If we could expand that table, table 3, please. Dr Snape's estimates are that in 1975 the approximate weight of the plasma pool used at BPL was 150 kilograms, and that that came from around 750 donations.

SIR BRIAN LANGSTAFF: That is assuming, of course, that each of the donations produces, what, how many? It's 20 -- 200, isn't it?

MR HILL: I think it is.

SIR BRIAN LANGSTAFF: Because on the assumption that five times 200 millilitres equals 1 litre, 1 litre is therefore 1 kilogram, assuming that that's the equation, which is I think the equation that's broadly within -- in line with the figures.

MR HILL: Yes.

SIR BRIAN LANGSTAFF: 150 -- that is 150 times that, so it's on the assumption of 200 per -- which is rather higher than the assumption which you've used.

MR HILL: Yes. It's also worth noting that later on -- if we look down, for example, at February 1988, and the batch is FHC, 2,400 kilograms; 10,000 donations. The assumption there is 240 millilitres.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Which may well reflect the growing use of SAG-M, the additive which allowed for more plasma to be taken from a single donation.

SIR BRIAN LANGSTAFF: Yes. It's between 86 and 88. It goes up from 200 to a higher figure.

MR HILL: Yes, that's right.

SIR BRIAN LANGSTAFF: 240, as is obvious from the figures there.

MR HILL: We have been using a different figure, 180 millilitres. That is not to say that we are right and Dr Snape is wrong, just that we have used those different figures.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Something that we recognise in the written presentation is that the figure of 180 millilitres, which we have stuck with all the way through for consistency, becomes less reliable as we move through the mid '80s into the late '80s because of the increased use of SAG-M. There aren't that many conversions that we do in the written presentation from that time, but it is something to keep firmly in mind.

SIR BRIAN LANGSTAFF: I suppose also there may be developments in the amount of Factor VIII activity that you can extract, known as ^check the yield.

MR HILL: Yes. Yes.

SIR BRIAN LANGSTAFF: Both going down possibly with the start of heat treatment, but then up again with the different processes.

MR HILL: Yes.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: We can come back and we can ask Dr Snape more about the assumptions that he made and how he drew this data. For now, we simply include it as a further data source for this presentation, and it is one, I should say, that does correlate relatively closely to other data sources, save towards the end of this period.

The weight of the donor pools, approximated, increases from 150 kilograms in 1975 to 450 kilograms in 1977, which Dr Snape equates to an increase from 750 donors to 2,250.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Then up to 600 kilograms in August 1980. The number of donors there is 3,000.

March 1981, it increases to 900 kilograms; number of donations, 4,500.

July 1982, the approximate weight is up to 1,200 kilograms. The number of donations is 6,000.

The same figures are given for April 1985.

I pause there to note that the figures from September '77, August 1980, March '81, July '82 and April '85 are all given by reference to specific batches of HL, the intermediate purity non-heat-treated product. So presumably Dr Snape has gone back to the records and checked those batches and given those figures accordingly. But he refers to the weight as an approximate weight, and obviously the donations figure is derived from the calculations that we have just been discussing.

July 1985 is the next figure in the table. That is again said to come from an approximate weight of 1,200 kilograms and 6,000 donations. That is for 8Y.

In November 1986, 8Y is again the batch code. The donor pool has gone up to 1,400 kilograms; 7,000 donations by this time.

The next figure is for February 1988. The weight has gone up to 2,400 kilograms; number of donations, 10,000.

June 1988, 3,200 kilograms; number of donations 13,500.

December 1988, 3,400 kilograms; number of donations 14,500.

Same figures for July 1989.

So that is what we get from Dr Snape's estimate.

A further secondary source that we have, a set of documents which are entitled "Batch histories". If we could go, please, Sully, to CBLA0014475. If we stay on this page for a second, we can see that this is a document that is prepared during the HIV Haemophilia Litigation. As with other such documents, we don't have a final document because the litigation was settled. So these kind of working papers weren't finalised, but they do provide us with some information from those who had been working on the case, as of 1989 and 1990, putting the documents that they had to hand in order.

If we could go to page 168, please. These are the batch histories that we have. It is really a list of batch numbers, the year issued, and then a column saying, "Number of donors". Then columns about whether or not the product has been heat treated, whether it has been tested for HIV or the pool has been tested for HIV.

The column stating "Number of donors" is not explained further. So we don't know whether they are basing this on a precise figure or on a maximum label, or what the basis of the number of donors is.

Thank you, Sully. We can take that off.

Having looked at the batch history, we have produced a table which is at page 12 and just going over into page 13 of the written presentation. If we could have that, please, INQY0000345.

Thank you, Sully.

Something to note here is that the batch history sometimes shows changes in donation numbers but it doesn't give a specific date for when that change has occurred. In order to be able to present this in tabular form, we have used January and July of a given year to reflect a change during that year. But that does not mean that the change came in July 1980, it's just our way of showing that during the year it changed, and the table is set out this way so that it can feed into a later graph.

We can see that the approximate number of donations, according to the batch history figures, were 2,250 in 1978 and 1979. That figure went into 1980 but, during 1980, it increased to 3,000 donations. That figure again went into 1981 but, during 1981, it increased to 4,500 donations. That is also the figure that we have for 1982 -- at the start of 1982, sorry -- but during that year it increased to 6,000 donations.

From 1983 to 1985, and even going into 1986,

that figure of 6,000 donations remains constant. But at some point in 1986 the approximate number of donations increases to 7,000 and that is also the figure given going into 1987, and that is where the batch histories table stop. So an increase from 2,250 in 1978 to 1979, to 7,000 at some point in 1986.

Of note there, sir, I've pointed out here it's reflected in some of the other data as well, but it's perhaps easier to point it out on this table, that that period between some point in 1982 and some point in 1986 sees a plateauing of approximately 6,000 donations per batch, after a period of increase before, preceding a period of increase afterwards.

The final table that I will take you to, which is from paragraph 43 of the written presentation, is a table that is drawn from contemporary reports that we have from BPL. When I say reports, these are reports that are given in letters, in memoranda, in minutes, and indeed in more formal reports as well in publications.

If we could go, please, to page 16 of the same reference. The table goes over into page 17 as well, please, Sully.

These are figures that we have extracted from various pieces of information that we have got from

the relevant periods. There are a series of caveats that go with them, which are set out from paragraph 36 of the written presentation. We have discussed those as we've been going along, sir. They are about the size of the -- sorry, the translation between volume and donation numbers, and weight and donation numbers, and weight and volume, and the one donor to one donation ratio that has been used.

It bears repeating that the figures that are contained in this table are, therefore, approximations. They show a trend, but they cannot always be relied upon to be precise at that particular moment.

The first entry is the one that we looked at, at the start of this presentation, which is the 830 donations that Dr Maycock said was the present figure on 8 December 1975.

The next entry for 11 January 1978 -- I'm not going to take you to the underlying documents, the next entry is 2,000-plus donations, 11 January 1978. At the 18 January 1978 the figure is 3,000 donations. Then other figures from 1978 are given by reference to volume, 400 litres, which translates at 2,200 donations if one takes 180 millilitres as the measure.

1979 and 1980, we can see an increase up to

600 kilograms, about 3,330 donations. We understand that to be linked to the Stop-Gap programme and I will come back to that shortly.

1980, 5,000 donations, for 1 September. A different figure at 3 September 1980, 3,500 donations. Now, this is not to say that pools were necessarily fluctuating at this time. It may be that we just have these little snapshots of data which may refer to the maximum possible size, whereas the 3,500 donations refers to an individual pool that was fractionated at that level.

A figure for March 1981 is 2,504 donations; but April 1981, 5,000 donations; February 1982, more than 3,000 donations; April 1985, 1,200 kilograms, which equates to about 6,660 donations.

Later in March 1985, 7,200 donations; in June 1988, so a significant gap there, three years, a 2,000-litre pool which would be a little over 11,000 donations; and then April 1990, so again another gap of two years, 25,000 donations, going -- said to go into a plasma pool.

April 1991, 20,000 donors; and 17 May 1991, 13,000 donations.

So these are little snapshots from different times, and, again, I stress they're helpful to show

a trend, and it shouldn't -- one shouldn't alight on a single figure and say that is what the pool size was for the entirety of that year.

Two graphs help to show this situation. First, same reference, please, Sully, page 18, please. The same caveat applies as I gave a few days ago, that data points on this graph are joined by a straight line but it shouldn't be assumed that there has been linear growth between those two data points. In fact, often you will see a step up when a pool size is increased.

There are three lines shown on this graph. The one in purple are -- is drawn from Dr Snape's estimates that we looked at earlier. The one in green is drawn from the batch history that we looked at earlier. The one in blue is drawn from the contemporary records table which is the table that we have just looked at.

The point that I take from these figures is that they correlate fairly closely up to January 1985. There is then less data in the later '80s, but again, there seems to be a correlation of a growth in pool size and steep growth after about 1986, 1987, so at the time of the redevelopment of BPL. Then the contemporary records go much higher, because they go

later into the '90s, whereas the other data stops in the 1980s.

So that graph illustrates that the tables that we have been looking at tell broadly the same story.

Then if we could turn over, please, to page 19.

SIR BRIAN LANGSTAFF: Yes, well, if you put a -- try to just envisage a line of best fit between those various data sources, it might look pretty much like a straight, upward line without any great increase in its rising up. So it's not a bell-shaped curve, not the sort of curve we've been used to seeing in respect of coronavirus.

MR HILL: No. That's right. Until 1986, 1987, 1988, at the point where the new BPL opens. And, granted, that we have far fewer data points after that, there does seem to be a sharp increase --

SIR BRIAN LANGSTAFF: At that stage.

MR HILL: Yes.

Another point to note about this graph is that in order to capture that late surge in pool size, if that's what it was, it's been necessary to extend the vertical axis up to 25,000 donations. So, inevitably, if one does that, then the rises in donor size at the start of the period look more modest than they would look if the vertical access was a -- had a smaller

figure in it, if that makes sense.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: If we could go over, please, to page 19. The same three lines are shown on this graph and this is just to compare them to the data that we have about maximum limits of pool sizes from the product labels and from the correspondence.

The product labels are shown by the yellow line, and the correspondence is shown by the red line.

I think it is fair to say from that graph that the maximum limits are higher than the data points that we have from the other sources -- Dr Snape's estimates for batch history and the contemporary records -- with a couple of exceptions which are very close to the line and may just be quirks of the way that the data has been put together.

So it would appear from that graph that while the donation size of -- while the pool size has grown in the period, it has not exceeded the maximum pool sizes given, either on the labels which accompany the product or in the correspondence with it.

Thank you, Sully. That can be taken down now.

That was for Factor VIII. As I say, the Factor IX data is, I'm afraid, much less satisfactory.

If we could go to INQ0000345, page 20, please.

I've given you the wrong reference again, sorry, sir.

INQY0000345. This is, at paragraph 52 in the table that is shown there, the best that we are able to do with the information that we have about the size of Factor IX pools at BPL from 1983 to 1987. We can see that the figures there contain the smallest batch, the largest batch, and the mode figure, which is the figure that appears most often. That is, we think, the better measure than an average figure at the time, given the data source that we've got.

These are taken from the batch history documents that were compiled as part of the HIV Litigation. As you will see, it's far less extensive than Factor VIII data. 1983 to 1985, the smallest batch, the largest batch and the mode are all 6,000 donations. In 1986, we see that the smallest batch and the mode are 6,000 donations, so the most common pool size in 1986, from the data that we have, was 6,000 donations. But the largest batch was 24,000 donations.

Now that may be explained by the fact that in 1986 your standard production was 6,000 donations, that there were experiments run or a batch run at 24,000 donations. Then in 1987, the smallest batch is 8,000 donations. The largest batch is 20,000 donations, and the mode, so the most common batch, is

18,000 donations.

If we could then, please, Sully, go to page 22 of the same document. This is a table that is drawn from the contemporary report that we have for BPL Factor IX so the same approach that we took to Factor VIII. Unfortunately, it's difficult sometimes to discern whether the references in the documents are specifically to Factor IX or whether there is an assumption that what applies to Factor VIII will also apply to Factor IX. That may not have been a safe assumption for the reasons that we'll come on to in a second.

But we can see there the figures obtained for January 1978 is over 2,000 donations; then a second figure a week later of 3,000 donations; July 1978, 400 litres, approximately 2,200 donations; April 1981, 5,000 donations; December 1984, 1,200 kilograms or 6,600 donations; June 1988, 2,000 litres, or a little over 11,000 donations; April 1990, 25,000 donations; April 1991, about 20,000 donors, which we equate to 20,000 donations.

Those are the figures that we have.

If we can have page 23, please, Sully. We can see a graph again showing similar rise to that which we've seen for Factor VIII.

But I would like to take you to the document that we looked at earlier, sir, because it does raise a question that we will perhaps come back to in evidence in due course.

It is CBLA0000253, please, Sully.

This is the minute from Dr Bidwell to Dr Maycock, dated 22 January 1975. We looked at the first sentence earlier, which was about the conversation they had had about labels at Elstree, and it was agreed that they would now say not more than 500 donations.

What Dr Bidwell goes on to say is this, and I quote:

"Mr Snape has pointed out to me that the batches of factor IX prepared from the Elstree material correspond to much higher than 500 donations and that the exact number is not known to us. If we pool the smaller batches here we know the number but again it is more than 500. I have told Mr Snape to have printed on the new labels 'not more than 1000 donations' but the whole subject of having anything at all on the label seems difficult. It is certainly not much of a guide to the clinicians any longer. Can we discuss this, please?"

Now, frustratingly, we don't have a document

setting out Dr Maycock's reply, and it may be that there never was such a document; the discussion may have been an oral one.

I am conscious that Mr Snape, or Dr Snape as he now is, is going to come and give evidence, so I won't speculate about what this means. But I will raise one possibility, which is that there is evidence to suggest that Factor IX was sometimes fractionated from Factor VIII pools which had been used to produce Factor VIII and then were re-pooled in order to make Factor IX and, if that is right, then it may be that there is a -- potentially a larger donor pool which went into a Factor IX product than a Factor VIII product. But as I say, Dr Snape is giving evidence next week, and we may return to that in due course.

Those are the figures, then, that we have for BPL. I'm going to go to a couple of documents now, which may shed some light on why the pool sizes increased and the processes involved.

If we could start with CBLA0000149, please, Sully. If we expand the top half, please.

This is a memorandum which is entitled "Notes on an outlined scheme for preparation of Factor VIII concentrate from 1,000 litres of plasma per week".

This document doesn't have a date, but from the

context of it, we know that it was before March 1974. I take that from paragraph 5 of the note, which I'm not going to take you to but refers to a timetable being achieved by March 1974, so we know that this document preceded March 1974.

What it says is that, and I quote:

"This scheme is intended to use, as far as possible, existing facilities in the lab.

"1. Pool sizes: 250 litres, 4 per week."

250 litres would equate to about 1,375 donors.

If we look just below where the handwriting is, we can see these words:

"The present working capacity of the large plant for 1,500 litres of plasma weekly includes 200 litres of supernatant from fresh plasma."

Now, it's hard to piece together what is contained in this document but what it appears to be is a proposal to move from fractionating plasma in pools of unknown quantity, but amounting to 200 litres per week, possibly one pool at 200 litres per week but we don't know that. Possibly that 200 litres could have been split into different pools. But what is proposed is a pool size, a new pool size of 250 litres and, as I say, that's about 1,375 donors.

The suggestion is to do that four times per

week, and that will increase the amount of product that is produced at BPL.

There are then technical discussions about what will be needed in order to achieve that is.

Then, Sully, if we could go, please, to BPLL0003721. This is Dr Maycock's memorandum of the 8 December 1975, which we went to earlier. I highlighted earlier that the present pool size was given as 830 donations 150 litres. The plan was to increase that pool size -- if we could go down, please, Sully -- to 270 litres and then 360 litres.

Then Dr Maycock said, and I quote:

"The large pool size can be defended on the ground that starting plasma and concentrates are tested by RIA."

That's radioimmunoassay. That is the test for hepatitis B surface antigen. So that is the "defence", to adopt the word used by Dr Maycock, that is being put forward for expanding the pool at that time.

Another memorandum from Dr Maycock, which I won't ask to be brought up on screen but is referred to at paragraph 63(b) of the written report, comes from 19 March 1976, where Dr Maycock agreed to the pool size of PFL Factor IX being increased to

500 litres, and he said that he was agreeing this "On the understanding that the final pool is prepared from two or three sub-pools, each of which has passed its safety tests, including RIA test for the presence of HBsAg."

So, again, a reference to the fact that testing is being linked to the increase in pool size.

I note from that memorandum that there is a reference to the Factor IX being prepared from two or three sub-pools, which may be that process that I was mentioning earlier, that once Factor VIII has been fractionated from the supernatant, the pools are then mixed to allow for Factor IX fractionation.

In the same month, March 1976, as we heard in the previous presentation, BPL made an application for a product licence for Factor VIII from Elstree, and that product licence said that the maximum pool size foreseen at Elstree is 450 litres. 2,500 donations are the figures that were given in the product licence application.

I note the word "foreseen" there, rather than the word being -- or words "being used" or "the present size".

The application also stated this, and I quote:

"Because of the large number of control tests

which have to be made, there is a trend towards larger pools, in order to lessen the amount of testing and reduce waste of valuable material."

The reference is given at paragraph 64 of the written presentation.

Moving toward 1977 and 1978, we get to the period of the Stop-Gap programme that we discussed before. And at that size, and as we heard, part of the Stop-Gap programme involved increasing the size of the plasma pools fractionated at BPL from 400 litres to 600 litres. That is approximately 2,200 donations to 3,300 donations.

That increase may shed light on something that we discussed before.

Sully, if we could have, please, INQY0000337, page 39.

Sir, is from Appendix 2 to the chronological presentation to England and Wales, and it's this confusing point that we discussed before about why it is that, in the fourth column there, the capacity of BPL, expressed in the amount of plasma that, in theory, could be fractionated, is given as increasing between 1977 and 1979, whereas the capacity, as expressed in the amount of product that could be provided, expressed in terms of international units,

remains constant.

Now, I don't claim to have an answer, but one possibility is that this increase in pool size helps to increase the figures between 1978 and 1979, and that is perhaps not reflected in conversations that were taking place about what the output was in terms of international units at the time, which is why we have the figures for 15 million there. I still can't resolve it, but I do note that the increase in pool size at this time may have played its role in helping to increase the capacity of fractionation as expressed in the weight of plasma that is fractionated.

While we are on this document, sir, it was pointed out to me by some of the Core Participants whose mental arithmetic is far superior to mine, that if you add the figure for 1977, 67,200 kilograms, to the figure for 1978, 57,600 kilograms, you get the figure --

SIR BRIAN LANGSTAFF: You do, yes.

MR HILL: I can see you nodding along. Again, your mental arithmetic is --

SIR BRIAN LANGSTAFF: In 1979.

MR HILL: They raised this because, as was pointed out, it's a very odd coincidence if it is indeed a coincidence. We agreed, and sir, we have gone back

and looked at the underlying documents to see whether or not this is just a function of somebody adding 1977 to 1978, and coming up with a figure for 1979.

We don't think that that is what happened. Having gone back to the original documents, the 1977 figure is based on a number given by Mr Watt of the SNBTS in a meeting on 11 March 1977. I won't take you to the reference, but for the record, it is SCGV0000001_172.

The 1978 figure is taken from a handwritten memorandum to Dr Lane dated 28 February 1978. The reference is CBLA0000738.

And the 1979 figure is derived from a document prepared by Norman Pettet of BPL, dated 27 February 1979, and the reference to that is CBLA0000916.

So three independent sources from at least two, possibly three, different authors, written at different times. So we are as satisfied as we can be that the fact that the 1979 figure is the sum of the 1977 and the 1978 figures is a coincidence, rather than indicating anything more substantive. It is, however, a very strange coincidence, and we're grateful for it being brought to our attention.

SIR BRIAN LANGSTAFF: It's curious, if it was additional,

that the international units actually produced at the far right-hand side aren't additive.

MR HILL: It is, sir. It is a period of unsatisfactory data --

SIR BRIAN LANGSTAFF: Yes.

MR HILL: -- if we put it that way. I'm afraid I don't have an answer for why these figures behave in the way that they do. The wider picture is that the Stop-Gap programme does allow an expansion of production, and it is taking place during this time, and, therefore, it might not be a step change but a gradual change which is reflected in some of these figures but not in others.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Going back, then, to pool sizes. Ms Richards, when presenting the work on Dr Lane, took you to two documents, that I won't take you back to, in which Dr Lane explained in September 1980 that he was content to expand the pool sizes at Dr Smith's request up to 900 kilograms on some days, as Dr Smith put it.

Dr Lane said that he was prepared to do this as, and I quote:

"I'm sure that once one has exceeded 100 to 200 kilograms pool size, one has already exceeded any possibility of small pool protection. I have

discussed this with John Craske, and he agrees exactly on this point."

The document you saw yesterday, I won't go back to it, but 100 to 200 kilograms pool size quoted by Dr Lane would approximate to about 550 to 1,100 donations.

Moving on to January 1982. Again, I won't take you to this document but it is at paragraph 76 of the written presentation. Dr Smith wrote to Dr Lane requesting permission to increase the pool size from -- sorry, requesting permission to increase the pool size to the equivalent of 1,200 kilograms or 7,500 donations, and he gave reasons for it, including making the most effective use of the freeze drying plant and helping to test new processes in preparation for the expansion of BPL. Those are all set out at paragraph 76 of the written presentation.

We then have that period where pool sizes appear to remain broadly constant from about 1982/83 to about 1985.

Then three documents to finish with, that we may come back to with Dr Snape. The first is CBLA0002190. This is a memo from Dr Snape to Mr Prince, copying Dr Smith and Dr Lane, dated 10 June 1985. It is entitled "Coagulation Factor Batch Sizes". Dr Snape

wrote this:

"Further to your memo of 25th April, 1985. I have assumed that a limit of 10,000 donations maximum will not restrict operations in the present building, but that an extension to 20,000 donations maximum will be required for the new facility. The higher figure will be used in any product licence applications."

So it appears to be gearing up for the redeveloped BPL.

If we could then go to CBLA0004791. This is from June 1986, so a year later. Again, from Dr Snape to Mr Prince and Dr Smith, copied to Dr Lane and others, entitled "Pool Size Limitations for heat-treated concentrates". It's important to stress that concentrates are by this stage heat treated.

Dr Snape wrote this, and I quote:

"Dr Lane has agreed that the maximum pool size may be extended to 25,000 donations for heat treated coagulation factor concentrates. The appropriate label revisions will be made as soon as possible. Please check that any manufacturing documentation is revised before the increased limit is implemented."

On the same day, Dr Snape wrote to Dr Smithies at the DHSS and this is at DHSC0002303_027.

Dr Smithies was the successor to Dr Walford as principal medical officer in the DHSS and the relevant division of the DHSS.

The document is dated 20 June 1986. It is entitled "Maximum donor pool size for coagulation factor concentrates", and what Dr Snape says or writes is this:

"I am writing to advise you of a proposed change in donor pool size limitation for BPL (and PFL) coagulation factor concentrates. It is proposed to increase the maximum number of donations to be pooled from 10,000 to 25,000 plasma donations. In taking this decision, we were mindful of the terminal heat-treatment of coagulation factor concentrates made from such pools and the fact that any increase beyond the already large 10,000 donor limit is probably not significant.

"I thought you should be aware of this proposal."

That is from Dr Snape. We will pick that up with him in due course. The terms of the memorandum you may feel, sir, are significant as to who was taking that decision and who was being informed of it.

That is where I will leave the BPL presentation and turn now to Scotland, which I'm happy to say is

a more straightforward story.

Again, there is a written presentation that has been provided on Relativity and on the Internet. The reference is INQY0000346. Mr Boukraa over the last couple of days has taken you through developments in Scotland, and I won't repeat that.

There is a shift from the use of cryoprecipitate to the use of factor concentrates, and a concentration of the production of blood products at the PFC in Liberton, as opposed to occasional alternative suggestions of having fractionation sites locally. I won't take you to any of the documents there.

There was a hope expressed at a meeting of SNBTS directors and Haemophilia Directors on 8 May 1975 that cryoprecipitate should be completely replaced by concentrates, and it was suggested that cryoprecipitate could be, and I quote, "obsolete in 5 years." The reference is paragraph 6 of the written presentation.

That was 1975. That did not come to pass, but factor concentrates did increase in use, as you have heard. The figure from 1976 to 1982 is an increase in PFC Factor VIII from about 1.3 million international units to 4.75 million international units. There was a corresponding decrease in cryoprecipitate from

1.27 million international units in 1976 to 681,000 -- sorry, 682,000 international units in 1982.

That increase in the use of factor concentrates seems to have had an effect on the pool sizes used at PFC. It appears that the pool sizes were in part determined by a desire to reach the level of production that self-sufficiency in blood products required in Scotland.

If we could go, please, to SBTS000309_023. This is a letter dated 16 March 1973, so very early on in this part of the story. It is a letter to Dr Macdonald of the Scottish Home and Health Department from Mr Watt, Scientific Director of the SNBTS.

At paragraph 1, we can see that Dr Watt wrote this:

"At present, we are between products in that one is being phased down whilst the other is being raised. As discussed yesterday, we are embarking on preparation of a 'high purity' fraction which we might, for convenience, call 'Supereight'. The planned production capacity for this product is one pool of 200 litres per week. This was deliberately chosen to meet a projected need to process 50,000 donations of plasma per annum to meet Scottish needs

for this product. We do not expect to reach this rate before mid-May, and capability beyond that date would be dependent on plasma supply, completion of clinical acceptance trials, clinical demand et seq."

So that is from March 1973.

There are also documents set out at paragraph 14 of the written presentation that indicate that pool sizes at PFC also increased because of a sense that it was advantageous, in terms of yield and reduction of loss, to fractionate in a larger pool size. I won't take you to that document but it is, as I say, set out at paragraph 14.

As demand rose for factor concentrates going into the 1980s, there was an exploration by Dr Foster and others of ways of increasing supply from the PFC. In a memorandum dated 29 December 1980, again I won't take you to it but it is at paragraph 15 on the written presentation, Dr Foster explored the limiting factors on production at PFC at that time. He concluded that the key limiting factor, both on the pool size and the frequency of processing, was the freeze drying capability at PFC.

Two freeze dryers were available for use. One was limited to freeze drying plasma pool of 300 kilograms, the other was limited to freeze drying

a plasma pool of 500 kilograms.

In that memorandum, Dr Foster suggests that one way of increasing production would be to increase the plasma pools by using smaller vials, which means that you could fit more into the larger freezer, and that would allow for a pool size of 700 kilograms.

The significance of this is borne out by Dr Perry's written statement to this Inquiry, in which he said, and I quote, that PFC pool sizes:

"... were designed and established to be aligned with anticipated process yields and the maximum capacity of freeze dryers used for the final stage of processing. At the time in question, PFC had two production scale freeze dryers of different capacities for this purpose."

That is paragraph 16 of the written presentation, Dr Perry and Dr Foster are both coming to give evidence, so I won't go into this any further, save to say that the data that we are about to look at seems to bear out the fact that pool sizes at PFC in the early 1980s were conditioned to an extent by the fact that the plasma from one pool had to fit into one dryer or the other.

Now, we have some data about the pool sizes at PFC at this time. If we could go, please, to

SBTS0000238_009. This is a review report from April 1984 from Dr Foster and Ida Dickson of PFC, looking at a Factor VIII recovery at PFC from April 1980 to September 1983. So it is not a report about pool sizes but it does touch upon pool sizes. If we go to page 8, please.

This is a table that was compiled as part of that report which refers to Factor VIII batches that were still in process, and, question mark, pending rework. what I take that to mean is that these are batches that have not been dispatched from PFC for various reasons.

You can see the reason for holding in the right-hand column.

What this helpfully shows is the size of the plasma pool for each of these batches. We can see in the top row a batch from 1978 to 1979 had a plasma pool of 114 litres. Three batches are there from 1979 to 1980. They are stated to be 167 litres, 175 litres and 300 litres. 1981 to 1982, we can see a number of batches. There are three that are 255, 260 -- sorry, two that are 260 and 290 litres. One is expressed as 255 vials, and we're not quite sure if a vial equates to a litre. But you have two at 290 and 260 litres, and then the other three are 450, 479 and 535 litres.

So it would appear that you have those two freezers, one of which can cope with up to about 290 litres, possibly up to 300 litres, of plasma, the other of which can cope with up to, on these figures, 535 litres.

It is a similar story for 1982 to 1983, that you have a split between seven batches, three are just under 300 litres, and four are between 495 and 555 litres.

If we could just go over the page as well, please, Sully.

We have another table setting out further batches that failed quality assurance tests, and we can see the size of those batches. And, again, similar story, from 1980 to 1981 and 1981 to 1982, where you have some batches which hover between 250 and 300 litres, and other batches which are about 500 -- in this case 540 and 555 litres for 1983 to 1984.

That information correlates with other sources that the Inquiry has. These are set out at paragraph 19 of the written presentation. I don't think there's a need to go to the underlying documents. But we can see at paragraph 19 that in a letter from November 1990, Professor Cash said that

pool sizes for Factor VIII at PFC were between 200 and 300 kilograms between 1978 and 1980.

Dr Perry in his written reason statement to the Inquiry says that the pool sizes increased during the early 1980s and varied between 300 and 550 kilograms.

Then Dr Perry's evidence is consistent with another report that we have for the period 1981 to June 1983 from the SNBTS Factor VIII Study Group which recorded pool sizes of either 320 or 550 kilograms.

If we could please put on screen, Sully, INQY0000346. Page 9. Table at the top of that page.

This is taken from the written presentation, and it draws together that information that we have just gone through. It is important to state that the table is comprised of limited data points, and it is possible there are other data points and other pool sizes that were used at the time, particularly in the early 1970s.

We have used in the final column the same measure of donations per litre, so 5.5 donations per litre, as we have used for England and Wales, although Dr Perry in his statement estimated that there were about 4 or 5 donations per litre, saying there is a degree of reasonable difference, depending on which translation one takes.

But looking at that, we can see that from the data, the estimated donations for a pool size of 114 litres in 1978 to 1989, is 627. That is just one data point that we have from that year.

1979 to 1980, we have a range of between 167 to 300 litres. That's a range of donors from about 900 to about 1,650.

1980 to '81, the pool size in litres is 144 to 290 litres; the range in donors, 792 to 1,595. That's 792 is a precise figure given but, of course, it is an approximation.

1981 to 1982, the plasma pool size in litres ranges from 260 to 540 litres. The estimated donations, 1,430 to 2,970.

1982-83, 283 litres to 555 litres, or 1,557 donors to 3,053 donors. That figure of 3,053 donors is also used for the single data point for 1983 to '84.

We have only limited data for pool sizes thereafter. One interesting point of data is -- I think we could have this on screen, please, Sully, it's PRSE0000965. This is a memorandum from Dr Perry to all staff, subject line "AIDS", date 31 January 1985. So this is just after the discovery of the Edinburgh cohort that Mr Boukraa referred to

and which you've heard evidence about before, the 16 people who were infected with HIV through the use of PFC products.

Dr Perry, in the third paragraph down, refers to the fact that all of the donors who contributed to this pool of Factor VIII had been identified or had sought to be identified, and he states that there were 4,000 such donors. So it appears that Dr Perry's conclusion is that the suspected pool was made up of 4,000 donors or donations. It is not entirely clear which metric is being referred to, but perhaps in this instance it doesn't matter.

That is a little higher than the figures that we have looked at in the table which took us up to 1983 and 1984.

You have heard from Mr Boukraa the steps that were taken in response to HIV and AIDS. They notably did not include steps to restrict the donor pool size at that time. There is a reference at paragraph 23 to a memorandum sent from Professor Cash to Dr Perry on 7 December 1984, in which he gave his view that any moves to restricting donor pools should be discussed by all directors. He said, and I quote:

"It is an exciting option that I suspect will have colossal cost and operational implications.

There is much to be done before we need consider this option."

The final piece of data that we have is an article from 1985 written by Dr Foster, and Alan Dickson of PFC. That recorded -- I needn't take you to it -- that at the time of writing, the pool sizes for continuous flooring ^wd were between 600 kilograms and 1,000 kilograms, adopting the 5.5 donations per kilogram conversion figure, that equates to 3,300 to 5,500 donations.

That is from 1985. The reference is at paragraph 24 of the written presentation.

There is a graph, sir, at page 12 of the written presentation. So that, Sully, is INQY0000346. I think perhaps we could try page 13.

Page 11? Found it in the end. If we could expand that, please, at the bottom. The same caveats apply to this graph as to the previous ones about the lines between the data points. There are two lines which show the lowest range and the highest range of the pool sizes at PFC. There is also a dotted line which shows the average pool size at PFC, but I'd suggest that perhaps isn't as useful because it does seem to be that the plasma pools are either one size or another depending on which of the freeze dryers was

being used.

But we can see that both of the lines do show an increase in the early '80s and then a further increase between 1984 and 1985. But I stress that the start and the end dates are based on very limited data points and so obviously come with a degree of caution as a result.

That is all I intend to say at this stage about pool sizes at PFC as well and you will, of course, be hearing further evidence in the coming days from Dr Foster about production at PFC among other matters.

That, sir, is all I have for you today.

SIR BRIAN LANGSTAFF: Well, thank you very much indeed, Mr Hill.

So tomorrow we have Dr Foster, don't we?

MR HILL: Yes.

SIR BRIAN LANGSTAFF: 10.00. 10.00 tomorrow.

(4.37 pm)

(Adjourned until 10.00 am the following day)

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