Tuesday, 15 March 2022

(10.00 am)

Presentation by Counsel to the Inquiry about self-sufficiency and domestic production of blood products in England and Wales

SIR BRIAN LANGSTAFF: Yes, Mr Hill.

MR HILL: Sir, we are turning to the issue of domestic production of blood products and questions around the self-sufficiency. There will be a series of presentations in the coming weeks and then some oral witnesses as well.

We are beginning with a presentation on production of blood products in England and Wales. We will follow that with some individual presentations on Dr Lane and Dr Smith, two significant figures from BPL, which will be done by Ms Richards towards the end of this week. Next week, Mr Boukraa will present a chronological account of blood product production in Scotland. We will also look at pool sizes that week, and then we will have the witnesses following up who are Dr Snape, Dr Perry and Dr Foster.

SIR BRIAN LANGSTAFF: And will we be examining in the -- although we're separating England and Wales from Scotland, and Northern Ireland is going to come in there I think next week, isn't it?

MR HILL: Yes.

SIR BRIAN LANGSTAFF: We are going to bear in mind, are we, that there may have been sources of production if one viewed the whole as United Kingdom.

MR HILL: Yes. That is something that will be touched upon today and examined in more detail next week by Mr Boukraa.

Northern Ireland will be dealt with more with Scotland because that is where product began to be made in the 1980s for Northern Ireland. Again, it will be touched upon today and some evidence as to why that arrangement came to be.

SIR BRIAN LANGSTAFF: Will we in the course of the presentations be looking at, or in the course of the next two or three weeks, be looking at the question of whether Scotland could have supplied more in respect of the UK's consumption than it did?

MR HILL: Yes, we will be looking at that. In preparing these presentations, we are very conscious of the fact that you have heard oral evidence. These presentations aren't an effort to try to surpass that oral evidence or even to try to analyse it. They are a piece of a jigsaw to go with the oral evidence rather than replacing it.

SIR BRIAN LANGSTAFF: Those who read the opening words of

the presentation will be left in no doubt this is not the view of the Inquiry. These are relevant documents and, to assist understanding, you put them in chronological order and made observations about them, but they are as good as the person who is making the observations.

MR HILL: Exactly so, sir. These are not our submissions. These are an account of what the documents seem to us to show.

SIR BRIAN LANGSTAFF: And you will be open to others who look at the documents to interpret them in a different way, if they think that is appropriate, and to persuade me in their submissions that that's the way I should look at them.

MR HILL: Absolutely, sir. Two people can look in good faith at the same document and come to differing conclusions, and that will be -- there will be an opportunity for all Core Participants to make those submissions in due course.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: This presentation that I'm going to start today, and I'm sure will go into tomorrow as well, doesn't attempt to be comprehensive. It is inevitably based upon a selection of the documents, otherwise we would be here for many, many weeks.

No special status is gained by a document being included or excluded and, as you've just been saying, sir, the Core Participants may well feel that there are other documents which are equally or more important, and they will have an opportunity to bring those to your attention in due course.

All conclusions, sir, are for you, and your counsel team do not seek to trespass on that territory at all.

The Core Participants will also be aware that a report has been provided from the expert fractionators instructed by the Inquiry. It is also on the Inquiry's website. We are not currently proposing to call the authors of the fractionation report to give oral evidence, and we are not seeking to explore that report in the next three weeks. It's there as background. It will have the same status as any other piece of evidence, expert or otherwise, and you can accept or reject it in part or in whole and give such weight to it as you feel is appropriate.

If Core Participants have any particular observations on the report, then they can be provided as part of their written closing submissions which the Inquiry has asked to be filed in late October.

I mention that so that everybody is aware of it.

It is there, but it is not a resource that I will be referring to in the next few days.

SIR BRIAN LANGSTAFF: Well, it doesn't deal directly with issues of self-sufficiency, though it does, I think, suggest that the first commercial anti-haemophilic fraction was produced in Sweden and marketed as AHF-Kabi or I-O, Kabi, and that was in 1956.

MR HILL: I think that's right, sir, yes. It brings me on to where we are with this presentation which begins in the 1970s. There are other places where one can begin, as the fractionators have, back in the '50s.

You, sir, have looked at some documents in the past from the 1960s, and in particular a letter from 1967, 22 August 1967. The reference is DHSC0100025_062. I didn't ask for that to be brought up, but that is a letter from Dr Rosemary Biggs to Dr Godber, the Chief Medical Officer, which raises in 1967 the question of domestic production of concentrates and suggests that 50,000 donors a year could be used to produce such concentrates in order to treat those who would most benefit from them at that time.

There is this pre-history, but this presentation is going to begin in the 1970s where the impact of increasing commercial products and the product

licences that we have seen were issued for Hemofil and Kryobulin, the impact those have upon the spur towards domestic production and a policy that was described as self-sufficiency. I use that word somewhat cautiously because it means different things to different people at different times.

SIR BRIAN LANGSTAFF: Just going back for a moment to Dr Biggs' letter to Dr Godber. That's a letter which, what, in April 1967 anticipates, does it, that there would be a need for investment to make sure that the BPL and PFC in Scotland were able to produce more. It envisages using red blood cells out of a donation of blood and harvesting the plasma, so it fits in very neatly with some of the evidence that I've been hearing over the past few weeks. And she does raise the question that if we don't get on with it, then we may have to rely upon commercial concentrates from elsewhere.

MR HILL: Exactly so, sir. Perhaps we can bring it up as good a place to start as any.

SIR BRIAN LANGSTAFF: It might be a place to begin. It's a contribution to the debate.

MR HILL: It is, and Dr Biggs is an important player in that debate, as we will see in the 1970s as well. It's DHSC0100025_62. We can see from the heading --

SIR BRIAN LANGSTAFF: I was wrong about the April. It's August.

MR HILL: It's August. 22 August 1967. We can see from the heading, should anybody need the reminder, that Dr Biggs was from the Oxford haemophilia centre, addressed to Dr Godber, Chief Medical Officer and what the letter says is this. The first paragraph is about thanking Dr Godber for an invitation to join the committee. Paragraph 2:

"I should like to take this opportunity to mention the question of preparations for the treatment of haemophilia and Christmas disease. These are mainly human blood products and do not, I suppose, class as proprietary preparations. The preparations I have in mind are concentrates from human plasma of factors VIII and IX used for the treatment of patients with haemophilia and Christmas Disease respectively.

"Both of these preparations are in very short supply in England, and at present they're also scarce everywhere in the world. They are so important for the treatment of these patients that their use makes the difference between life and death in many cases, and the difference between quick recovery and long, drawn, painful illness with residual crippling in many others. At present, many haemophilic patients are not

aware of the great efficacy of this treatment and do not attend as they should for treatment. In the next year or two, I would expect that these patients will attend for treatment.

"I have estimated on the basis of our practice that a minimum quantity of these concentrates required at present is the product from about 50,000 donors a year."

I pause there, sir, to say that there are various measures that are used about the quantity of plasma that is required to produce concentrates. In the period here and into the early 1970s, the metric tends to be donors or donations.

SIR BRIAN LANGSTAFF: Well, they didn't yet have an International Standard for Factor VIII activity, did they?

MR HILL: That's right. That's right.

SIR BRIAN LANGSTAFF: When did that come in?

MR HILL: That comes in the mid-1970s when, firstly, there is a reference to units and then it becomes international units. That refers to the end product, how much is actually made. The way that how much plasma goes in to make that end product is described in various ways, initially from donations, later it comes to be referred to either by weight, by kilogram,

or by volume, by litre. But in this early period it is donations.

It is quite hard sometimes to translate between the different figures and must be done with a degree of caution. I'll come back to that on Thursday when we look at some statistical analyses and graphs of plasma supply and blood product production in England and Wales.

But at this period, we're talking about donors or, probably more accurately, donations. 50,000 is the figure given here and that is a figure to keep in mind as we go forward through the 1970s.

Returning to the document. I quote:

"When all of the patients come for treatment more would be needed. The supply of plasma as starting material for fractionation would, I think, be no problem since the use of the red cells can be organised. This shortage of material to treat these patients is not new, but at the meeting I attended recently, the plans made by the United States to deal with the shortage were outlined. I have good reason to believe that within the next year or two very large amounts of these products will become available on a Commercial basis in the United States. I estimate that the product from more than 1,000,000 donors

a year will be processed. When this material comes on to the market we shall be obliged to buy it at a very high cost for our patients unless the English shortage can be remedied."

Going on to paragraph 5:

"In this country we have pioneered this treatment, we have the personnel who know how to make the products, we could easily have enough plasma to serve as starting material. It would seem to me a great pity if we cannot make our own material in this country for lack of the organisation, apparatus and buildings in which to work. The purchase of the finished products in the United States will undoubtedly be very costly. A part of the United States product will be made on contract by the American Red Cross and will presumably not be available for sale aboard but a large amount will be made by commercial enterprises and on sale. On present prices a course of anti-haemophilic treatment for one emergency purchased from the United States would cost $1,500 to $5,000. Surely it would be less costly to us to do everything to expedite the manufacture of these fractions in England and in particular to accelerate as much as possible the new fractionation buildings at Elstree and Edinburgh.

I feel that it is perhaps time to try to reassess the quantities of these products that might be needed and to try to work out an emergency plan to try to meet the need."

That's Dr Biggs, August 1967.

As you say, sir, some of the themes that come out of that letter include the reference to red cells, and that's the idea that one can separate red cell concentrate from the plasma, thereby allowing more plasma to be fractionated, the red cells to be used in blood transfusions, a more efficient use of a blood donation. There is also reference to the potential cost of the imported products, and a plea, that is not to put it too high, to start thinking about what can be done in England and Scotland to produce more products domestically, given that, as Dr Biggs said, the relevant expertise was available in the country.

But the reference to Elstree and Edinburgh: Elstree is a reference to the Blood Products Laboratory and Edinburgh to what becomes the Protein Fractionation Centre, the discussion of various building works that were ongoing at that time.

SIR BRIAN LANGSTAFF: She refers also, in one word, I think, to the necessary organisation to do it --

MR HILL: Yes.

SIR BRIAN LANGSTAFF: -- which we've heard, again perhaps, a lot about just recently.

MR HILL: Yes, that will be something that comes up again repeatedly in the '70s. Of notice, the fact that the letter was addressed to Dr Godber at the Department of Health --

SIR BRIAN LANGSTAFF: Yes.

MR HILL: -- or, as it was then called, the Ministry of Health, later becomes the Department of Health and Social Security.

I will be coming on to the '70s shortly but, just so there is a route map of where we are going to go, the intention of a presentation is to trace the rise in demand for Factor VIII concentrates in England and Wales and the associated calls for national self-sufficiency, which pick up on what Dr Biggs said in that earlier letter, and indeed are amplified by Dr Biggs herself.

We will look then at how that fed into estimates for future usage and planning on how to increase both plasma supply and the production of blood products. We will consider the response of the DHSS, and the Regional Health Authorities, then a discussion of the announcements in late 1974 and early 1975, about which you've heard some evidence from Dr Owen and others,

the £500,000 of central DHSS funding to increase plasma supply for fractionation.

We will look at how that money was spent, what was said about it and what was achieved. We will then turn into increases in demand for factor concentrate in the second half of the 1970s, and the revised estimates that follow.

We will look at the related need to redevelop BPL at that time, both through increased capacity and in response to the Medicines Inspectorate report. This led to what was called, originally, the Stop Gap programme, which, as the name suggests, was an interim measure for some redevelopment before a full redevelopment of BPL. That programme was later changed to be called the MARP01 programme, MARP standing for Medicines Act Rehabilitation Programme, and again, as the name suggests, you can see how Stop Gap has been knocked off course by the Medicines Inspectorate report, although there is a great deal of overlap between those two programmes.

At that stage, sir, the presentation comes to a point where Dr Walford's presentation to you began, which is discussion about the full redevelopment of BPL. To lapse into an analogy, the camera, at that point, is going to pan out, both in the written

presentation and the oral presentation, to give an overview of the events that led to the redeveloped of BPL but there is no intention to try to repeat the detailed evidence that was given by Dr Walford and by reference to the documents about that period.

There is similarly going to be an overview of the introduction of heat treatment at BPL and at its sister plant, the Plasma Fractionation Laboratory, PFL, in Oxford. More detail is going to be provided on those matters when Ms Richards takes you through the presentations on Dr Richard Lane and Dr Jim Smith. So I will touch very lightly, if at all, orally on those, but there is an overview in the written presentation, which may assist to provide some background, some context for what is to follow.

Having gone through the events chronologically, the intention is then to zoom in again with the camera on a couple of thematic points looking at the data the Inquiry has identified on three issues. The plan is to do this looking across the 1970s and the '80s, so that we can see the patterns developing without the chronology getting in the way.

The first is about the estimates that were made for Factor VIII usage during the '70s and '80s. The second issue was the level of plasma supply to BPL and

PFL, and the third issue is the amount of Factor VIII concentrates that BPL and PFL could have produced and did produce during that time.

By looking thematically at those matters, it is hoped that this will help to identify the shortcomings that meant that clinicians in England and Wales continued to use imported concentrates throughout this period.

The written presentation will be published on the Inquiry's website; I'm not quite sure if it is up there yet, but it will be there soon if not. It is also available on Relativity. I understand, at the moment, it is only available to the legal representatives of the Core Participants but it will be made more generally available on Relativity. It is accompanied by seven appendices that will be published and disclosed in the same way and they provide more detail on specific points, for example the detail of how the £500,000 was spent on a region-by-region basis, and the documentary evidence about the role of the SAG-M additive in the plasma supply.

Now, I won't seek to summarise all of those appendices, they're intended to assist on more technical and more granular details that are important, and I would invite everybody who was

interested to read those, but, for reasons of time, we will not be going through those in enormous detail. The exceptions are Appendix 1 and Appendix 2, which will form the mainstay of that thematic presentation that I've just discussed.

The focus of this presentation is on Factor VIII, the product that was more widely used in England and Wales and posed more problems for Government and fractionators in terms of providing enough of it. England and Wales was largely self-sufficient in Factor IX for much of this period. There were imports, particularly following the introduction of heat treatment, and that's something we will touch upon, but the focus will be on Factor VIII. There will also be a presentation next week on the specific question of the pool sizes that were used in BPL and in PFC and indeed in Oxford as well.

As you know, sir, it will be myself and Ms Richards and Mr Boukraa who are giving these presentations but we have been assisted enormously by the hard work of the Inquiry legal team in preparing them, their names have been added to the appendices and the main presentation as well. We are extremely grateful for everything they have done.

Before diving into the 1970s, it may be helpful just to explore briefly a few themes that emerge in this period on this topic. The first theme is really to identify the three elements that determined how much domestic Factor VIII concentrate could be produced. Those three elements were the plasma supply, the ability of BPL and PFC to fractionate that plasma, and the planning assumptions that went into both plasma supply and fractionation capacity, and those assumptions were based on estimates of demand for the products. Those are the three elements that we will look at repeatedly.

The second theme, and something that you, sir, have already touched upon, is the lack of a central body with executive powers to direct and coordinate those with the responsibility for those three different elements.

Plasma supply fell within the remit of the Regional Transfusion Centres and the Regional Health Authorities that funded those Regional Transfusion Centres. Fractionation fell within the remit of the Blood Products Laboratory and the Protein Fractionation Centre. The DHSS, funded both of those elements but it did so indirectly, in general, with one exception that we will come to look at. The

clinicians were working within the NHS and, again, the funding came ultimately from the DHSS, but there was a strong value placed on clinical freedom and clinical independence.

Ministers and civil servants had little power or inclination to dictate policies to doctors, transfusion directors and fractionators, and they equally may not have taken kindly to attempts to do so.

These different groups were both interdependent and independent.

The third theme associated with that lack of a central executive body was the lack of a single accepted definition of what self-sufficiency meant. This a matter on which you have heard evidence before. Did it include prophylactic treatment? Behind that question lay the wider issue of the type of life that those with haemophilia should aspire to lead. We will hear some of the debate that took place on that point. It is covered in particular in appendix 2.

Throughout that theme, there is an underlying question of whether or not an assessment should be made of clinical need rather than clinical demand. Clinical demand reflected what patients and clinicians would like; clinical need reflected what those more

centrally thought should be supplied.

SIR BRIAN LANGSTAFF: At some stage, we may have to think about, and I don't necessarily suggest in this week, how both of those, demand and need, reflect what the patient wanted.

MR HILL: Exactly, exactly. That is not something that we will be looking at in detail this week, because the focus is rather at the other end of the telescope about how fractionators and civil servants and regional administrators responded to what they understood the demand to be. It is not a question of how that demand was formed, in terms of how much information patients had, and what their views were compared to the views of the clinicians.

That is not something that I seek to discuss in the next couple of days. It is a very important point and it is not one that -- I know, sir, that it is not one that you will overlook but it is not the focus of this presentation.

SIR BRIAN LANGSTAFF: It's just that it can be difficult to talk about clinical need across a group, when one person's needs may be something for that person to have an input into, as opposed to something which is determined by the body looking at what they need in their opinion, and that was what I had in mind --

MR HILL: Yes, absolutely. It's the top-down and bottom-up approach.

SIR BRIAN LANGSTAFF: -- how those two, personal autonomy and clinical decision making or, for that matter, strategic decision making, fit together.

MR HILL: Yes.

The fourth theme that we've identified is the importance of the availability of commercial products in pushing forward both demands for self-sufficiency and pressures on clinicians, on politicians and civil servants, and on fractionators. Those commercial products threatened, at least in some eyes, the very existence of the UK's voluntary donor system. As we will see, in the early stages of the development of the policy on self-sufficiency, the drive comes from cost and the need to try to produce a domestic product that wasn't as expensive as the commercial imports and to provide enough of it to ensure that the commercial imports didn't dominate the UK market.

Later, principles about safety and altruism also developed within the argument. The protection of the voluntary donor system is something that weighed very heavily, particularly on Dr Owen.

Finally, sir, a theme which runs throughout the earlier period is the financial pressure on all

involved, particularly in the 1970s and start of the 1980s. It's a common theme across those different bodies, the clinicians, the fractionators, the civil servants, the Regional Health Authorities, in that period, in the 1970s. No attempt is made here to try to describe the difficult economic environment in which these decisions were taking place, but that is, of course, a factor which weighed very heavily upon all of those involved.

With that production, sir, and mindful as well of the letter that we've looked at from Dr Biggs, we're going to turn to the early 1970s, and the impact of commercial blood products.

If we could bring up, please, Paul, OXUH0000673. This is a letter dated 18 July 1972, and if we could turn, please, to the second page, Paul, just at the bottom we can see who it's from and to.

From Dr Rizza, of the Oxford Haemophilia Centre, and it's sent to W Trillwood who is the director of pharmaceutical services, the relevance of his role there is -- will become obvious as we read through. We can see that it is copied to Dr Biggs, Dr Bidwell, who worked at the Protein Fractionation Laboratory in Oxford, and Dr Maycock, who was the director of BPL and consultant adviser on blood transfusions to the

DHSS at that time.

What Dr Rizza says in the letter is this:

"Dear Mr Trillwood,

"During the past twelve months we have been experiencing increasing difficulties in meeting the needs for AHG for our haemophilic patients."

A pause there, sir, to say it is a reference to antihaemophilic globulin. It is used, often interchangeably, in this period with the word "concentrate". I have used the word concentrate more consistently in the report just so it is clear what he is talking about, but here he is referring to Factor VIII concentrates.

"At present we rely entirely upon human cryoprecipitate supplied by Dr Grant of the Regional Blood Transfusion Centre and freeze-dried human AHG concentrate supplied by Dr Bidwell of the Plasma Fractionation Laboratory, supplemented by a small amount of human AHG from the Lister Institute of Preventative Medicine, Elstree."

Pause there, sir, that's what becomes BPL.

"During 1971 we received and used concentrates of human blood clotting factors derived from more than 20,000 blood donors. This material was mainly from donors in the Oxford Region and we are deeply indebted

to the Regional Blood Transfusion Service for the co-operation over the years which has made it possible for them to channel plasma from nearly a quarter of the total donations of the Region into the fractionation process.

"Despite this seemingly excellent supply, we are chronically short of material to treat the ever increasing number of patients that come to Oxford. This shortage is not new and we have always had to give priority for treatment to emergency cases and to the treatment of children to prevent crippling deformity. This restriction has meant that the surgical waiting list for patients requiring non-urgent operations has grown and at present 25 patients are on the list. About half of the patients treated in Oxford during 1971 were from the Oxford Region and half were from other parts of the United Kingdom."

Go on to the next part of the letter. Thank you.

"Until recently this shortage of therapeutic material was unavoidable since no suitable commercial material derived from human blood was available. There are now two sources of supply, one is from the Hyland Laboratories and the other is from Immuno AG of

Vienna."

Pause there to note that's a reference to Hemofil and Kryobulin.

"Both are expensive and it would require material to the value of £2,000 to treat one operation case. Both of these preparations are clinically effective and have been used extensively in other countries. The Immuno concentrate has the advantage of being derived from blood which has been tested and found to be free of Hepatitis Associated Antigen, thus diminishing the risk of hepatitis.

"At present we are often forced to balance the needs of one patient against those of another in allocating treatment. This potentially dangerous practice was reasonable when there was no alternative supply of therapeutic material. We feel now that good material is available commercially our supply should be supplemented by the use of this commercially available concentrate. It seems to us quite unethical to continue to withhold treatment from patients when material exists to supply their needs.

"We therefore ask that the Immuno AG Factor VIII concentrate be bought at an estimated cost of about £15,000 per annum for use at the Oxford Haemophilia Centre. About half of the patients for whom this

material would be used would come from other regions and most of the material would go to cover patients requiring major surgery. This additional supply would much increase the safety margin for the treatment of urgent cases and would permit us over the years to lessen the waiting list for non-urgent operations."

That is Dr Rizza, 18 July 1972.

A couple of things to pick up from that. First is that many of the predictions that Dr Biggs had made in 1967 were now coming to reality, albeit perhaps a few years later than she had anticipated in her earlier already. It's notable that Dr Rizza's request for funds was based on a medical assessment of clinical needs and was framed by reference to medical ethics. It is also notable that it's the recent availability of commercial concentrates which have prompted his concerns in that regard. We also highlight the fact that Dr Rizza expressly acknowledges the expense of those concentrates.

Finally, we note that the request that Dr Rizza is making is about obtaining material to facilitate surgery. No reference is made at the time, in 1972, to either home treatment or wider prophylactic treatment.

As is set out in the written presentation,

Dr Rizza's concerns were shared by others and refer to the paragraph [14] of the written presentation. I won't go to all of the documents that were in it. We can see there that in October 1972, there was a meeting that took place of Haemophilia Centre Directors and, following that meeting, the Chair, Professor Edward Blackburn of the Sheffield Centre, wrote to Sir George Godber, the Chief Medical Officer, and requested that the DHSS establish an expert committee. That committee, he said, should consider the supply of therapeutic materials in relation to the treatment of haemophilia and allied disorders.

In the letter and at the meeting, Professor Blackburn expressed that his colleagues had referred to a preference for concentrates over cryoprecipitate, which is something we will pick up in some further documents, and he also mentioned the desirability of home treatment.

In his letter, and I won't take you to it but I will just quote the concluding section, he said:

"The directors feel there is an urgent need to increase supplies of Factor VIII concentrates, in particular those of freeze-dried concentrate. Many feel that if a British preparation cannot be made available very shortly, the commercial preparations

should be bought."

An interesting distinction there, perhaps, sir, that the first sentence, the need to increase domestic supply, appears to enjoy the unanimous support of the directors. The second sentence about buying commercial products in the interim, is expressed by reference to "many" feeling that way, so not unanimity on that one.

Professor Blackburn's letter was copied to Dr Richard Maycock, who I have said was the consultant adviser and also the director of BPL. He expressed concern over the cost of commercial concentrates and supported the proposal of a working group being set up to look at this matter.

In a memorandum dated 7 February 1973, which is referred to at paragraph [19] of the written presentation, Dr Maycock said that, in his view, and I quote:

"As far as possible, the UK should aim to be self-sufficient in the supply of preparations of antihaemophilic globulin and Factor IX."

He goes on to say that the preparations made in the UK can be as good as any commercial preparation and are available more cheaply. He also adds that there is insufficient supply at the moment, and

pressure from those who are using the products, because of the commercial material that is being made available to them.

The interventions of Professor Blackburn and Dr Maycock led to the DHSS establishing an expert group. We can see that thought is being given to this at the most senior levels within the department because in an internal minute dated 20 February 1973, at paragraph [20} of the written presentation, Sir Philip Rogers, who was the Permanent Secretary and so the most senior civil servant of the department, was said to be, and I quote, "Concerned about the possible financial consequences and is anxious that these should be quantified as soon as possible, bearing in mind the scope for meeting blood product requirements from home sources."

So he is expressing concern about the cost of commercial imports and the question of what can be done domestically to meet the supply demands.

On 6 March 1973, Dr Godber, the CMO, sent a circular to all senior administrative medical officers, has copied it to Haemophilia Centres and other regional health administrators, and informed them that the expert group would be formed. That circular is referred to at paragraph [21] of the

written presentation. We can see from it that concerns about cost are, again, at the forefront of Dr Godber's mind.

There is reference to the commercial products which are being provided, and Dr Godber says, and I quote:

"It has come to the notice of the Department that one of the firms is already engaged in active promotion of this expensive product. The firm has indicated that they can supply a large quantity of human AHG concentrate, and this could result in very significant expenditure if amounts were bought in excess of immediate needs."

I stress those last words, sir, because that is again hinting at this debate about what these concentrates should be used for. "Immediate needs" may suggest -- is often referred to as on-demand treatment; a response to a bleed, and possibly also emergency surgery.

There is in this document the circular that was sent by Dr Godber no reference to safety concerns about imported commercial concentrates.

The expert group on the treatment of haemophilia is the body that was set up to examine these questions, at the prompting of Dr Maycock and

Professor Blackburn, and it met for the first time on 20 March 1973. At that meeting, it considered a paper that was presented by Dr Biggs. We will look at that paper first before we then look at a discussion that followed.

If we could go, please, Paul, to PRSE0002553. We can see that although the paper is marked "Draft", we think that this is the version that was seen. It is entitled "Factor VIII concentrates and the treatment of haemophilia". We can see from the title page that it is Dr Biggs who has written it.

If we could go on to the next page, please. I'm not going to read all of the way through this document. I'll point out how the document was structured and some of the calculations within it before turning to the conclusions and also highlight one or two passages as we go through.

What Dr Biggs is setting out to do is trying to discuss the pros and cons of cryoprecipitate and factor concentrate and to work out the needs of patients with haemophilia in the UK. And she begins, as we can see halfway down the first page of the report, by discussing the number of patients with haemophilia per 100,000 of population.

And if we could turn to the second page, please,

Paul. The figures that she adopts, or the range that Dr Biggs adopts, is between 1,754 and 3,000 patients. And we can see that that is expressed to be for Great Britain. I read that as meaning Great Britain and Northern Ireland, but that's my interpretation, not something which is expressed in the document. Dr Biggs stresses that that is an estimate and it is not based on exact data. There was no central database at that time.

On the figure for 1,754, she says that this is the number of patients known to have attended Haemophilia Centres. But she says that we know that there are more than that number of patients because cryoprecipitate is also sent elsewhere and has been used in other hospitals as well. So she says the lower limit for the number is 1,754; likely to be more. The upper limit is not known for certain.

If we look at the next section, the Factor VIII preparations at present used to treat haemophilic patients, I'm just going to read a few paragraphs from this because it's --

SIR BRIAN LANGSTAFF: That would be severely affected patients, would it?

MR HILL: This is an attempt to calculate the total number of patients. We will see later in the document that

there is an estimate of the number of most severely affected.

SIR BRIAN LANGSTAFF: Well, the reason I say that is if we look at the top of the page, she starts off talking about the United States estimates, and she says:

"The estimate for the severely affected patients in the USA indicates about 12,000 patients in a population of 200 million. For Great Britain, the total would be between 1,754 to 3,000."

That looks as though that's for severely affected. Presumably people who were severe haemophiliacs is what she means by that, but that, again, is an assumption which may be wrong.

MR HILL: I think so, sir. A problem with many of these documents is that it's not entirely clear what it is that -- or what the numbers represent, whether or not this is intended just to be people with severe haemophilia or others as well.

As we will see in the debate that follows, there is a number that is given. And tempted though I am to try to pluck it out of my memory, I would undoubtedly get it wrong if I do, so I will resist the temptation, but we will see that number given later for the amount of people that are considered to be or -- who would benefit most from the concentrates being provided at

home. And that figure may correlate more closely to those with severe haemophilia. Certainly, the data on which she draws is a US study about people with severe haemophilia, and then she extrapolates that over to the UK. And in fairness to Dr Biggs, she emphasises repeatedly this is not exact.

Turning, then, to the Factor VIII preparations at present used to treat haemophilic patients. This is helpful just to gain an understanding of the base level, where they were at that time, before considering what they planned to do about it. If we -- if I read from that, Dr Biggs said this, and I quote:

"At present, the treatment of bleeding in a haemophilic patient consists in giving a calculated dose of an anti-haemophilic factor (Factor VIII) preparation as soon as any symptoms of spontaneous bleeding arise and of giving enough material during and following operations to maintain normal haemostasis.

"Each of the haemophilic patients treated at Haemophilia Centres during 1971 had on average received material from 122 donor units. This figure refers to the total amount of material that the patient received. It does not refer to the number of

donors to whose blood patients have been exposed through the use of pools of plasma.

"Most of this treatment was for on-demand treatment which is given whenever a patient feels that a haemorrhage is occurring and for major surgery and for dental extraction. At many Haemophilia Centres, the directors feel that they could use at least twice as much material as they receive but that the present shortage of materials leads to a dangerous selection between more or less urgent cases for treatment and the accumulation of patients on long waiting lists for non-urgent operations."

That last comment, sir, is one that echoes the letter from Dr Rizza that we looked at earlier.

If we could turn to the next page, please, Paul. Electronic page 5. We can see that Dr Biggs then goes into a comparison of concentrates and cryoprecipitate and, in particular, compares four different aspects. The first is the yield of Factor VIII activity. Here it is -- the word "yield" is being used as a measure of the efficiency of both concentrates and cryoprecipitate in using a blood donation and providing the necessary treatment to the patient. Elsewhere, "yield" is used in a more technical sense.

The second criteria is the convenience of

a material in preparation and in use.

The third criteria is the reliability of material from batch to batch.

The fourth criteria is the complications which might attend treatment with the various preparations.

I will summarise Dr Biggs' findings at paragraph [28] of the written presentation. I won't take you all the way through the document. If I summarise briefly, on "yield", Dr Biggs' ultimate conclusion is that the two products are equally efficient.

On convenience of manufacture, cryoprecipitate was stated to be easy to manufacture in small doses, but, I quote:

"On a large scale and widely distributed over centres with very different facilities, the method is less satisfactory."

Concentrates, by contrast, required a higher capital expenditure but were, in her assessment, probably less expensive in the long run.

On convenience of use, Dr Biggs referred to the need to thaw cryoprecipitate. The fact that the process of making up cryoprecipitate was, in her words, open to many abuses. She stressed the variety in the activities of individual doses in cryo and the need for a deep freeze. She contrasted that with

concentrates which she said were, and I quote, were "very convenient to use".

On reliability from batch to batch, Dr Biggs referred to data from the study that had been conducted and found that cryoprecipitate was very variable, and concentrates in contrast could be assayed to give a reliable estimate of dose activity per dose.

On the final criteria, the complications, I will take you to the document. I will take you in particular to electronic page 10. This is a section which I think has been put in evidence before, but it's helpful to see it in the context in which it was written and the context of the debate which is to follow. The heading is "Complications of treatment", and what Dr Biggs wrote is this:

"About 1 in 800 donors is a carrier of hepatitis B antigen. The larger the number of donors concerned in the preparation of concentrate, the greater the risk of exposing the recipient to material containing hepatitis B antigen. The use of freeze-dried concentrate, which is made of pools of 200 donors (or even higher numbers for commerce material) must carry a higher risk than single donations. But there is the possibility that the

development of jaundice may be dose related and that single infected bottles may be more dangerous to the individual patient than pooled material in which the virus is diluted. Despite this, the frequency of hepatitis in severely affected patients does not seem to increase significantly with increased use of freeze-dried concentrates. This is shown by a low incidence of jaundice in patients treated in Oxford (who have half of the material given to them as freeze-dried concentrate) and in those treated at other British centres. The conclusion is also supported by data collected in the United States."

Reference is made to an article -- letter by Kasper and Kipnis from 1972. The reference to that is in the written presentation:

"An exception to this rule concerns the mildly affected patients to whom very little treatment is given. These patients do seem to have a higher incidence of hepatitis if large pool fractions are used. Kasper and Kipnis 1972 showed this, as did also the British Survey where female carriers of haemophilia treated with concentrate had a high incidence of hepatitis.

"Since the majority of patients are in the multi-transfused category, the increased risk of

exposure to hepatitis would not seem to be an important disadvantage to the use of concentrates from pooled material. Hepatitis is, in any case, a complication which should decrease with universal screening of donors for hepatitis antigen.

"The incidence of Factor VIII antibodies does not seem to be related to the type of material used ..."

And a reference is made there to the British Survey.

So this is a document which dates from 1973, and so the discussion of hepatitis there is of hepatitis B, rather than non-A, non-B hepatitis.

SIR BRIAN LANGSTAFF: And the comment about the incidence of Factor VIII -- sorry, that complication should decrease, I think universal screening of donors for hepatitis-associated antigen, hepatitis B antigen, have been introduced in 1972.

MR HILL: I think that's right, sir. The test gradually improves in its sensitivity over the years as well.

SIR BRIAN LANGSTAFF: So what she is reporting on is material which was -- some of which probably was collected and manufactured into product, so far as it was concentrate, before it was screened.

MR HILL: Yes.

Going back to the paper, we can see that the next issue that Dr Biggs turns to is the amount of Factor VIII concentrate required to treat haemophiliacs in Great Britain. And we can see from the paragraph that follows that she bases many of her calculations on work that was done at Treloar's, in which observations were done of the students there of the number of bleeds they had per year. And then from that, Dr Biggs makes a number of assumptions -- necessary assumptions in order to do the calculations but assumptions nonetheless -- about the number of bleeds per year, the amount of material that is required per bleed, average patient weight.

If we go over to the next page, please. I won't take you through all the calculations. We can see there is also reference in the second paragraph to the amount of plasma that can be taken from each donation, and the figure there is 200 to 220 millilitres of plasma. And we'll see in later papers reference in England and Wales at least is made to 180 millilitres, so this may be optimistic as to how much plasma can be obtained per donation.

Dr Biggs goes through these various assumptions and calculations to try to provide a figure for how much Factor VIII will be required per year. It's

important to note that she is talking here about on-demand treatment. And then in the next section, if we go over to page 13, she then adds in major surgery, and then in the next section, page 14, dental extractions. So these are the calculations that are being done. And when she puts all of this together, page 15, we can see at the top of the page the ultimate conclusion that Dr Biggs makes is this:

"Thus for all types of bleeding (spontaneous, at operation and dentistry and after) the total material required is likely to lie between 400,000 and 750,000 donor units per annum."

I pause there, sir, and contrast that with the 1967 figure of 50,000. Dr Biggs's assessment now is that it's between 400,000 and 750,000, and this estimate included on-demand treatment.

SIR BRIAN LANGSTAFF: Just one question. She's talking here, is she, about England and Wales as a whole?

MR HILL: She refers to Great Britain.

SIR BRIAN LANGSTAFF: Great Britain, so that's the UK?

MR HILL: I think that may be -- yes, a misonym For Great Britain and Northern Ireland.

SIR BRIAN LANGSTAFF: When she spoke about the 50,000 earlier, she spoke about it on the basis of "our practice", and her own reference in, I think, the

earlier letter of '67 was 20,000 units.
MR HILL: Yes.
SIR BRIAN LANGSTAFF: So this may not be comparing like with like --
MR HILL: No, I was about to say, sir, it is not a direct comparison. She does refer to "our practice" and --
SIR BRIAN LANGSTAFF: Which may mean Oxford, and Oxford was recognised as a centre, wasn't it?
MR HILL: It does and, from the context of her letter, she refers not just to Oxford but to patients who were coming into Oxford.
SIR BRIAN LANGSTAFF: Yes.
MR HILL: So it is a significant proportion of England, but it is not the same figure here, which is between 400,000 and 750,000. Of course, Dr Biggs, in her 1967 letter, wasn't seeking to project into the future the demand that would be required in six or seven years' time; she was talking about what, in her practice, at that time, was needed then. That was the 50,000.

The figure here now is between 400,000 and 750,000 donor units.

Now that, she stresses, is for on-demand treatment, so bleeds, major surgery, dental extraction.

A little further down the page, she goes on to

talk about prophylactic treatment, and I read from that section now:

"Prophylactic treatment to haemophilic patients would require much more material since this treatment envisages regular administration of factor VIII once or twice a week to the patient regardless of whether or not bleeding has occurred. The estimate of the amount required for such treatment in the USA is 13 million donor units [reference to Stengle in 1972]. So for Great Britain an estimate would be about 3 million donor units. Lazerson (1972) estimates 636 donor units per patient for prophylaxis which would give a maximum figure for Great Britain of about 2 million donors units. It is not at present certain that this prophylaxis is desirable for even the most severely affected patients. It is certainly at present impracticable. In the USA about 4 per cent of patients receive prophylaxis.

"Home Treatment should be distinguished from prophylaxis. Home treatment involves the administration of therapeutic material in the home by a relative, by the patient to himself, or by the General Practitioner. This form of treatment is becoming accepted and should not involve the use of more material than good Hospital care. In fact, the

experience of Lazerson (1972) suggests that more material is not used for home care. There is no doubt that the freeze dried concentrate is the best material to use for home care. Were the most severely affected 1,000 patients allocated to home treatment this would require about 250,000 donor units of freeze dried concentrate but this would be instead of, not in addition to, the doses given on demand in the hospital."

We will come back to those figures in a second, sir. I note that that 1,000 patients who are most severely affected was the figure that I was trying to recall earlier. I would have got it right. I should have guessed.
SIR BRIAN LANGSTAFF: But this may be no more than a calculating figure, because "were the most severely affected 1,000 patients", it isn't saying "of the patients, 1,000 are most severely affected". It is calculating how much would be needed for the worst cases.
MR HILL: Yes. Yes. So it's not saying that is the total number of people with severe haemophilia in the country.
SIR BRIAN LANGSTAFF: Yes.
MR HILL: I'm just mentioning in parenthesis here, sir,

that the assumption that is made there about home treatment, and that it shouldn't involve the use of more concentrate than in hospital, is an important assumption, which plays out in the estimates that follow. It is one that is later challenged. There is a suggestion that more concentrate is used, particularly in the early stages of home treatment, than would be used in hospital.
SIR BRIAN LANGSTAFF: Well, I think we saw some evidence of that when we were looking at the haemophilia centres and the use of concentrate, that home treatment was thought to add something -- this is a very broad recollection, I may be wrong -- but something in the region of a third on top, to the amount that might be needed compared to on demand.
MR HILL: There is a debate which emerges about this. There is a sense that the higher use of home treatment, initially, is making up the previous under-treatment, which was done in hospital, and the reference to "good hospital care" by Dr Biggs may be hinting at that.

There is also a subsequent debate, which is not quantified in the papers that I have seen, that the earlier treatment of bleeds at home leads, ultimately, to less concentrate being used than would be used in

hospital because the bleed does not become as severe.

SIR BRIAN LANGSTAFF: That certainly was the suggestion early on and used to justify, in part, home treatment, quite apart from the convenience for the individual, it might be thought, but I think the objective evidence, so far seen -- as far as I remember it, is that it added to the consumption.

MR HILL: That would certainly fit with what we see in terms of the demand curve, once home treatment becomes more widely used.

SIR BRIAN LANGSTAFF: Indeed, it was, I think, one of the suggestions made at the time that people became aware of the risk that blood products might transmit whatever it was that was causing AIDS, that a suggestion was to reduce the amount of people on home treatment or reduce home treatment, thereby lessen the need for factor concentrate and thereby lessen the need for reliance upon imported factor concentrate.

MR HILL: I think, sir, we will see in some of the later papers that there is an acceptance that the assumption made here by Dr Biggs is not one which is borne out in practice.

Dr Biggs goes on in the paper to discuss the economics of treatment. This is a short section in

which she points out that the cost of treating patients with haemophilia is high but she doesn't try to compute the figures. But she does make the point, at the end of that paragraph, that proper treatment is probably no more expensive than that of renal patients requiring dialysis.

Then we come to the conclusions of Dr Biggs's paper, page 17. I will read through these and then I will come back to some of the numbers that are contained within them.

Conclusion 1:

"Calculations suggest that the amount of material required for optimum treatment of all the haemophilic patients in Great Britain would be derived from 400,000 to 700,000 blood donations a year. The present supply is of the order of 300,000 per year of which most is in the form of cryoprecipitate.

"2. Comparisons of cryoprecipitate and freeze-dried concentrate made in Oxford suggest that from the point of view of conservation of the factor VIII activity of the donor plasma and of recovery of infused activity in the patient the two preparations are equally efficient.

"3. The cryoprecipitate is more difficult to make up for administration and much factor VIII

activity may be lost when inexperienced staff handle the material prior to giving the infusion. Moreover the material varies in activity from one Centre to another. There is evidence that the Oxford material may be among the best.

"4. The pool size used in the preparation of concentrate does not affect the incidence of factor VIII antibodies nor of clinical jaundice in multi-transfused patients.

"5. For home treatment it is our opinion that only the freeze-dried concentrate is useful in most cases. The gradual introduction of the most severely affected patients who have the most frequent bleeding to home treatment would reduce hospital management of haemophilia by about half. To give this proportion of patients home treatment would involve the use of concentrate from about 250,000 donors a year. The present total supply is of the order of 25,000 a year."

"6. We think that the subject should be set to provide factor VIII concentrate from 250,000 donations by 1975 and that, over ten years, an attempt should be made to provide all of the necessary material in this form. By 1975 the magnitude of the problem should be more exactly defined by surveys being made by the

Haemophilia Centre Directors.

"7. It may be noted that freeze-dried material of good quality is now available commercially. At present patient treatment at many of the Haemophilia Centres in this Country involves a dangerous policy of balancing the needs of one patient against another and of denying patients reconstructive orthopaedic surgery which would greatly improve their lives. We feel it very important that the material made in the UK, which is second to none in quality, should be substantially increased in amount. Otherwise we feel that material should be bought from commercial sources which now provide material of good quality both from the point of view of factor VIII activity and from the point of view of screening the donors for Hepatitis Associated Antigen."

If we could just turn, please, to page 21, Dr Biggs referred to Table II. That is a table which is appended to her report, and we can see there that it is a representation of therapeutic materials for the treatment of haemophilia.

We can see the four different types of material in the first column, whole blood, plasma, cryoprecipitate, and freeze dried concentrate, and then the assessments for Dr Biggs made of Factor VIII

activities, and the post-infusion level of plasma Factor VIII, as a percentage of normal. We can see that, although I didn't take you to the sections on whole blood and plasma, Dr Biggs's conclusion is, in essence, that they're not much use for treatment of haemophilia.

Then we can see, in the final column, the approximate donor units at present made. We can see that, at that time, about 25,000 units were dedicated to concentrate, 220,000 to cryoprecipitate and 44,000 to plasma.

Just before the break, sir, I will go back to some of those figures that are given in the report, just so that we have in mind what they represent. I'm afraid that this gets complicated and will become more complicated as different estimates develop.

But the first figure is that figure of 400,000 and 750,000. That is the range of donor units per annum that Dr Biggs calculates is required for on-demand treatment. Now, expressed in its raw form, that could be treatment either of cryoprecipitate or of Factor VIII concentrate and, as they're equally efficient, the question is simply how you divide those two. So you could have 200,000 cryo, 200,000 concentrate, and that would be your 400,000.

Later in the conclusions section, Dr Biggs refers to 400,000 to 700,000 donations per annum being required for optimum treatment. So 700,000 rather than 750,000, I'm not quite sure why that distinction is there. She says that the figure at the time is 300,000 donor units, so below even what she considers to be the minimum.

SIR BRIAN LANGSTAFF: For optimum treatment?

MR HILL: Optimum treatment is 700,000 or 750,000.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: The requirement for on-demand treatment, as she puts it, is 400,000. So, in her analysis, there is, at that time, under-treatment, and that's consistent with what she has said in her letters and what Dr Rizza has said in his. As mentioned earlier, that figure should be the same whether that treatment is given in hospital or on home treatment, in Dr Biggs's analysis discussed there.

Prophylactic treatment, on Dr Biggs's analysis, is going to require much more material, and she put a range of estimates between 2 million and 3 million donor units per annum, based upon the American experience.

SIR BRIAN LANGSTAFF: She says it's impracticable.

MR HILL: Impracticable and, at that time it wasn't

necessarily clinically advised either. We will see -- I'm not going to go through the debate on prophylactic treatment in the 1970s but, every now and again, it crops up in the papers and we can see that it is something which has been considered at this early stage, but it is not inevitable in the mind of Dr Biggs, and indeed others, at this time, that prophylactic treatment is going to come in but they are aware that it is a possibility.

The final set of figures, or the final figure to refer to, is this figure of 250,000 donor units, a figure which is going to be important in the debate that follows. That figure, 250,000, is, as you said sir, for the 1,000 patients who are most severely affected and would most benefit from home treatment. So Dr Biggs is plainly not saying 250,000 donor units per year will provide self-sufficiency. The figure for on-demand self-sufficiency, as we've seen, is between 400,000 and 750,000 units at that time, or expressed as 400,000 to 700,000 for optimum treatment.

We will also see from the conclusions that there is a sense that there should be a push, firstly, to produce those 250,000 units of concentrate by 1975, and that will be a tenfold increase from the 25,000 units then dedicated to factor concentrates, and that,

over a longer period, given as 10 years, an attempt should be made to provide all the necessary material in the form of concentrates.

So that is all between 400,000 and 700,000 or 750,000 units. I pause there just to note that, although it is expressed in that way, I'm not sure that should be read literally as meaning that there should be no cryoprecipitate produced anywhere. Earlier in the report, Dr Biggs had referred to the preference, at that time, for single donor units to be given to people with mild haemophilia, based on the evidence that she then had.

So this paper isn't necessarily making an assessment about how treatment should be done 10 years down the line. So I'll just add that as a slight caveat into perhaps reading too much into that word. But, certainly, the thrust paper is that more should be dedicated to concentrate, at the expense of plasma, which was dedicated to cryo.

Sir, I note the time. I wonder if that's a good place to stop for our break.

SIR BRIAN LANGSTAFF: Yes, well, let's take a break until 11.50, shall we? 11.50.

(11.21 pm)

(A short break)

(11.51 am)
SIR BRIAN LANGSTAFF: Yes.
MR HILL: Sir, a couple of points of housekeeping just at the start. First of all, the presentation I understand is now up on the website and so people will be able to access it there. It should also have been provided on the CP work spaces.

The second point is that I earlier referred to some paragraph numbers from the written presentation. Due to my own error, these are out by five. So if I said paragraph 9, it should be paragraph 14. I won't bore you with the reasons for that, but I will be careful about doing that in the future, and we will arrange for the *[draft]* transcript to be corrected so that the correct paragraph numbers are given.
SIR BRIAN LANGSTAFF: Thank you.
MR HILL: Turning back to where we left off, sir, which was the expert group on the treatment of haemophilia and its first meeting on 20 March 1973. We've looked at Dr Biggs' paper which was considered by the group. Dr Maycock also provided two papers dealing firstly with capacity figures for the production of Factor VIII, and, secondly, dealing with the responses to a survey that he had conducted of haemophilia clinicians about their preferred use of product.

I won't take you to those documents. I will just point out that paragraph 39 -- that is the correct reference -- on the presentation, Dr Maycock set out the different capacities of BPL, PFL and PFC. His calculation was a total capacity to fractionate 1,145 litres per week once certain works had been completed.

He also said that in order to meet the preference of haemophilia clinicians, four-fifths of blood donation, so 80 per cent of blood donations, should be assigned to concentrate production which he put at a figure of about 330,000 donations per year.

He summarised the survey responses by saying that 33 of 34 Haemophilia Centres had responded to him. Of those, two were said to prefer using cryoprecipitate, 14 were said to prefer using concentrate, and 17 preferred to use both. We will come on later to some other assessments made of preferences between cryo and concentrate.

So those were Dr Maycock's papers. We will turn now to the minutes of the meeting itself. If we could go, please, to PRSE00047064. The first page, we can see that this is the expert group on the treatment of haemophilia meeting, held on 20 March 1973. In the chair is Dr Reid. We can also see the other members:

Dr Biggs, Professor Blackburn, Professor Douglas, Dr Maycock, Dr Rizza, Dr John of the DHSS, Dr Macdonald of the Scottish Home and Health Department, Dr Thomas for the DHSS, Mr Walters for the DHSS, Mr Gardiner of the DHSS and Dr Sheila Waiter of the DHSS who was with Mr Gardiner, the secretary.

Dr Waiter is a significant figure in the months to come. She was the predecessor of Dr Walford in the role that Dr Walford would take from 1978 or 1979.

The terms of reference on the first page -- just a little bit lower down, Paul. Those terms of reference are:

"To advise the Department on trends in methods of treatment of haemophilia and allied conditions, and to consider possible future requirements for the treatment of a condition and the consequences for the supply of therapeutic agents."

I pause to note that a different version of the terms of reference refers to the departments, plural, which may reflect the presence on the committee of Dr Macdonald of the Scottish Home & Health Department. I believe that Professor Douglas was from the University of Aberdeen as well. Regardless of whether or not the department is given in the single or the plural, there was certainly SHHD representation at

this committee, and so whether they were advised or merely informed is perhaps a moot point.

If we could go over to the second page, please, Paul. I'm not going to go through all of this paper because much of it repeats the analysis that Dr Biggs has given in her paper. We can see that there is the comparison of therapeutic materials, and then discussion of cryoprecipitate and freeze-dried concentrate. If I pick it up from the final paragraph, there is this said about the safety aspect of concentrates, and I quote:

"A possible disadvantage arises from the fact that AHG concentrate is prepared from a larger pool of donations, and in theory, therefore, the risk of hepatitis is greater. About 1 in 800 of the donors who present to the Transfusion Service is a carrier of hepatitis B antigen.

"The present policy of rejecting donations which give a positive test for hepatitis B antigen will reduce the incident of virus in the blood used to make plasma pools. In practice, studies in several centres have shown that the incidence of hepatitis among severely affected patients who have been treated with freeze-dried preparation is not very much higher than that of the centres not using freeze-dried

concentrate, and this suggests that the development of hepatitis in these multi-transfused patients may be dose related. It was agreed that the theoretically increased risk of acquiring hepatitis, which does not seem to be borne out in practice, should not be a deterrent to using the freeze-dried preparation, and in any case this complication will decrease if universal screening of donors for hepatitis antigen."

That is what is said at the meeting, obviously building on what is said in Dr Biggs' paper.

If we go down to section 4, "Future requirements of therapeutic agents". If we just read from this section until the end of the document, and I quote:

"During 1972, considerably more cryoprecipitate from freeze-dried concentrate was issued in terms of donations of blood. It was generally agreed that 400,000 donations would be required to treat UK sufferers from haemophilia of all degrees of severity, and more if strenuous efforts were made to clear surgical waiting lists and if home treatment, or eventually prophylactic treatment, became accepted ways of dealing with the problems of haemophiliacs. Life-saving surgery has been undertaken for some time using the therapeutic agents which are available, but clinicians must now look to the possible improvement

in the quality of life of boys and men who suffer from haemophilia.

"Since more freeze-dried AHG concentrate has become available from two foreign sources, the prospect of improved management of day-to-day bleeding episodes using this therapeutic agent has become realistic. If the anticipated annual uptake of 20 million units of freeze-dried AHG concentrate is to be met from foreign commercial sources, the cost will be of the order of £2 million per annum, (assuming the cost to be 10p per unit).

"At present, UK production is considerably less than the required amount of the freeze-dried preparation. It was agreed that there was an immediate need to discuss the advisability of central purchase and distribution of the two commercially produced preparations. There is also a pressing need to seek ways of increasing UK production with the intention of reducing and, as soon as possible, ending purchase from foreign sources.

"Freeze-dried AHG concentrate is made at the Blood Products Laboratory, Elstree, at the Plasma Fractionation Laboratory, Oxford, and at the Blood Products Laboratory, Edinburgh."

Note the phrasing there is slightly wrong, but

we will move on:

"It is essential the production and distribution of the therapeutic agents concerned should be considered as a UK exercise.

"In any consideration of increased UK production of freeze-dried AHG concentrate, the immediate problems are those of the organisation and cost of increasing donations of either whole blood or plasma (by plasmapheresis) and the difficulties, including cost, of increasing the capacity of the laboratories at present engaged in production.

"Close cooperation between England (including Wales and Northern Ireland) and Scotland will be required in order to coordinate and optimise blood collection and transport. The fractionation processes, distribution of therapeutic agents and utilisation of other blood fraction by-products.

"Recommendations by the expert group:

"1. DHSS should give early consideration to central purchase of freeze-dried AHG concentrate from the firms who have recently been granted product licences.

"2. Distribution to other Haemophilia Centres and hospitals should be through the regional centres, three of which are in Oxford, Manchester and Sheffield

in England, one in Scotland (Edinburgh or Glasgow), and one in London (to be decided). The establishment of such a distribution scheme would be a prerequisite of recommendation 1 in order to ensure the most effective use of available material.

"3. At the same time, the UK should aim to become self-sufficient as soon as possible by increasing home production of freeze-dried AHG concentrate.

"4. The Regional Transfusion Directors should be consulted about the consequences of recommendation 3 in terms of increased demands upon the Blood Transfusion Services throughout the UK. Discussion should take place between DHSS and the directors about problems of decreasing productions of cryoprecipitate, increasing production of fresh frozen plasma for fractionation, and the possibly increased collection of plasma by plasmapheresis.

"5. There should be further meetings of this expert group at times to be arranged. Several subjects need to be discussed further, including home treatment and, in due course, prophylactic treatment.

"6. The expert group membership might be expanded to include representatives of each of the regional Haemophilia Centres, a representative of the

Regional Transfusion Directors, and possibly a SAMO [which is a Scientific Area Medical Officer]."

I will come back to SAMO, but a regional scientific medical officer of some form:

"It was also suggested that the National Medical Director of the Scottish National Blood Transfusion Association and Mr Watt of the Edinburgh BPL should be invited to join the group."

Edinburgh BPL is a reference to the PFC in Edinburgh.

So we can see there, sir, support for the position put forward by Dr Biggs. Reference to a need for 400,000 donations to treat UK sufferers from haemophilia of all degrees of severity, which is one of the questions you were asking earlier, and more if strenuous efforts were made to clear surgical waiting lists and if home treatment or eventually prophylactic treatment became accepted. So 400,000 as the minimum.

Reference as well to the costs of commercial imports, £2 million a year.

And two strands of development proposed. One is a central contract to buy commercial products, and the other is efforts to increase domestic production. The meeting referred both to the need to increase plasma supply and to consider the fractionation capacity of

the different fractionation centres in the UK.

SIR BRIAN LANGSTAFF: If we just look at what is currently on screen at the moment, just before we get to "Recommendation", it sounds a bit like another recommendation in the very last paragraph, "Close co-operation".

MR HILL: "Close co-operation between England (including Wales and Northern Ireland) and Scotland will be required in order to co-ordinate and optimise blood collection and transport, the fractionation processes, distribution of the therapeutic agents, and utilisation of other blood fraction by-products."

Yes, sir. A point which is, in fact -- that is a repetition of the point which was made earlier in the meeting as well, so something that the group considered to be very important.

You'll note there, sir, that Northern Ireland is grouped with England, at that stage, rather than Scotland because, at that time, the blood products were obtained from BPL. Later, of course, it would be PFC.

On the point about cooperation, I referred back to the discussion at the start of looking at this document about the presence of Dr Macdonald of the SHHD at this meeting.

SIR BRIAN LANGSTAFF: I think you said Dr Douglas as well.

MR HILL: Dr Douglas from Aberdeen.

That was what the expert group said. The response to that group within the DHSS can be seen in a series of letters, which are summarised in the written presentation. I won't take you to those. I will, however, flag the fact that one of those letters from Dr Reid to Dr Waiter, which is described at paragraph 47, ruled out spending £2 million per year on blood products but suggested that if £250,000 to £500,000 could be found in the current financial year so that is financial year from 1973 to 1974, then it would provide time to explore the possibility of the UK expanding production. Those figures, £250,000 to £500,000, will reoccur later on.

The working assumption within those internal DHSS documents is that it would take around two years before domestic production could meet the total demand. So it's talking about 1975 as a possible date for self-sufficiency, as defined by the requirements set out in that document.

A meeting was held to discuss the expert group recommendations in May 1973. If we could go to that, please, Paul, it's DHSC0100005_022.

We can see that present at this meeting were

Mr Gidden of one of the divisions of the Health Service division of the DHSS, so an administrative civil servant and somebody who is important in the development of the policy that comes; Dr Macdonald again from the SHHD, Mr Taylor from DHSS; Dr Maycock in his capacity as consultant adviser to the DHSS; Dr Duncan Thomas; Dr Waiter; and then Mr Pearson and Mr Walters and Mr Fenner, all of different divisions within the DHSS.

Reading from the minutes, paragraph 1:

"Mr Gidden said that the meeting had been arranged to consider the issues arising from the recommendations of the Expert Group on Haemophilia, including possible arrangements for central purchase and distribution of commercially produced AHG concentrate, and for expansion of UK production.

"Mr Taylor referred to the anticipated UK annual uptake of 20 million units and said that if it was decided to purchase the material commercially, the estimated cost of £2 million would almost certainly have to be met from existing financial allocations. It was most unlikely that the Treasury would make additional funds available."

I pause there, sir, to say that is a prediction which has proved accurate. So in the discussion which

follows in the coming year, the references to budgets are always to the internal DHSS budget. If the money is going to come from somewhere, it has to come from within the DHSS. There isn't additional Treasury funding being made available for the increased purchase of blood products or for the development of blood products domestically.

Back to the document, at paragraph 3:

"Dr Maycock said that professional opinion was that the clinicians and the pressure group representing patients felt strongly that the quality of treatment would be greatly improved if there were sufficient supplies of freeze dried AHG concentrates to replace a large proportion of the cryoprecipitate at present used. Dr Waiter and Dr Thomas supported this view and stressed that the development of AHG concentrate was a major advance in the treatment of haemophilia. Clinicians prefer to treat episodes of bleeding by giving infusions of freeze-dried concentrate as early as possible. Programmes of home treatment and possibly in future prophylactic treatment, which will be feasible when the freeze-dried material becomes more widely available, would in the long-term reduce treatment costs and the demand on hospital facilities. Dr Maycock thought

that the cost of increasing production in the UK to meet estimated requirements should be less than the cost of importing material from commercial sources. Dr Macdonald said that he had not looked at the problem solely from the cost point of view. He felt that Departments should, wherever possible, avoid involvement with commercial firms on all matters concerning blood transfusion, including the production of AHG concentrate. His view the Blood Transfusion Service should be self-sufficient in all respects."

Pause there, sir, to pick up a couple of points from that paragraph. The first is, again, we see reference to the preference of clinicians for the use of concentrate over cryoprecipitate, expressed forcefully by Dr Maycock and supported by Dr Waiter and Dr Thomas.

Also reference to home treatment and possibly, in the future, prophylactic treatment, stated -- the latter stated to be in the future.

Dr Maycock gave his view that, ultimately, there would be a cost saving of domestic products because it would mean you had to import less of the more expensive commercial products, though it is important to note that is not quantified in this document, the calculation presented.

Interestingly, Dr Macdonald, from the Scottish Home & Health Department, puts forward a more principled view of the need for self-sufficiency. So leaving cost aside, as a point of principle, he feels that the domestic Blood Service should be self-sufficient. When I say "principled", I mean putting it forward as a point of principle, not a judgement value if that is a more morally sound position.

Paragraph 4 of the minutes of the meeting:

"Dr Maycock said that one estimate was that the plasma from around 416,000 donations of blood would be needed annually in order to prepare the materials considered necessary to treat haemophiliacs in accordance with present views of ideal treatment. At present, about 228,000 donations in England and Wales were used annually for the preparation of these materials. He thought that the BPLs at Elstree and Liberton, when the latter was operational, would have the capacity to increase production of AHG concentrate to meet UK demand, but that some additional staff and equipment would be required at both laboratories. Dr Macdonald said that the new building at Liberton should be open and functioning by the end of 1974; he had some reservations about pursuing Mr Watt's

statement that the laboratory would be able to prepare AHG concentrate from 2000 litres of plasma per week. After discussion, it was agreed that the Blood Transfusion Service should increase production of AHG concentrate to meet all UK requirements, provided that the necessary addition of funds could be made available."

Pause there, sir, just for -- to refer to a couple of matters from that paragraph. A question which may be in your mind about what happens next from 1974 to 1975 period is why there was no decision taken, at that stage, to redevelop BPL more fundamentally than the incremental changes that were made. Part of the answer to that question may lie in Dr Maycock's analysis here, which is repeated in later documents that we will come to, in which he says that, if you look at Elstree and Liberton together, then, as long as there are some additional staff and equipment made available, then they would have the capacity to increase production of AHG concentrate to meet UK demand. The suggestion there is that the two fractionation plants can cope with what is going to be asked of them, subject to those pieces of equipment of the staff being made available.

If we go to the end of the document, the

following action was agreed. Point 7, the first action point is:

"Supply Division (that's a division within the DHSS] should be asked to start negotiations with a view to arranging a central call-off contract for the purchase of freeze dried AHG concentrate on the basis of a demand for 20 million units per annum from about 40 haemophilia centres."

Then point (iv), as well, if we go on to the next page, please:

"The question of UK production to be referred to the proposed Joint Steering Committee on Blood Products Production for consideration."

So again, sir, two strands. One is the central contract to purchase commercial concentrates and the second is further work and a new body, the Joint Steering Committee, to look at joint production. Those were the action points suggested at that meeting.

SIR BRIAN LANGSTAFF: So if we just go back to the previous page, Supply Division starting negotiation "on the basis of a demand for 20 million units".

Now, earlier in this meeting we said there was no additional money for that. So what was being proposed, presumably, was that this would come from

existing budgets?

MR HILL: Yes. We will see how this -- how it plays out in the documents that follow, I won't take you to all of them, is that the DHSS arrange the central contract. They do so to try to take advantage of economies of scale, and that is a contract with the providers of Hemofil and Kryobulin. However, that is arranged centrally but, for each of the regions who wish to purchase the commercial product, they must fund that out of their own budget.

There is a debate about whether or not this is going to be centrally funded or regionally funded and that is answered by the DHSS saying it has to be regionally funded. So the regions will have to decide how much concentrate they want, how much they can afford, and then they will use the concentrates obtained by the DHSS as their source of material, but they will be the ones who are paying for it.

Just to finish that section off, sir, it's set out in the written presentation from around about paragraph [55], that the take-up by the Regional Health Authorities of the commercial concentrates that DHSS had arranged to purchase from the providers, that take-up was well below the anticipated demand. I won't take you to the document, but a memo from

July 1974 states this, and I quote:

"Because of a high cost [that's the high cost of the concentrates] and authority's current financial difficulties, the uptake of the material during the first seven months of the contract has been far below the originally estimated level of demand: Travenol, Hemofil, 1.35 million units, 47% of the estimate; and serological products [that's Kryobulin], 244,000 units", which was about 8 per cent of the estimate.

So, although the commercial contract goes ahead, it is of limited success in increasing the amount of commercial concentrate that is available to clinicians because Regional Health Authorities are reluctant to buy the concentrates because of their cost. If we think back to October and November, when we were looking at the pharmaceutical companies, we discussed, briefly, the central contract there and the figures that it gave rise to and the costs that it gave rise to.

That is all I will say on the central contract. We turn then to the second strand, which is the work that was done on increasing domestic production, and you'll have seen from the last meeting that the first step is to set up a new body, the Joint Steering Committee on Blood Products, and that met for the

first time in June 1973.

If we could go Paul, please, to PRSE0004359, this is summarised at paragraph 59 of the written presentation.

We can see from the heading that this is the note of the first meeting and it was held on 20 June 1973. The list of those present, Dr Maycock is in the chair, and then I won't go through all of the names but there are various Regional Transfusion Directors, another representative of the Blood Products Laboratory, representatives of the DHSS, and representatives of the Scottish Home & Health Department, including Dr Macdonald and Dr Bell. From the DHSS, we just note that Dr Waiter was one of those who was present.

If we could turn -- I won't go through all of this document, but if we could turn, please, to electronic page 5, paragraph 19. There is a discussion of Dr Biggs's paper and the previous discussion that had been held about haemophilia treatment. It says there that, and I quote:

"The main points that emerged from the discussion were:

"a. It was decided that in principle to treat the UK as a whole and that the first target should be

Dr Biggs' lower estimate of the plasma from 400,000 donations with 700,000 donations as the ultimate target.

"b. The initial aim should be to provide anti-haemophilic globulin concentrate from 250,000 donations by 1975.

"c. The UK should opt initially to meet most of the requirement with an 'intermediate potency product' but about 10% of the total output should be a 'high potency product'.

"d. DHSS was considering making 'call-off contracts' for two commercially produced anti-haemophilic globulin concentrates which would be available through Haemophilia Centres. It was agreed that it would be of considerable interest to the Joint Steering Committee to have details of the rate of purchase by the Centres.

"e. The UK should aim to be self-sufficient by 1975."

Again, sir, we see the different figures, the initial aim of 250,000 donations, that is part of a first target of 400,000 donations, which is part of a way to an ultimate target of 700,000 donations.

SIR BRIAN LANGSTAFF: Is there any further detail as to what the distinction, what distinction was seen

between intermediate potency and high potency? We've had descriptions of intermediate purity and high purity before, which is explained by removing unnecessary proteins from the fraction. What's potency? This is the amount of activity?

MR HILL: I think, at least I read this as what would later be described as high purity, intermediate purity and --

SIR BRIAN LANGSTAFF: It might, however, mean extra concentrated.

MR HILL: It --

SIR BRIAN LANGSTAFF: Just as one buys a bottle -- to use a home-spun analogy -- a bottle of squash and then you can get a smaller bottle, which is supposed to be three times as concentrated.

MR HILL: It could mean that, sir. My -- I can't take you to any document which shows this, but my sense is that it is probably referring to what later becomes termed "purity". But I cannot be sure about that.

SIR BRIAN LANGSTAFF: Yes. I mean, if there's no other document that helps, well, that's just a mystery and we'll assume that it means one or the other.

MR HILL: We can look into it and see if we can find anything. The terminology in this period is a little looser than it becomes later.

SIR BRIAN LANGSTAFF: Well, they knew what they meant.

MR HILL: They knew what they meant, yes. Certainly, the sense is that there should be two forms of product, one which will be for general use, as it were, and one which is for a more specialised use.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: The next meeting of note is on 20 July 1973. I won't take you to the document, but it was a meeting of the Regional Transfusion Directors, which discussed the issue of domestic production, and considered a paper, which is referred to in the written presentation at paragraph 60.

At that meeting, it was proposed that the figure of 250,000 should actually be increased to 275,000, and the basis for that was a recalculation of how much plasma could be assumed to be obtainable from a single donation. As we saw earlier, there was an estimate from Dr Biggs of 200 to 220 millilitres, and at this meeting, the Regional Transfusion Directors thought that 180 to 190 millilitres was a more realistic target. Because you were obtaining less plasma from each donation, you would therefore need more donations, hence the figure of 275,000 donations.

The same meeting heard that there was an overall deficiency of about 100,000 donations per annum, and

that was by reference to the first goal of 400,000 donations. So there were about 300,000 donations at the time, and there should be about 400,000 to meet overall need, and of those, 275,000 should go to concentrates. That was the maths that was being done.

Now, interestingly, the meeting discusses how that shortfall of 100,000 donations could be made up by the increased use of red cell concentrates. So as we were discussing earlier, the separation of the whole blood donation into red cell concentrates and plasma. And appendix 7 of -- that is attached to the written presentation provides some further data on this, and we will look at that in due course.

But the shift towards red cell concentrates as a way of increasing domestic production is seen as one of the things that can be done and can be done relatively quickly at this time.

There was also discussion about how a donation target should be distributed amongst the different Regional Transfusion Centres in proportion to the total number of donations that they collected. So the idea there of setting each centre a target for the number of donations that it should provide.

Now, the meeting was told, paragraph 4 of the note, and I quote:

"It was expected that the necessary fractionation capacity would be available at BPL."

And that goes back to the point, sir, that I mentioned earlier about why there was no concerted effort at this time to seek an expansion of the Blood Products Laboratory at Elstree.

SIR BRIAN LANGSTAFF: That meant BPL Elstree, did it?

MR HILL: Well, again, the terminology isn't absolutely clear. And it could mean -- sometimes BPL is used as a term to cover both Elstree and Liberton. From the previous documents, the discussion was very much that you would need -- to provide self-sufficiency across the UK, you need both. Both plants. And my reading of this is that that is what was intended to be meant, even if that's not necessarily expressly recorded.

There was a further meeting of the Regional Transfusion Directors on 27 September 1973 where some of the practical issues and difficulties involved in increasing plasma supply were discussed.

That brings us to January 1974 at which point a significant reconsideration of future demand took place. And if we can go, please, Paul, to PRSE0002350. We can see, sir, that this is a paper, but it's a report from the Medical Research Council's transfusion research committee working party on the

cryoprecipitate method of preparing AHF concentrates. So it is an MRC working party which has been put together, and we can see who is on it from the front page. Dr Biggs in the chair, and then other members include Dr Rizza, Professor Blackburn, Dr Delamore, Dr Dormandy, Professor Ingram, and Dr Maycock among others.

This working party produced a report, and it drew very heavily on Dr Biggs' earlier work and earlier paper, so I won't take you through all of it. But there is a slight -- a significant, sorry, adjustment of the figures for the donations required. And if we could turn, please, Paul, to page 21 of the document, we will go to the conclusions.

Conclusion 1 is that:

"Calculations suggest that the amount of material required for optimum treatment of all the haemophilic patients in Great Britain would be derived from 547,540 to 750,000 blood donations a year. This material would be used for on-demand treatment of all patients, including home treatment of the 1,000 or so patients who might benefit from it. The present supply is that derived from approximately 300,000 blood donations a year, of which most is in the form of cryoprecipitate."

Just pausing there, sir. I'll deal first with that figure. So it has gone up from 400,000 to 750,000 to 547,540. The explanation for that is that there had been a recalculation of the minimum number of people with haemophilia in the UK. I'm going to use the term "the UK" because I'm very confident that this refers to the UK, not just Great Britain.

Now, previously, Dr Biggs had said that that figure was at least 1,754 and was almost certainly more than that. In this paper, the lower figure is 2,434. That is taken from data which had been obtained from Haemophilia Centres and certain other assumptions which are explained in the paper. So that explains why the lower figure has gone -- the lower estimate for the number of blood donations required has gone up from 400,000 to pretty much 550,000.

I would also note, sir, that this paper is later published in the British Journal of Haematology, and a slightly different figure is given there, which is between 511,000 and 720,000 donations. So not quite as high as is covered in this paper, but certainly closer to that than the original estimate of 400,000.

The first conclusion also addresses some of the issues that we have been discussing earlier. There is

a reference to "all patients", so presumably meaning patients with severe, moderate, and mild haemophilia. And included within that figure is, again, this 1,000 or so patients who would most benefit from home treatment. The most severely affected. And very clearly stated that this is about on-demand treatment, so the same assumptions that had informed Dr Biggs' earlier paper and the discussions of it. That on-demand treatment was to include the home treatment of the 1,000 or so most severely affected patients.

Returning to the conclusions. I won't take you through all of them because they are echoes of Dr Biggs' earlier work. There's a discussion at conclusions 2 and 3 about comparisons between cryo and concentrates.

At paragraph 4 on the next page, and I quote:

"For home treatment, it is our opinion that a freeze-dried concentrate is the therapeutic material of choice. The gradual introduction to home treatment of the most severely affected patients who have the most frequent bleeding would reduce hospital management of haemophilia by half. To give this proportion of patients (approximately 1,000) home treatment would involve the use of factor VIII concentrate from about 250,000 blood donations a year.

The present (1973) total of factor VIII concentrate is derived from 40,000 to 45,000 donations a year."

Just pause there to note, sir, that we're back to the 250,000 figure, rather than the 275,000 figure which the Regional Transfusion Directors had arrived at. And I also note that the figures of donations devoted to concentrate had gone up by 1973 to 40 to 45,000 from the original 25,000.

And back to the document in paragraph 5:

"The number of donations contributing to pools of plasma used to make concentrates does affect the probability that a particular pool may contain hepatitis virus. However, the incidence of jaundice in multi-transfused patients seems to be, to some extent at least, dose related. In practice, the incidence of jaundice in multi-transfused haemophilic patients does not rise very greatly with the use of freeze-dried concentrates. In any case, with universal screening of donors for hepatitis B antigen now in operation, the danger of infection will decrease to some extent in the future. The incidence of anti-factor VIII antibodies is not affected by the type of human material used to treat the patient.

"6. We think that within the next few years a great effort should be made to increase the amount

of plasma which is fractionated in the United Kingdom. From the point of view of patients with haemophilia and Christmas Disease, present estimations suggest they need for 547,540 to 750,000 donations to be fractionated annually to produce freeze-dried factor VIII. On a national scale, this need for factor VIII must be coordinated with other demands of the Transfusion Service, for example the need for albumin fraction. Clearly, a 20-fold increase in fractionation cannot be achieved overnight, but it is to be hoped that very substantial increase may occur without too much delay. The present estimate of the need for factor VIII is based on data now available, and as time passes and more concentrates become available, the true amounts of factor VIII required will be defined more certainly. Our present opinion is that the provision of freeze-dried material from 500,000 blood donations annually will do as much to improve the lives of haemophilic patients as was achieved several years ago by the provision of cryoprecipitate.

"7. Freeze-dried factor VIII concentrate of good quality is now available commercially. At present, patient treatment at many of the Haemophilia Centres in this country involves a dangerous policy of

balancing the needs of one patient against those of another and of delaying reconstructive orthopaedic surgery which would greatly improve the lives of many patients. We believe it very important that the material made in the United Kingdom, which is second to none in quality, should be substantially increased in amount. In the interim period before the United Kingdom product is available in adequate amounts, commercial factor VIII should be bought in quantities sufficient to satisfy the needs of these patients."

SIR BRIAN LANGSTAFF: Can you just help? The claim is there made that the material made in the United Kingdom is quote "second to none in quality".

MR HILL: Yes.

SIR BRIAN LANGSTAFF: Is there any description anywhere as to how quality was to be assessed?

MR HILL: There isn't a single document, I think, that sets that out. There is discussion in some of the other meetings which really echoes what is said there: that the domestically made product is as good to use as the commercial products. Now, I have inferred from that discussion that that is a reference to things such as the solubility of the product, the lack of inhibitor reactions to it, the ease of storage, for

example, but that is not expressly stated. The discussion on safety is that at paragraph 5 and echoes the discussions that were previously had.

I'm just going to go back over those numbers again, sir, because I'm conscious that we have a different set of numbers, and it's helpful, perhaps, to just pause and take stock of what they are. So the MRC are saying -- have presented three figures in their conclusions. The first is that range from 547,540 to 750,000 donations, and that is stated to be the overall need for donations for optimal treatment for all people with haemophilia.

It is presented in conclusion 1 as a figure that encompasses both Factor VIII and cryoprecipitate, and it is compared with the current position of 300,000 donations. However, later, there is a discussion about how there is a desire for all or most of that figure to be made up in concentrates in the long run.

So that is 574,540 to 750,000, an increase, as we've said, on the previous estimate of 400,000 to 750,000.

The second figure is that figure of 250,000 donations for home treatment for the 1,000 most severely affected patients. That is consistent with what Dr Biggs had said before and, as we've seen, the

Regional Transfusion Directors have said, actually, that figure should be about 275,000 to adjust for the amount of plasma that can be taken from a blood donation.

The third figure that the MRC give is 500,000 donations, which, in their view, should be dedicated to concentrates in order to improve the life of people with haemophilia, as much as the introduction of cryoprecipitate did.

The final recommendation is about how the UK should both increase its own domestic supply and also buy commercial concentrates to cover the shortfall in the interim.

This paper was presented by Dr Biggs, who I take to be the lead author of it, to the directors of Haemophilia Centres and Blood Transfusion Centres at a meeting that was held on 31 January 1974.

Paul, please could we go to CBLA0000187.

We can see from the top of that page that this is a joint meeting and it is held to discuss Dr Biggs's paper, among other matters. The Chair is Professor Blackburn. I won't go through the full list of those who attended and sent apologies. There were 41 representatives from Haemophilia Centres and hospitals; five representatives from Regional

Transfusion Centres; Dr Maycock was present from BPL and Dr Waiter was among those present from DHSS.

If we could go, please, Paul, to page 4 of the paper, of the minutes, and we can see that item 3 is "The present and future supply of Factor VIII", and Dr Biggs introduced the MRC Working Party report that we have just looked at.

If we go down just to the bottom of that paragraph we can see that Dr Biggs said that the report suggested a need for material derived from 500,000 to 750,000 donations annually. That is the range that she is giving there.

There then followed discussion, if we look at the next page. The first item was how many people with haemophilia there were in the United Kingdom. I won't go through that discussion but if I could just ask Paul to go to point (iii), a point raised by Dr Ingram, who:

"... spoke on the long term forecast of factor VIII requirements ... and stressed that the incidence of haemophilia is likely to rise as treatment improved. Any assessment of the amount of [antihaemophilic globulin] required for therapy must take this into account."

So Dr Ingram flagging the point that, as the

population increases, due to better treatment, it will need more factor concentrate.

Then I will read the next part of the discussion, which is "What kind of material was best for treatment?" I quote:

"There was a wide ranging discussion about the relative merits of cryoprecipitate and freeze dried concentrates with regard to ease of manufacture, recovery from the original plasma, ease of administration and recovery of activity in the patients. It was generally felt that larger supplies of concentrated preparations were required now and urgently and some felt that it was rather meaningless to ask doctors if they would prefer freeze dried concentrate to cryoprecipitate when no freeze dried concentrates were available to them. When the discussion was completed the meeting was asked to indicate whether anyone would in fact prefer to have cryoprecipitate if freeze dried concentrate were freely available. It was clear that none of those present would prefer cryoprecipitate."

The next section of the meeting discusses how much material was likely to be needed and we hear a dissenting view from Dr Bowley, who was a Regional Transfusion Director. I'm afraid, I -- Sheffield.

Sheffield Blood Transfusion Centre.

Dr Bowley, I won't go into this in detail, but he criticised Dr Biggs's figures and thought that she was overestimating the amount of future need and he suggested that it was lower. It's not a view which gains much traction so I won't go into it in any further detail.

But, if we go to the bottom of that page, it says, and I quote:

"In view of all that had been said, the Chairman concluded that with one exception [I take that to be Dr Bowley], the Meeting" --

SIR BRIAN LANGSTAFF: I think we need -- thank you.

MR HILL: -- "the Meeting supported and wholeheartedly endorsed the Appendix B Document [that is the MRC report]. Again it was stressed that the estimates in Appendix B are just for present but in five years' time there may be a need for more material.

"ACTION. The Chairman agreed to write to the DHSS saying that the meeting of Haemophilia Centre Directors and Transfusion Directors, approved the contents of Appendix B and recommended that this document be used as the basis for planning future requirements for factor VIII in the United Kingdom.

"The meeting then went on to discuss problems

which would arise in trying to increase the supply of factor VIII freeze dried concentrates.

"It was felt that once the new fractionation laboratories in Edinburgh and at the Lister Institute [BPL and Elstree] were in full production, they should be able to meet the needs of the country provided sufficient plasma was available.

"Some Blood Transfusion Centres felt that plasmapheresis which was already being carried out on a large scale in some Centres might be the answer to the problems of plasma applies. Dr Cleghorn described his procedure and said that his donors found it acceptable and not distressing.

"There was no doubt that the 'processing' of more blood to obtain plasma for manufacture of factor VIII would require more staff, equipment, mobile vans with cold storage facilities, etc, and that this would add to the Blood Transfusion Centres' costs.

"Dr Waiter could give no statement as to how this extra expense would be met but she said that it should in the first instance be referred to the DHSS. She made the point that the purchase of commercial AHG was already costing the DHSS a lot of money.

"The meeting digressed for a short time to

discuss the problems of genetic counselling ..."

I won't take you through that.

"Several directors said that they did not treat all the patients at their Centres since this was too inconvenient for the patient and too difficult. On the other hand, they were aware that the materials might not be used properly. This raised the question of home therapy. It was stressed that home therapy was becoming more accepted and widespread and was improving the quality of the patients' lives. Cryoprecipitate was not ideal for home therapy from many points of view. Some directors were buying commercial AHG for use in home therapy."

If we could just go back to the previous page, Paul, just to pick up a couple of points from that. The joint meeting of the Haemophilia Centre Directors and the Blood Transfusion Directors, therefore, gave a ringing endorsement of the MRC paper that we have already looked at and of the estimates that it contained, in particular, at least 500,000 to 750,000 donations per annum.

They recommended that the MRC report should be used as the basis for future planning. We can see about halfway down the page a statement again that, once the new fractionation laboratories at PFC and BPL

were up and running in full production, then they should be able to meet the needs of the country, provided sufficient plasma was available.

Again, sir, I'll go back to that question of why it is that BPL was not redeveloped at that time and this may be the answer. That plays out in the way that the £500,000 that Dr Owen makes available is subsequently spent, something that we will come to later.

Finally, just a couple of points on what Dr Waiter is recorded as saying. She said that, in the first instance, the costs of increasing plasma production, which had been raised at the meeting, should be referred to the DHSS. I take that to mean that there is a need to consider that centrally, in Dr Waiter's view, rather than, in first instance, in the regions. This gives rise to significant debate in the months that follow, about who should pay for the improvements that were needed in order to increase plasma supply.

The second point that Dr Waiter made was that the DHSS, looked at cumulatively, was already paying a lot of money for commercial concentrates, and that could be offset against the cost of future production. I don't think it is too far of a stretch to say that

one can see here that Dr Waiter is sympathetic to this argument but, of course, Dr Waiter is one individual within the DHSS, as --

SIR BRIAN LANGSTAFF: Well, what she seems to be saying is the DHSS is paying centrally to buy a commercial product, the production -- the greater production of which is capable, on the basis that the meeting decide, capable of being fulfilled by BPL, Elstree and PFC in Liberton, if they're given enough plasma. That requires enough plasma, that'll cost a bit more money, but because it's going to save money with the DHSS currently paying centrally, that's where you get your money from. It's the subtext.

MR HILL: Yes, and that is an argument which is made repeatedly in the papers by various people, including Dr Waiter.

SIR BRIAN LANGSTAFF: But, as you say, it cuts against the principle of regional payment.

MR HILL: It does, sir. What we will see in the papers that follow is that, in order to expand plasma supply requires significant upfront capital costs and, indeed, revenue costs that occur. Those will be incurred upfront, and you won't get your plasma -- increased plasma supply until sometime afterwards because it takes a while to work through the system.

Buying concentrates commercially will cost less in the short-term than your significant capital costs, and you will get the concentrates immediately. So there is a trade-off between a short-term and a long term cost, both for the Regional Health Authorities and, indeed, for the DHSS generally. That is perhaps a dynamic which is important in the events that follow.

The response of the DHSS to this meeting is considered from paragraph 73 of the written presentation. I won't take you to the documents there. There was a minute from Mr Jackson of the DHSS, dated 14 February 1974, in which he refers to the fact that 8 out of 14 Regional Transfusion Centres had provided the DHSS with estimates as to how much money would be required to increase plasma supply, and he had extrapolated from those estimates that, across the country, about £160,000 would be needed for extra accommodation, equipment, staff and transport, and that BPL would also require about £45,000 for capital works.

That is, as Dr Jackson says, a calculation which is a rough one, and is not based on data from all of the centres.

Now, Mr Jackson says, in that minute, and

I quote:

"The cost of increasing the production of plasma is modest", when compared to the cost of production products.

So the point that we have just been discussing.

Mr Jackson's minute triggers a debate amongst DHSS officials about whether central funds should be provided or whether the regions should be left to fund these improvements themselves. It's clear from the relevant documents that there is an awareness, an acute awareness, that this debate is taking place at a time of great pressure on public expenditure. To quote from one document, I quote that public expenditure reductions have, and I quote:

"... been so severe that Regional Health Authorities will be unable to carry through all the products that the department would like to see."

So there is a recognition that the regions are very pushed for money. But, as of 19 April 1974, we have a minute from that date, the position of the DHSS was that no central funds would be made available to the regions. By that time, the estimate for how much the improvements were going to cost had gone up to being not less than £1 million, and the point made in the documentation is that the savings on the cost of

commercial concentrates would be savings that benefited the regions, therefore it was for the regions to put forward the capital costs to improve the supply of plasma, in order to get the benefit of those savings.

Now, that lack of central funding coming at the same time as the DHSS and others are pushing for an increase in plasma supply caused tension, as one might expect. And just to give one example of that, if we could go, please, Paul, to DHSC0100005_094. This is a letter which is written from Mr Scott, who is the regional medical officer of the Trent Regional Health Authority, and it is written to Dr Maycock. It is dated 16 May 1974, and it is entitled "Provision of plasma for Factor VIII concentrate". And what Dr Scott says is this, and I quote:

"I have recently received from Dr Wagstaff [the director of the Regional Transfusion Centre] a request for £17,000 capital and £29,000 recurrent revenue to meet the cost of providing fresh frozen plasma for the manufacture of Factor VIII concentrate. It seems that the DHSS was expected to meet these costs, but not unexpectedly it has referred the matter to regions.

"I cannot comment on other regions' finances at this time, but in the light of information currently

available to me, there is no hope whatsoever of the Trent Regional Health Authority meeting these demands.

"I find this situation disturbing because a national edict of this kind threatens to distort other regional priorities. Equally, I am very unhappy at not being able to offer encouragement to the Sheffield Centre which has always prided itself on being to the fore in such developments.

"I would value your comments and advice."

That was sent, as I say, by Dr Scott. An indication of the tension that had developed between the region and the DHSS in this area.

I note the time, sir, and wonder if that might be a good point to stop for lunch.

SIR BRIAN LANGSTAFF: Yes. Well, we will take a break now, shall we, until 2.00. 2.00.

(1.02 pm)

(The Luncheon Adjournment)

(2.01 pm)

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Just to pick up on three things from this morning, sir. First, SAMO stands for Senior Administrative Medical Officer. Apologies. There's so many acronyms. Sometimes they slip through the net.

SIR BRIAN LANGSTAFF: Well, I'm sorry couldn't help you. I was trying to work out what the "A" meant.

MR HILL: The second point, this question of potency and purity. If we could have on screen, please, WITN3431001, page 32. This is the witness statement of Dr Snape from whom we will hear at the tail end of this block of hearings. We'll have paragraph 90 when it comes up. Page 32, paragraph 90. The context is not relevant for today's purposes, but we can see here what Dr Snape says about potency and purity. In the parenthesis he says:

"The term 'potency' refers to the concentration of factor VIII in units/ml, whereas purity, or more accurately 'specific activity', describes the ratio of assayed factor VIII to measured protein content expressed as units of factor VIII per mg of protein. Specific activity is important in this context since it reminds the fractionator and the treating physician how much non-factor VIII protein is going to be infused."

We can see there the distinction that Dr Snape draws in his statement. The reference earlier was to the potency of the product --

SIR BRIAN LANGSTAFF: Yes.

MR HILL: -- which, in Dr Snape's usage, will therefore be

this --

SIR BRIAN LANGSTAFF: Well, he can tell us if that's right, but thank you for that. It looks as though there was a proper distinction to be made.

MR HILL: Yes.

SIR BRIAN LANGSTAFF: Thank you.

MR HILL: Finally, a measure that I didn't introduce earlier but will introduce now. We looked at the MRC paper, Dr Biggs' paper that was later enthusiastically endorsed by various meetings and was recommended as the basis for planning. That expressed the amount of blood donations required as the measure for achieving the requisite amount of blood products. The same paper also expresses that amount in terms of Factor VIII units. The figure that is given in the paper, and it is page 18 of that document, is that --

SIR BRIAN LANGSTAFF: Is that PRSE0002553?

MR HILL: It's PRSE0002350. Electronic page 18, internal page 17. Perhaps, actually, we will bring it up, Paul.

PRSE0002350. Electronic page 18. We can see at the top there the figure that we discussed earlier, 547,540 to 750,000 blood donations per annum. If we go down a few lines, it says:

"Expressed as factor VIII units, the range is

a reference to the concentration in units of Factor VIII per millilitre.

SIR BRIAN LANGSTAFF: It's the degree of concentration. It's the -- my example of the concentrated squash or the concentrated washing up liquid.

MR HILL: Exactly, sir. Exactly so. The wider context of that discussion is that 90 per cent of what may be referred to as standard Factor VIII was required and 10 per cent of the higher potency --

SIR BRIAN LANGSTAFF: He makes the point here that the two might be linked, possibly, in this sense: that if you are using less volume to give you the necessary Factor VIII, you are therefore providing less volume of other proteins --

MR HILL: Yes.

SIR BRIAN LANGSTAFF: -- which may *(unclear)*, by the way, but they're there. So it is also going to be more equivalent to higher purity although -- because it's -- high purity refers to the amount of excess protein that you get, doesn't it?

MR HILL: That is my understanding, that the two will be closely related. A higher potency Factor VIII product may be an increasingly pure Factor VIII product.

SIR BRIAN LANGSTAFF: Yes, on the other scale.

MR HILL: Dr Snape I hope will be able to take us through

likely to lie between 38,327,800 and 53 million factor VIII units."

So expressed in slightly more simplified terms, it's between 38 million and 53 million Factor VIII units. Now, I understand that to be a reference to what later becomes referred to as international units.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: We will see increasingly, as the '70s goes on, the measure of blood donations is dropped in favour of weight or volume for the amount of plasma and international units for the amount of Factor VIII that is produced. This is a translation between the two presented by Dr Biggs. There are various ways of trying to calculate how many international units come from each donation, and it rests on a series of assumptions. So it can't be seen to be an absolute definitive figure, but in Dr Biggs' mind, what she is thinking about is the need for between 38 and 53 million international units of Factor VIII per annum.

SIR BRIAN LANGSTAFF: Yes. Just one other measure while we're talking about measures. I understand there is a clear link between volume and weight if you're looking and thinking of water, which I think is how the MKS system of measurement works and converting

from kilograms to volume. Plasma plainly is not the same specific gravity as water, so it will be heavier, presumably, per volume. Do you know what the conversion is?

MR HILL: The conversion that I have found, and I stress this is a layman essentially looking online to try to find the conversion, I think it's in the region of 1.024 kilograms.

SIR BRIAN LANGSTAFF: Thank you.

MR HILL: But there will be others who are far better placed to be able to make that conversion.

SIR BRIAN LANGSTAFF: So it's very close to a kilogram being equivalent to a litre.

MR HILL: You will see in appendix 1 and appendix 2 when the Inquiry legal team have had to do that calculation in order to be able to compare data points, the conversion used is 1:1.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: But it is stressed that that is a rough approximation. And as we will hear when we come on to look at those figures, they come with a lot of caveats, the core of which is that they are helpful in showing a general trend but they shouldn't be relied upon to be absolutely precise at all points as to exactly how much is being either produced or supplied.

SIR BRIAN LANGSTAFF: I suppose it might be said that it would give a degree of apparent accuracy, which isn't necessarily completely accurate, knowing that different plasma donations will have different levels of Factor VIII activity in them, depending upon how much the donor had.

MR HILL: Yes. There are so many variables, it is never going to be possible to say this figure is exactly this figure in equivalence.

SIR BRIAN LANGSTAFF: You'd expect the donations to approximate if there are enough of them in a pool, to a hundred per cent activity, that being the average, but you don't know.

MR HILL: Exactly, sir.

SIR BRIAN LANGSTAFF: I see.

MR HILL: Returning, then, sir, to the chronology. The tension that we were exploring before the break was between the DHSS and the Regional Health Authorities about who was going to fund the expansion of plasma supply.

There was also a tension that was growing between clinicians and the DHSS, and no doubt with their regional administrators as well, about the amount of concentrate that was being provided to them.

Two examples of that come from Dr Biggs. The

first is a letter that she wrote to Dr Waiter at the DHSS on 23 May 1974. And, Paul, if we could have that on screen please. CBLA0000206. What Dr Biggs wrote is this. It's in response to a letter sent by Dr Waiter on 10 May 1974. Dr Biggs wrote, and I quote:

"I wonder if there is some impression in the Ministry of Health and Social Security that the haemophilic patients in this country are now not undergoing any real inconvenience? I cannot give you figures about 'crippling' because it is hard to say exactly what is meant by crippling. However, many of our child patients arrive at hospital in ambulances on crutches and with knees and ankles so painful that they cannot put a foot to the ground. Elsewhere, I am sure that patients with these bleeds are at home in bed. In the long run, all of these patients will have arthritis and deformity. In the bad old days, this would occur before the age of ten. Now, hopefully, most patients who attended Haemophilia Centres (about half the total) should at least reach adult life able to walk. Our modest objective is to get enough factor VIII delivered to the patient to delay the onset of arthritis to middle age for all patients."

You can take that down.

Dr Waiter replied saying that her colleagues in the department had been left in no doubt of the requirements. And she also pointed out that if money were to be made available for more Factor VIII, then it would come at the expense of something else in the health budget.

I should add, sir, that although that letter was addressed to Dr Waiter, I think that we can see from the papers that Dr Waiter was sympathetic to the cause being made by Dr Biggs and others.

Dr Biggs, in the same letter, told Dr Waiter of her intention to send a letter to The Lancet on this matter, and that was published on 29 June 1974.

If we could go to that, please, Paul, it's PRSE0002515. I'm going to read the entirety of the letter, because it is significant in the effect that it has on some Parliamentary opinion:

"Letters to the Editor

"Supply of Blood-Clotting Factor VIII for Treatment of Haemophilia."

Dr Biggs wrote this:

"Sir -- The treatment of haemophilic patients involves a replacement in their blood of an essential substance which they lack. In this respect, the disease resembles diabetes or pernicious anaemia.

Factor VIII to a haemophilic patient is literally his expectation of life. Haemophilia differs from diabetes or pernicious anaemia in that the missing factor VIII can only safely be provided from human blood. The haemophilic patient is thus indebted to society and in return is the responsibility of society in rather a special sense.

"Without treatment, before the middle of this century, few patients reached adult life and those who did were helpless cripples. Over the past 12 years, blood products containing factor VIII have gradually increased in amount. In the early part of this time, medical attention was centred on the cure of life-endangering bleeding and on the protection during essential major surgery. As more material became available, patients were treated for particularly dangerous muscle haematomas and haemarthoses in the hope of reducing somewhat the severity of crippling and delaying the age of onset of deformity. The present, but still modest, objective is to treat all developing musculoskeletal bleeds as early as possible, hopefully to prevent the occurrence of severe deformity in all patients. This form of therapy is called 'on demand' treatment. Very many of the patients treated on demand arrive at the hospital

on crutches, in ambulances, and with painful swollen joints. Most such episodes of musculoskeletal haemorrhage resolve with treatment, but there can be no doubt at all that in the long term these patients will have arthritic joints long before those of the normal population. An extension of on-demand hospital therapy to the home (home therapy) so that treatment is given by the patient to himself, by a relative or by a general practitioner would undoubtedly reduce the damage and also the anxiety under which patients and their families now live. It should be noted that even home therapy is a modest objective when comparison is made with prophylaxis. In prophylaxis, treatment would be given to prevent the occurrence of bleeding altogether. Prophylaxis is, of course, the rule for patients with diabetes or pernicious anaemia; its application to haemophilic patients would treble the present estimated requirements of factor VIII.

"Those who treat haemophilic patients in the United Kingdom have in the past of necessity tolerated the chronic undertreatment of their patients and have put much time and effort into spreading the inadequate amounts of therapeutic material thinly so that deprivation should be least damaging. Essential but non-urgent operations have been postponed and are

still being postponed. Economy has also been achieved by calculating the those for each lesion for every patient to the absolute minimum dose. In addition, patients have not been put onto home therapy who would greatly benefit by this treatment. Even with dire economy, some centres have been hard pressed to main minimum treatment. For example, the treatment of the boys at Lord Mayor Treloar College at Alton in recent years has been maintained against a background of begging and borrowing from other centres from one week to the next. Were the school not supplemented in this way, it is calculated that there would be a deficit of about 260,000 factor VIII units annually. There is, in fact, evidence that 90% of haemophilic patients in the United Kingdom receive less (and in some cases much less) than optimum treatment for their complaint. The consequences of this undertreatment include subjecting the patients to unnecessary, painful, and destructive bleeding into joints and muscles. Ancillary effects of undertreatment include loss of educational time and inability to holding continuous employment.

"The question that arises is for how long should this shortage of factor VIII be considered to be a reasonable feature of haemophilia treatment? Two

things, in my view, make continued limitation both unnecessary and unethical. The first of these is the fact that three commercial companies are now licensed to sell good-quality human factor VIII in this country and they have between them amounts of material adequate to supplement the present provisions of the National Health Service. In fact, at the time of writing, one commercial firm has over 1,000,000 units of factor VIII awaiting use.

"The second consideration which renders adequate provision of factor VIII both feasible and desirable is the fact that blood can now be collected in plastic containers, which makes it possible to use the red cells for patients who are anaemic and the plasma for patients who lack some plasma components. The blood donated in the United Kingdom is freely given by responsible citizens; the best use of this valuable resource clearly lies in the best use of all parts of the blood. With regard to the provision of factor VIII by the NHS, we can say with certainty that we have the skill, experience, and capacity in this country to provide factor VIII of very high quality in the amounts required.

"Why, then, is there still a chronic shortage of factor VIII in the clinics where the patients are

treated? The reason is that factor VIII is expensive, whether bought commercially or made by the NHS. Over the country as a whole, a supply of commercial human factor VIII sufficient adequately to supplement that made at present by the NHS would cost an annual £1-2 million. It is claimed that a sum of money of this order cannot be found from current allocations to the NHS without reducing money spent on other necessities. To make increased amounts of factor VIII in the NHS is also likely to be expensive since it would require substantial expenditure on organisation of blood supplies, on staff, apparatus, and buildings for fractionation. Set against this financial argument, it must be remembered that poorly treated haemophiliacs also cost a lot of money in their role as hospital inpatients and in receipt of social-security benefits. But of course the financial argument takes no account of the misery and anxiety attached to frequent painful episodes of bleeding and inability to hold a normal place in school and society. In the long run it will probably be found cheaper to pay for these patients' treatment rather than to pay for the inevitable consequences of undertreatment.

"When, as a director outcome of years of

research, lifesaving therapeutic materials suddenly become available to a population of patients previously chronically undertreated, there surely should be some means of assimilating this welcome advance, otherwise it is stupid to undertake the research in the first place. How this should be achieved is an administrative and political problem rather than a medical one. Perhaps there should be a special fund in the NHS set aside every year for the practical implementation of research discoveries. Perhaps an organisation should be set up to collect money on a charitable basis to supplement the NHS funds available for the introduction of new treatments. Whatever solutions there may be for problems of this sort in general, some immediate solution should be found for the ridiculous impasse of large available stocks of therapeutic materials locked up in stores because no-one will buy them and, on the other hand, patients in dire need of this same material."

That is Dr Biggs's letter to The Lancet on 29 June 1974. That letter, as I hinted, prompted a number of Parliamentary questions about Factor VIII supply and home treatment from Lewis Carter-Jones, the Labour MP for Eccles. These are the first

Parliamentary questions that the Inquiry legal team have been able to identify from Hansard on the topic of Factor VIII supply. They were addressed to the then Secretary of State, Barbara Castle, but they were answered by a minister, Dr Owen, on 9 July 1974.

If we could bring up on screen please, Paul, LDOW0000032, I believe this is a document that Dr Owen referred to in his evidence, certainly in his written evidence. I think in his oral evidence as well. This is a written Parliamentary answer. Dr Owen wrote this:

"The supply of Factor VIII produced within the National Health Service is at present insufficient for the optimum treatment of haemophilic patients. I hope that it will be possible to increase our supplies, and meanwhile product licences were issued last year to two firms to market imported Factor VIII in the United Kingdom. Adequate stocks, I understand, are held of this commercial material. It is not the Department's normal practice to make central purchases of health service supplies, but central contracts were arranged to facilitate the purchase of this material by Health Authorities.

"I recognise the desirability of enabling these patients to receive treatment at home but progress in

this direction is likely to depend largely on the extent to which production of Factor VIII within the National Health Service can be increased."

SIR BRIAN LANGSTAFF: Just as a matter of interest, it doesn't directly affect self-sufficiency but it may affect other points of accuracy, in her letter, Dr Biggs speaks of three commercial firms, I think, whereas Dr Owen speaks of two. When we had the presentation in respect of the pharmaceutical companies, I understood that Hemofil and Kryobulin were the two which were authorised to be distributed in 1973, licensed. What was the third?

MR HILL: From memory, and I stress it is from memory, I think it was Factorate, Armour's Factorate, which came on to the market third.

SIR BRIAN LANGSTAFF: Factorate. Because Profilate came later?

MR HILL: Yes, I will check on that.

SIR BRIAN LANGSTAFF: Because I thought the date of that was after '74 but, plainly, that's a mis-memory on my part.

MR HILL: Well, the licence, I think, was after '74 but it was provided off licence on a named-patient basis.

SIR BRIAN LANGSTAFF: Well, that would be so of any product.

MR HILL: Yes, yes. My recollection, I will check it over the break or overnight, is that Factorate is the third product that enters the market, and rapidly --

SIR BRIAN LANGSTAFF: But it may not be the third she was referring to, if she was talking about named-patient basis.

MR HILL: It may not be. But, again, my recollection from last autumn is that Factorate pretty quickly establishes a very strong market position, partly because it's cheaper. So it may well be that Factorate is the one that she is referring to.

Dr Owen, in his reply there doesn't seek to rebuff the central charges that Dr Biggs --

SIR BRIAN LANGSTAFF: My own note, actually, is that Armour Factorate, was licensed on 25 March 1976, which would be a couple of years after this, and Abbott's Profilate was earlier in '75, so I am just wondering if there was something which we've missed.

MR HILL: I can look back, sir. I will look at the letter and see if there is anything else that can tell us which product she is referring to.

SIR BRIAN LANGSTAFF: Thank you.

MR HILL: Dr Owen, in his response then, not seeking to deny the central charges that Dr Biggs had made in her letter, and seeming to accept that the question of how

great a number of concentrates can be provided, is tied heavily with how much domestic supply can be increased, and that is the question for the wider National Health Service, which is not inconsistent, in any way, with what Dr Biggs said in her letter: that it was essentially a question of politics and finances as to why there wasn't a greater domestic supply.

Sir, we can see from this increasing tensions and increasing public concern being raised about Factor VIII supplies to patients. In this atmosphere, the Regional Transfusion Directors met on 3 July 1974.

If we could go please, Paul, to NHBT0016495, we can see from the document that Dr Maycock was in the chair and the list of Regional Transfusion Directors, but also you can see Dr Waiter and Mr Jackson from the DHSS attending.

If we could turn, please, to page 4, we can see that the heading "Provision of Plasma for Anti-Haemophilic Globulin Concentrate and Other Plasma Fractions Including Specific Immunoglobulins", what is recorded in the minutes is this:

"The meeting considered Dr Maycock's letter of 12 June 1974 to Directors about the need to provide more plasma for fractionation and [the paper] which summarised information from Queensland, Western

Australia and New South Wales, Canada and Switzerland about the number of donations collected and the use of concentrated red cells."

Over to the next page:

"Dr Maycock said that as a result of a number of factors that were operating or had operated, the NBTS now found itself in a position of some difficulty and facing a shortage of certain preparations of human blood. These factors, not necessarily in the order of importance, were:

"(a) The need to provide antihaemophilic globulin concentrate equivalent to about 275,000 donations. This was the preferred preparation and was essential for home treatment which was being increasingly used. The department had been advised that the NBTS should reach the position of being able to supply this amount of concentrate by 1975, but this was clearly not possible.

"(b) An increase in demand throughout the world for albumin fractions."

I won't go through the rest of that paragraph, sir, but I do pause to note that we, of course, are focusing on Factor VIII here, but the debate about self-sufficiency is wider than that. Albumin forms a particularly important part of that debate.

SIR BRIAN LANGSTAFF: What the fractionators say in their report is that either a first step or a precursor to cold ethanol fractionation is the removal from the -- from what remains of Factor VIII and the proteins that tend to come with it, the proteins such as fibrinogen. It's later on in the same fractionation series that you get albumin. So, presumably -- but this may need a specific question -- my assumption had been and it may still be that there is no conflict between (a) and (b) in this sense: that if you get more plasma supplied to BPL, they can make more, or get more Factor VIII out of it, but they also have the supernatant which remains in the process from which you get more albumin. So the need to supply more plasma is essential for both, and the same plasma provides both --

MR HILL: That is my understanding as well.

SIR BRIAN LANGSTAFF: So this is not setting up something which is a contradiction.

MR HILL: No.

SIR BRIAN LANGSTAFF: It's basically saying we need more plasma because it will serve these various different needs.

MR HILL: That's right, and we will see later under a group called the Working Party on Trends, they're

trying to work out how much plasma is needed to be fractionated. The measure that they take is the amount needed for albumin, and they say, "If we get this amount for albumin, then it's going to be enough for Factor VIII as well." So, as you say, it's not a contradistinction between the two. It's just -- (overspeaking) -- you need to consider albumin as well in the wider picture, is what they're saying.

SIR BRIAN LANGSTAFF: If, however, one were to use the plasma, I suppose, for cryoprecipitate production, you wouldn't have it necessarily available for albumin.

MR HILL: That's right. And, indeed, for other blood components as well. And you may remember Dr Walford, when she was discussing the arguments about reverting to cryoprecipitate, drew attention to Dr Lane's statement, something that we will look at in due course, where he said: if you are going to revert to cryo, you need to think of a way to make sure that we at BPL have sufficient plasma supply in order to be able to produce albumin ,Factor IX, Factor XIII, other blood components which are not going to be covered by cryoprecipitate.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Returning to the document at point (c), and this is the third of Dr Maycock's factors that are causing

difficulties for the NBTS, he says, and I quote:

"The need to depend, at least temporarily, upon supplies of AHG concentrate and possibly PPF [that's protein plasma fraction] from commercial sources posed a potential threat to the unpaid voluntary donor system: (i) a permanent demand for commercial preparations might arise; (ii) it had been suggested that NBTS should provide plasma to commercial firms for the preparation of coagulation factor concentrates which are needed by clinicians responsible for treating disorders of coagulation."

I pause there, sir, to note that this is one of the first references that we have been able to find about the argument being raised that an inability to provide domestic Factor VIII and albumin may threaten the very existence of the voluntary donor system in the UK.

That is an argument that will be developed in the papers that we'll go on to look at:

"(d) Dr Maycock reported that two meetings between representatives of the DHSS and SHHD [Scottish Home & Health Department] had recently been held at the request of the SHHD ..."

I skip a few sentences, and it says:

"As a result of these meetings, the following

principles have been reaffirmed:

"(1) The system of unpaid blood donation must be preserved in the UK.

"(2) In order to preserve the system, the Blood Transfusion Service services in UK must be self-supportive."

Going on to the next page, and this is a slightly different point, Dr Maycock says:

"There should be agreed UK targets for provision of preparation of human blood."

There is then a discussion of Scottish targets for PPF and a discussion about why those targets were higher than those in England and Wales.

Picking it back up again with the paragraph "In the present circumstances", the minutes record:

"In the present circumstances, increasing the number of donations used as concentrated red cells seem to be the most practicable way of improving the amount of plasma for fractionation. In the Glasgow region, 40% of donations were used as concentrated cells.

"The present position in RTCs is ..."

And then a table is set out. I won't go through all of those figures, but we can see that, in comparison to Glasgow, 40 per cent of plasma going --

coming from -- sorry, 40 per cent of donations being split between plasma and red cells. In comparison to that, in England and Wales, the figures range from nil in Tooting to -- the highest figure is 33 per cent in Oxford. We can see just to pick a few others, Cambridge is well below Oxford at 10 per cent; Leeds, 20 per cent; Sheffield, 6 to 7 per cent; Bristol, 25 per cent; Cardiff, 20 per cent.

In the right-hand side of that table, we can see the needs listed in order to increase the proportion of red cell concentrates, and we can see that those include staff. It says, "Plastic equipment" in respect of Newcastle. And that I take to be a reference to the fact that some of these centres were still using glass bottles to collect blood donations which weren't conducive to separation into red cell concentrates. You needed the plastic bags to do that.

Other references are to space, to the need for a centrifuge. Again, references to equipment and staff, and also a reference to the need for a haematologist and three technical staff.

So those are the reasons given by the RTCs as to why they can't produce more in the form of red cell concentrate at that time. It's a point that we will

come back to when we look how Dr Owen's money was spent.

If we move then to the next page, page 7, the paragraph underneath number 6:

"The meeting concluded that the immediate aim should be to raise the use of concentrated red cells to 30 to 35 per cent but that in order to reach this level, additional capital and revenue expenditure would be necessary. The chairman asked RTDs to do everything they could within the limitations of their present budgets."

The key points that we take from this document are as follows: firstly, there is a reference to the donation target of 275,000 donations, and we have seen before lunch where that figure comes from. An acceptance that that would not be reached by 1975. The introduction of the new argument about the risk to the domestic voluntary donor system. We will see that is to prove an influential argument with Dr Owen. The emphasis that is being placed on red cell concentrates as a way of increasing plasma supply. And those final words from the minutes that it is for the Regional Transfusion Directors to try to do everything that they can within their budgets to increase the supply of red cell concentrates. So no

central funding. This is going to have to come from the regions.

That was a meeting of 3 July. The directors met again, the Regional Transfusion Directors, on 9 October 1974. I'm not going to take you to those minutes, but as is set out in the written presentation at paragraph [85], there is a sense from them of a very tense meeting and of a situation coming to a head. The meeting reported that little progress had been made on increasing red cell concentrates, and that, and I quote:

"Progress was likely to continue to be slow until money was provided by one means or another."

Mr Jackson from the DHSS was recorded as saying, and I quote:

"The department was fully aware of the financial difficulties of RHAs and centres regarding Factor VIII concentrate."

A tense meeting and little progress being made, as of October 1974.

Also in the same month, the Expert Group on the Treatment of Haemophilia met again. Reference to that is made at paragraph [87] of the written presentation. I won't take you to those documents.

The position that was reached by October 1974 is

that we are now some 19 months after the initial meeting of the Expert Group on the Treatment of Haemophilia. The original goal of using 250,000 donations, later 275,000 donations, annually for Factor VIII, fractionation, had not been met, and it was recognised that it was not going to be met in 1975.

There were also concerns over the domestic production of albumin. The more ambitious proposals put forward by Dr Biggs and others for between 500,000 and 750,000 donations being used for fractionation were, of course, still more distant.

The central call-off contract had been arranged, but Regional Health Authorities had been slow to increase their expenditure on commercial concentrates.

There had also been an unwillingness or an inability to prioritise spending to increase plasma supply to BPL.

Tensions had grown between the DHSS and the regions about who should meet the additional costs, and between clinicians and the administrators about the shortfall of concentrates.

Concerns were now openly being expressed about the threat to the voluntary donor system in the UK. And running through all of this was an emphasis on the

lack of available funding.

And that, sir, is the context in which the announcement made by Dr Owen of £500,000 of spending took place. And it's to that that we will turn.

The origins of that policy announcement lie in a letter that was ultimately sent by Mr Gidden of the DHSS, and we saw his name this morning, to regional administrative officers, where there's a string of correspondence within the DHSS when the letter is drafted and redrafted, and thoughts are given on it.

I'm going to take you to the letter now. This is what results from all of these discussions. It is at CBLA0000239. I'm going to read all of this letter, sir, because this, ultimately, is the document that Dr Owen approves, which amounts to the approval for the spending of £500,000 of central funds from the DHSS. The letter, addressed to "Regional Administrators" and dated 24 December 1974, says this:

"Blood Products Production

"1. The National Blood Transfusion Service is currently unable to meet the demands of clinicians for certain operations of human blood. There is an immediate need to provide more AHG concentrate (equivalent to about 275,000 blood donations annually). AHG concentrate is now the preferred

therapeutic agent for the treat of haemophilia and considerable benefit could be brought to these patients if adequate supplies could be made available for their treatment. There is also an increasing demand for albumin fractions, mainly plasma protein fraction (PPF) which is replacing dried plasma and plasma substitutes. Over the next few years the need for PPF may rise to 200,000 bottles per annum.

"2. At present, part of the demand for these blood products is being met by expensive imported material which is now marketed in this country, and as the demand increases commercial firms may consider it worth their while to establish panels of paid donors in this country in order to obtain their supplies of human blood. Such a development would constitute a most serious threat to the voluntary donor system upon which the NBTS is founded. The Department therefore regards it as of the greatest importance, quite apart from the question of cost, that NHS should become self-sufficient as soon as practicable in the production of PPF and other blood products (the cost of purchasing AHG and PPF from commercial firms on the scale envisaged in paragraph 1 would be around £6 million a year).

"3. The current output from the Blood Products

Laboratory, Elstree is limited by the amount of plasma supplied by Regional Transfusion Centres (RTCs). This amount in turn depends upon (a) the number of blood collected and the extent to which clinicians are prepared to use blood in the form of concentrated red cells, and (b) the facilities available at RTCs for separating the whole blood into concentrated red cells and plasma. At present, less than 10% of blood donations in England and Wales are used in the form of concentrated red cells compared with 30-40% in Scotland. If this percentage could be raised to 40% in England and Wales it would be possible for the NHS to meet the demand for AHG concentrate and to increase the production of PPF from the current figure of 78,000 bottles to 136,000 bottles ... To reach the medium target of 200,000 bottles of PPF per annum mentioned in paragraph 1 would also require an increase of 400,000 blood donations from the present figure of 1.6 million per annum. It is intended that the production of blood products in Great Britain should be co-ordinated and that some of the increased output of plasma produced in RTCs in England and Wales should, by arrangement with the Scottish Home and Health Department, be processed at the Plasma Fractionation Centre, Liberton, Edinburgh.

"4. To achieve a 40% use of concentrated red cells will require the full co-operation of clinicians. Clearly no steps can be taken towards this objective unless parallel action is taken to ensure that RTCs have sufficient facilities to separate more plasma from whole blood and thus to meet the increased usage of concentrated red cells. For this purpose the cost of providing the necessary facilities such as additional equipment and staff might be up to £0.5 million in England and Wales, part of it recurring (the cost of collecting 400,000 additional donations annually might be of the order to a further £1.0 to £1.5 million). The extent to which the capacity of RTCs to produce plasma can be increased will vary from Centre to Centre.

"5. It would clearly be considerably cheaper to produce these blood products within the NHS than to buy them from commercial sources.

"6. If the normal procedure for financing of health services were to be followed, authorities would need to agree, collectively, to accord blood transfusion priority for additional resources over a period of several years, within a co-ordinated programme of expansion. However, additional expenditure is bound to be some what disproportionate

as between Regions if realistic targets are adopted with the aim of making NHS production sufficient to meet clinical needs. It has therefore been decided that since the Department would in any case have to co-ordinate a programme for the increased production of blood products, earmarked finance of up to £0.5 millions should exceptionally be provided for this purpose. The Department proposes to invite estimates of requirements in RTCs for the increased production of plasma, with the primary aim of making the NHS self-sufficient in AHG concentrate in 2 to 3 years.

"7. Additional copies of this letter are enclosed for the Regional Medical Office, the Regional Treasurer, and the Regional Transfusion Director."

It is signed by Mr Gidden.

The letter and the internal DHSS correspondence that was circulated during the drafting of the letter indicate that this programme is something of a hybrid between national and regional funding. The decision is made, and it is stressed to be an exceptional decision, to provide £500,000 of central DHSS funding in order to increase the production of blood products, with the aim of self-sufficiency in two to three years.

The terms of the letter, the reference in the

letter to the immediate need to achieve 275,000 donations for concentrate, refer back to the immediate target, as set out by the MRC, rather than the longer term -- medium and longer term targets by the MRC, which were of 500,000 to 750,000 donations per year.

The reference is to a sum of £500,000 coming from Central Government. In order to expand plasma production further, there would be a need for continuing funding, and the hope within the DHSS was that the £500,000 would meet initial costs and that the Regional Health Authorities would then be persuaded to invest further, in order to avoid the costs for more expensive commercial concentrate in the future.

To give a couple of pieces of correspondence which evidence that, in June 1976, the DHSS official then leading the initiative, Timothy Dutton, described the provision of central funds, the £500,000 in the following terms -- for reference, I won't take you to it, but the reference is DHSC0103283_102. Mr Dutton said that this was, and I quote:

"A pump priming operation to start the AHG concentrate plasma production programme. Thereafter, it was expected that regions would continue the programme from within their normal allocations, which

include an element for the programme, revised in the usual way to take account of cost increases."

Back in 1974 Dr Waiter described the rationale behind the £500,000 proposal in the following terms, and I quote:

"It is an initial injection of money by whatever mechanism is now available to ensure such a programme would get under way. At present, it shows little likelihood of so doing."

The reference for that DHSC0003616_038. So both Dr Waiter and Mr Dutton see this as, essentially, a way of kickstarting production or increased production of plasma for fractionation. The exceptionality of this central funding, which Mr Gidden was at pains to stress in the letter to the Regional Health Authorities, was also something that was referred to by Dr Maycock in 1976 in a document about -- in which he provides comments on a paper about decision making structures in the NBTS. Dr Maycock says this:

"While it is true that the Department [that's the DHSS] can, if it wishes, provide additional money for Regional Health Authorities and direct how it should be used, I think it is important that the reader of a paper understand that the Department has

for some 20 years rarely, if ever, used this ability, although there would have been occasions when to have done so would have enabled simultaneous and uniform advances to be made. To the best of my knowledge, the ability has been used only for AHG and then only after prolonged and vigorous prodding."

That's Dr Maycock looking back in 1976. The reference is DHSC0003738_047.

The reference to "prolonged and vigorous prodding" is an interesting one and we have seen in those RTD, Regional Transfusion Directors, meeting minutes the tensions that were growing up in the second part of 1974, that the policy is announced only towards the end of that year when those tensions have built up.

The letter from Gidden goes out on 24 September 1974 and it does so after Dr Owen becomes involved in the debate and gives his authority to this policy. The earliest reference we can find to his involvement is in a document, if we could go to this please, Paul, DHSC0100005_189.

This is a minute to Mr Alexander, who I understand to have been Dr Owen's private secretary, and it comes from Mr Gidden. It's dated 9 December 1974. It says at paragraph 1:

"Since Dr Raison and I discussed with the Minister of State last week the question of supplies of AHG concentrate, we have established within the office that earmarked central finance to the extent of £0.25 [million] capital and £0.25 [million] revenue can be made available to Regional Authorities to increase NHS production of this material. We have asked to draw attention to the fact that a decision to make this special allocation of resources to blood products production inevitably means that less money overall will be available for other high priority Health Authority services eg mentally ill, mentally handicapped, family planning, and certain centrally sponsored projects, such as schemes to reduce waiting times. But there is broad agreement that such an allocation would be justifiable."

The minute then goes on to suggest a form of words that could be used in answer to questions which have been raised by several MPs on this point, which shows the political pressure that was building for a policy development on this front as well. If we could go over to paragraph 3, please:

"It will be necessary to inform Regional Authorities of this decision, and I attach for information a rather fuller draft of a Dear Sir letter

which I suggest should issue at about the same time as the Minister of State's letter to MPs."

I pause there to note that that was a draft of the letter that was eventually sent out by Mr Gidden:

"During our discussion last week mention was made of a possible arranged PQ (which could be based on the last three paragraphs of the draft above). I am somewhat doubtful about this since the main pressure is for additional money to buy commercial product now. However, you will no doubt take the Minister of State's views on this."

Signed by Mr Gidden, 9 December 1974, so the reference to the previous week means that Dr Owen was involved in discussing this policy in early December 1974.

Also perhaps of note, the political pressures to which Mr Gidden is alluding are to buy commercial concentrates straight away, rather than to take a longer term development of domestic production.

The response from Dr Owen comes in a minute from Mr Alexander to Mr Gidden on 11 December 1974. This is DHSC0100005_191. Mr Alexander wrote this, and I quote:

"Dr Owen has seen your minute of 9 December 1974 and has agreed the submission. He would like one

change made to the suggested new standard reply for MPs. In place of the second paragraph you propose, he would like inserted suitably amended versions of the first and second paragraphs of the draft letter to regional administrators which you also submitted for approval. He has commented that, and I quote, 'It is time MPs knew the full arguments.' He would like to know if there is any objection to this.

"With reference to paragraph 4 of your minute, Dr Owen has commented, 'I agree that we should not court publicity'."

Picking up the last point first that is about whether or not there should be a planted Parliamentary question to make the announcement, Dr Owen says no.

The reference to the fuller draft, including the second paragraph of the letters to regional administrators, that is a reference to the risk to the voluntary donor system which Dr Owen suggests should be put in the replies to MPs as well as being sent to the regional administrators.

In response to that, Dr Gidden advises Dr Owen not to do that. He says that the reason for that advice is to avoid controversy and because he was aware that there were some advocates within the UK, he was suggesting that the voluntary donor system should

be perhaps replaced or at least supplemented with paid donors. And Mr Gidden -- the tenor of Mr Gidden's advice is "Let's not go there. Let's not raise this issue."

Dr Owen accepts that advice, and we can see his response at LDOW0000344, please, Paul. This is 17 December 1974 from Mr Alexander sent to Mr Brandes. In it, it says:

"Dr Owen has seen Mr Gidden's minute of 13 December 1974 [that's the one I've just summarised] about the standard draft letter to MPs on the treatment of haemophilia. He has said that he will accept this advice. Dr Owen has gone on to comment more widely on related issues."

And this is a quotation from Lord Owen:

"I would like, however, the department to consider a legislative ban on paid donor panels for blood and semen and, indeed, any human biological material."

And discusses a way in which such a ban could be put into legislation:

"The philosophy and spirit of Richard Titmuss's book *The Gift Relationship* is one to which I attach immense importance. The concept of altruism is one which Government should not be neutral over but

actively promote. I will never be party to the National Blood Transfusion Service not being available to all."

Mr Alexander goes on to ask for a note on the points raised by Dr Owen.

We know, sir, from Dr Owen's evidence that he had reviewed *The Gift Relationship* back in 1971, and Dr Owen stressed in his evidence the importance that he attached to the idea of a voluntary donor system in the United Kingdom.

Those were the internal discussions about the policy. As we have seen, they led to the letter being sent out to the regional administrators on 24 December 1974.

In terms of public announcements, the first that we have been able to find is on 22 January 1975, and it is a written response to a Parliamentary question. If we could go, please, Paul, to DHSC0000274. Towards the bottom right of that page under the heading "Haemophilia", the question has come from Mr George Cunningham asking the Secretary of State for Social Services:

"... what deficiencies exist in the supply of Factor VIII (cryoprecipitate) for the treatment of haemophilia; and what action she proposes to take to

deal with the problem."

That is a reference to Barbara Castle. Dr Owen provides the answer.

He wrote:

"The amount of Factor VIII materials, including cryoprecipitate, produced within the National Health Service is not sufficient and, in particular, there is an immediate need to provide more human antihaemophilic globulin concentrate -- AHG concentrate -- which is now the preferred treatment for haemophilic patients. There is also an increasing demand for certain other blood fractions.

"At present, part of the demand for AHG concentrate is being met by imported material, but this is very expensive and, for reasons which I well understand, Health Authorities feel they cannot afford to buy as much as they would wish to, given the various claims on their resources.

"I believe it is vitally important that the National Health Service should become self-sufficient as soon as practicable in the production of Factor VIII, including AHG concentrate. This will stop us being dependent on imports and make the best-known treatment more readily available to people suffering from haemophilia. I have, therefore,

authorised the allocation of special finance to boost our own production with the objective of becoming self-sufficient over the next few years."

That is, so far as we can tell, the first announcement of the policy.

Dr Owen was asked about Factor VIII again in oral questions on 25 February 1975, and he was pushed to commit to central purchasing of what was described as "this drug" and to home treatment. And if we could go, please, to HSOC0015202, we can see how he responded to that. He says first:

"I have authorised the allocation of special finance of up to £500,000, about half of which would be recurring, to increase the existing production of Factor VIII, especially in the form of antihaemophilic globulin concentrate, AHG, within the National Health Service. The first effects of this will, I hope, be felt by the end of the year."

Mr Watkinson, who was asking the questions, welcomes the reply, and then goes on to talk about the need for central purchasing. He also asks if Dr Owen will accept that this is far and away the best treatment for haemophilia.

Dr Owen responds by saying this, and I quote:

"I confirm that in most cases I think it is the

most desirable form of treatment, but one cannot avoid the fact that this is one of the many costly treatments which are competing on priorities. The present system whereby a doctor can persuade his local area health authority that his patient needs this form of treatment most is the best way of proceeding, and not by central allocation. If we were to go to all-commercial purchase of this factor, it would cost an additional £1.5 million to £2 million annually."

If we could go back to the full screen, Paul. Thank you.

A further question is asked by Mr Martin, with particular reference to the under-treatment of children, and he asks whether or not Dr Owen can go a stage further and give more of a lead to Regional Health Authorities. Dr Owen replies by saying this, and I quote:

"They are aware of our concern and have had ample demonstration of it by the fact that we are prepared to divert scarce resources to make the National Health Service self-sufficient, but I concede that it will take two or three years before we are at full production. During that time, I am sure that they will weigh very carefully the individual cases and will be sympathetic to the sort of hardship which

can arise."

Mr Shaw asks a further question where he compares the position in the UK to that in Israel, and Dr Owen says, and I quote:

"I know my [honourable] Friend's concern, but honourable Members must face the fact that with limited resources we have to choose, and these are very difficult choices and priorities. When confronted with an ill child, everyone wants to get the best that is available, but there are many other aspects of childcare which also have priority and we are not always able to meet all the demands."

That is 25 February 1975. I stress again, those are oral answers to questions, whereas the previous section of Hansard was a written answer.

On the following day, 26 February 1975, Dr Owen published some further written answers to Parliamentary questions. I won't take you to these, but they included -- the questions included concerns over the provision of concentrates, and about domestic production. Dr Owen repeated his previous comments on the £500,000 which had been made available, and I quote:

"... to increase the existing production of Factor VIII within the National Health Service."

He noted the expense of the commercial products and the resultant reluctance of Regional Health Authorities to buy them. He then stated, and I quote:

"I believe that it is vitally important that the National Health Service should become self-sufficient as soon as practicable in the production of Factor VIII, including AHG concentrate. This will stop our being dependent on imports and make the best-known treatment more readily available to people suffering from haemophilia."

Those are the answers that he gave in January and February 1975. There is no reference in those answers or in Mr Gidden's letter to the regional administrators to any perceived safety advantage of domestically produced concentrates when compared to commercial concentrates.

I'm about to move on to how that £500,000 was spent and what was achieved by it, and what was said about it.

I wonder if it would now be a good time to have a break and come back to that.

SIR BRIAN LANGSTAFF: Yes, well we will take a break for 25 minutes and come back at 3.40.

3.40.

(3.16 pm)

(A short break)

(3.40 pm)

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Sir, before turning to how the £500,000 was spent, just a couple of points that we have checked over the break.

The first refers to the point that you raised from Dr Biggs' letter to The Lancet, where she said that three commercial companies are now licensed to sell good quality human Factor VIII in this country, and that is from a letter dated 29 June 1974. I'm afraid we haven't got to the bottom of this because Hemofil and Kryobulin were licensed in 1973, as we know. The third licence, as you said, sir, is Profilate, the product from Abbott, which was dated May 1975, and then Koate and Factorate follow in 1976. Now, we know from the previous presentations that several of these products were available on a named-patient basis at an earlier stage. We also know from a document that was referred to in the earlier presentations that there are promotional materials from Profilate in the Oxford haemophilia centre archive from 1975. The reference for that is BPLL0008067. And we can a complements sheet signed by Dr Bidwell there, and also evidence of Dr Rizza having

seen it. Obviously, Dr Biggs worked in the same centre, so it is possible that she saw these promotional materials. We don't know if those were promotional materials that were provided to the UK market, or whether or not they were materials that were obtained from the United States by somebody connected to these clinicians and brought back to the UK.

But in any event, the licence is not granted before Dr Biggs' letter of June 1974, so we are not sure why she refers to three companies being licensed. Perhaps she is confusing a product which is provided on a named-patient basis with the licensed product, or perhaps we have missed something. But we don't know.

SIR BRIAN LANGSTAFF: If you keep on looking, I'd be grateful. It may simply be that she has seen a change of name from the producer which isn't a real change of name. We know that happened. It may be something like Speywood which she has in mind. I don't know. But if we can work it out, we will. Otherwise, we'll have to rely upon what we know from other materials.

MR HILL: Yes, sir.

SIR BRIAN LANGSTAFF: And it's a shame she's not available to us to explain.

MR HILL: Yes. What I would say is from the documents

that we looked at in November, when Dr Walford comes in the early '80s to try to tot up who was providing which products, those are the products that she refers to. There is no other licensed product within the United Kingdom that she is referring to at that time.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: I'm afraid I can't assist more than that at the moment.

SIR BRIAN LANGSTAFF: There will be perhaps some indication given if we looked at the UKHCDO returns and saw what was on their list, if they had a list at that stage, for the different sorts of concentrates because they did have pretty early on a list, didn't they?

MR HILL: I believe so. There is ongoing work trying to put together all of the returns and interrogate them in order to provide some useful data for you. We will feed this question into that.

SIR BRIAN LANGSTAFF: It doesn't -- this particular little point, it's intriguing, but it doesn't actually affect your presentation on self-sufficiency does it, really?

MR HILL: No, it doesn't. No.

A second point concerns Hansard references. The Inquiry legal team, as I said, had identified the question that was posed of Dr Owen following Dr Biggs'

letter as the first Hansard extract that we had found that referred expressly to Factor VIII. We are grateful to the Collins team who have pointed out a question and answer in Hansard from 15 June 1966 in which Mr Pavitt, MP, asked the Minister for Health what information he has of advances recently made in the treatment of haemophilia and if he will make a statement. And the answer given by Mr Robinson is, and I quote it in full:

"Concentrates of anti-haemophiliac factor have been available for some years in this country on a limited scale for the treatment of special cases, and arrangements are now being made for preparation on a wider scale. The method of preparation recently reported from the United States is under investigation in several centres here."

That is the answer that was given on 15 June 1966.

SIR BRIAN LANGSTAFF: Yes. Again, it's intriguing, isn't it, because although I think that Kekwick and Wolf developed a form of AHF concentrated in 1959, maybe '57 but certainly in the mid-'50s, mid- to late '50s, I don't think there was any great production of it for a while. And the reference to developments in the United States may refer to the method which Dr Pool

had found of using the cryoprecipitate, which she already knew existed, but using it for therapeutic purposes by being able to have a system of closed bags and isolate it without losing its efficiency.

MR HILL: It could do, sir. I'm afraid I cannot go any further beyond that Hansard answer.

SIR BRIAN LANGSTAFF: Yes, but at least there is an answer, and there is something about that, so I'm grateful to Collins for having pointed that out.

MR HILL: Turning, then, to the £500,000. Appendix 3 to the main presentation is a detailed analysis prepared by the Inquiry legal team on how that money was spent. And it is a centre-by-centre analysis at points.

I'm not going to take you to all of the documents in that, or indeed take you to the substantive material that's contained there. It's there for people to read both on the website and on Relativity should they wish to do so.

What the appendix shows, if I may summarise it, is that the announcement of the £500,000 was followed by a dialogue between the DHSS and the regional centres. The regions were given targets by the DHSS for how many donations were expected of them, and they in turn provided indications to the DHSS about the amount of money that was going to be required for them

to be able to make those donations.

The discussions took into account local factors, and as we saw in the documents before the break, there was inevitably a degree of variation as to how much would have to be spent on different centres in order to increase production.

There were extensive negotiations that followed, more extensive with some regions than with others. The target of donations rose from 275,000 to around 340,000 per annum, which was about a 20 per cent increase. The reasons for that rise and the different figures are contained in the appendix. I don't think that I need to explain those now, but it's to do with different centres explaining how much they could reasonably expect to produce.

The analysis of your team, which is supported by a spreadsheet as well, which is referred to in the appendix, is that just over £500,000 of special allocation funds were spent in the year 1975 to 1976. That is if one includes the announcement on BPL. And a further 433,000 was spent in the financial year 1976 to 1977.

The money was spent on a wide variety of items. As I mentioned earlier, some of the centres were still collecting blood in glass bottles at that stage, and

so some of the money was used to transfer to plastic bags. Equipment such as freezers and centrifuges were purchased, as was laboratory kit. Several centres required money to be spent on building works, often referred to as "accommodation" within the budgeting documents. Others incurred additional staff costs.

The position of Wales in this process isn't entirely clear. There was some prior consultation between the DHSS and the Welsh Office before the announcement of the £500,000 funding, but it was for the Welsh Office and not the DHSS to make the necessary funds available to the Cardiff Transfusion Centre. That said, there was an awareness that Cardiff was, and I quote one document which was written by Mr Gidden:

"... unlikely to be able to do much in the way of increasing its output of plasma."

Mr Gidden didn't explain the reason why that was so.

The first set of regional targets that were sent out by the DHSS did contain a target for the Welsh Regional Transfusion Centre, but later documents don't. And there were discussions between the Welsh Office and the DHSS about what was being done in respect of increasing plasma production.

The results of this programme were that the target of about 340,000 additional donations for fractionation was achieved by mid-1977. That's about two and a half years after the policy was announced.

BPL also received sums, and those are set out in the appendix 3. Those sums seem to have been part of BPL's annual budget, rather than part of the special funding, and they were much smaller than the overall special funding.

Dr Lane, in his fifth draft proof of evidence about which you'll hear much more later in the week, calculated that BPL received £58,000, and he says this was, and I quote:

"... for the purchase of additional equipment."

That sum allowed for a significant increase in production at BPL on PFL. The figures, which are set out in paragraph [112] of the written presentation, are that in 1973, production was estimated at 2.7 million international units per year. In 1975, that had dropped to 2.19 million international units per year. But it rose by 1976 to 6.1 million international units per year, and in 1977, it's up to 11.5 million international units.

We will go into those figures and the sources for those figures and their reliability a little more

probably on Wednesday or on Thursday this week. But the short point to take from it is that BPL's production rose substantially in this period.

The documents demonstrate that Dr Owen asked for and received various updates on the progress of the scheme, that he was engaged in the policy and keen to encourage more rapid progress where that was possible. The documents also show that officials were aware of the importance that ministers, and in particular Dr Owen, attached to this scheme. I won't go through the references, but they're at paragraph [114] of the written presentation.

One document that I will take you to is at DHSC0001774, please, Paul.

This was a minute sent by Mr Jackson on 11 July 1975 and it is sent to Mr Lillywhite, who I understand to have been Dr Owen's private secretary. It is a minute that is sent in response to a Parliamentary answer, which has been given to a question that was posed on 22 April. It is not a question I took you to earlier, but Dr Owen, on that occasion, said that:

"I hope that the NHS can become self-sufficient in the production of all forms of Factor VIII within two or three years."

You will see from the opening paragraph of this minute that Dr Owen commented on that.

"Once again we are at a 2-3 year time-scale. I have asked if we can improve on this. Can I have a note?"

So that is Dr Owen chasing civil servants for an update about this. This what Mr Jackson provides in response, if we pick it up from paragraph 2:

"Since then [which is since the Parliamentary question], as a result of our discussions with Regions, we have given them targets which will produce plasma from 337,000 blood donations. This is some 20% more than the total of 275,000 recommended by the Expert Group on Haemophilia but that figure must be regarded as the minimum."

"Minimum" is underlined.

"All Regions, except two, have now indicated when they expect to achieve their share of the target of 337,000."

There is a summary of the table there showing that by June 1977, 87 per cent of the target is expected to have been achieved and the two other regions make up the remaining 13 per cent.

Paragraph 4, Mr Jackson says:

"The main reason why the programme cannot be

completed earlier is that in four Regions extensive alterations have to be made to the Transfusion Centres before they are in a position to provide more plasma. In one case the work will take six months, in two cases one year, and in the fourth 21 months."

Paragraph 5:

"We are taking steps to clarify the position of the two Regions whose ability to contribute to the programme is at present uncertain."

Then at paragraph 6:

"It is difficult to be precise in estimating a date for achieving self-sufficiency, not least because not all are agreed as to what constitutes self-sufficiency; some Haemophilia Centre Directors envisage prophylactic treatment whereas the Department's programme is based upon home treatment of those patients for whom treatment at home can be recommended. It remains to be seen whether RTDs will be successful in persuading clinicians to accept a steadily increasing proportion of blood in the form of concentrated red cells; this may be a possible limiting factor. AHG concentrate has not previously been prepared in the NHS on the scale envisaged and this in itself will almost certainly give rise to some problems.

"However, accepting these qualifications, the figures in paragraph 3 suggest we can improve on the previous estimate of achieving self-sufficiency within two to three years. We can now say that we expect to be self-sufficient within two years or, alternatively, that within about a year we will be able to meet some 2/3rds of present requirements and become self-sufficient in 1977."

That was sent to Dr Maycock and to Dr Waiter, and we know that it was seen by Dr Owen because on the first page, the top right-hand corner --

Sorry, the top right-hand corner of the first page, please, Paul. Could you just scan out on the first page so we have the whole thing. It doesn't seem to be coming up on my screen at least. Ah, perfect, thank you.

We can see some handwriting in the top right-hand corner which reads:

"This is excellent and I recognise that everyone is doing everything possible. I believe we should keep up the pressure. Can I be kept informed on the centrifuges and also the two regions? Why are there difficulties and what can be done? I would not easily accept that they should not contribute."

That is handwriting from Dr Owen.

We can see within that minute, Mr Jackson discussing the different definitions of self-sufficiency, before, at the end of that minute, saying that it can be stated that "we expect to be self-sufficient within two years", which is from July 1975.

Lord Owen returns to Parliament in July 1975, 7 July 1975, where he described the Government's policy as being, and I quote:

"... to make the NHS self-sufficient in the production of Factor VIII as soon as practicable."

In a letter to Andrew Bennett MP, dated 4 December 1975, he used similar terminology, and I quote:

"I regard it as most important that the National Health Service should become self-sufficient as soon as practicable in the production of AHG concentrate."

He went on to explain that funding had been provided by the DHSS and said, and I quote:

"I hope that in about a year we will be able to meet some two thirds of the present requirements for AHG concentrate and that within two years we may be able to reach the target we have set ourselves."

The references for those documents are at paragraph [116] of the written presentation.

On 29 April 1976, Dr Owen addressed the World Federation of Haemophilia Congress. This is a document that you have been taken to before, during Lord Owen's evidence. It is LDOW0000045. This is the text of Lord Owen's speech to the Closing Ceremony of the World Federation of Haemophilia, which was held at the DHSS building in Elephant & Castle.

I won't read the whole thing but, if we pick it up from the second paragraph, Dr Owen says this:

"This of course is the World Federation of Haemophilia and I would like to state quite clearly to you how strongly I believe all the nations of the World should support the objectives and policies of the World Health Organisation and none more so than in the policy of the WHO that each country should be able to supply its own blood and blood products to meet clinical needs. The previous speaker, Dr Rosemary Biggs, told you quite bluntly the facts which are that the NHS was not at present able to provide sufficient Factor VIII concentrate needed by haemophiliacs in this country for the management of bleeding, and that Health Authorities are having to buy expensive imported products. I think we ought to have made ourselves self sufficient rather earlier than we will now be able to do so. But we have made

the decision in principle to become self sufficient. We have made a special allocation of half a million pounds last year and substantial progress I am glad to say is now being made in building up production capacity in our country, and self sufficiency of home produced Factor VIII we expect to be reached around the middle of 1977. There is still some argument about the overall level of supply that we should be aiming at and I am not certain that we have necessarily got it right at the moment. It might well be that as it becomes more readily available the products will be used more effectively, but I cannot stress enough to you, as an International Congress, that I think all nations, particularly the richer nations of the World, ought to be able to be self sufficient and not to drain the supplies which are often much needed in other countries in the World."

You will see there, sir, that there is a degree of nuance in what Dr Owen is saying about the debate about the level that should be aimed at. If we go to the press release which accompanied that speech, which is at LDOW0000044, we can see in the third paragraph, I quote:

"Following a special allocation of £500,000 last year, substantial progress was now being made in

building up production capacity in the NHS, and self-sufficiency in home produced Factor VIII was expected to be reached in mid-1977."

That is the press release and that doesn't have a reference to the discussion about the overall supply.

Dr Owen left the Department of Health in 1976 and so he wasn't in post when the targets set by the DHSS were achieved in 1977. The following year, Max Madden MP tabled a series of written questions on self-sufficiency which were answered by the then Secretary of State Mr Roland Moyle. If we could go to those, please, Paul it's DHSC0000291.

I will read through the entirety of this exchange. These are written questions and written answers:

"**Mr Madden** asked the Secretary of State for Social Services, in view of ministerial statements, made in 1976, indicating that Great Britain would be self-sufficient in Factor VIII, used in the treatment of haemophilia, by the middle of 1977 if self-sufficiency has been achieved; and, if it has not, if he will explain the reasons."

I pause there, sir, just to say that the reference to ministerial statements made in 1976 might

be a reference to the press release and what Dr Owen said at the World Federation of Haemophilia. The Inquiry legal team haven't been able to find references in Parliament from 1976.

Mr Moyle's answer is this:

"The production target of Factor VIII set for June 1977 was attained; however, new opportunities in the treatment of haemophilia and associated disabilities have been developed which have made further clinical demands for Factor VIII.

"**Mr Madden** asked the Secretary of State for Social Services how much of the authorised amount referred to in ministerial statements, made in February 1975, indicating ministerial authorisation for the allocation of up to £500,000 to increase the existing production of Factor VIII, especially in the form of a new concentrate, within the National Health Service had been allocated.

"**Mr Moyle:** The whole sum was used to increase Factor VIII concentrate production within the National Health Service.

"**Mr Madden** asked the Secretary of State for Social Services how many units of Factor VIII concentrate are being produced by each of the fractionation centres at Elstree, Oxford, and Glasgow.

"**Mr Moyle:** Production of Factor VIII concentrate at Elstree and Oxford is currently at the rate of approximately 15 million international units per annum. The National Blood Transfusion Services, in addition, produces approximately the same amount of Factor VIII in the form of cryoprecipitate. I have no information about the production at Glasgow but I have asked my right [honourable] Friend the Secretary of State for Scotland to write to my [honourable] Friend about the production at Liberton, Edinburgh.

"**Mr Madden** asked the Secretary of State for Social Services what is the current shortfall between British National Health Service production of Factor VIII and British demand for Factor VIII concentrate; and, if there is a shortfall, what action is being taken to remedy it.

"**Mr Moyle:** The current amount of Factor VIII produced in England and Wales is approximately 30 million international units per annum; total usage of Factor VIII in England and Wales is estimated to be approximately 45 million international units per annum. Regions are being asked to provide more fresh frozen plasma to the central processing laboratories where the National Health Service concentrate is produced. In the meantime, quantities

of commercial Factor VIII continue to be purchased to meet clinical demands."

If you go over to the next page, please, Paul:

"**Mr Madden** asked the Secretary of State for Social Services what additional central funding has been allocated to the Blood Transfusion Service to improve blood fractionation.

"**Mr Moyle:** In 1978 to 1979, a total of £145,000 has been allocated to the central processing laboratories in England to enable them to increase the production of blood products, mainly of Factor VIII concentrate.

"**Mr Madden** asked the Secretary of State for Social Services if the three fractionation plants supplying concentrate drugs for the treatment of haemophilia are working at full capacity and where supplies are allocated.

"**Mr Moyle:** The Blood Products Laboratory at Elstree and the Protein Fractionation Laboratory at Oxford are both working at present full capacity, but this is being increased. Factor VIII concentrate is supplied by the central processing laboratories to the regional blood transfusion centres who, in turn, supply the haemophilia treatment centres.

"**Mr Madden** asked the Secretary of State for

Social Services what is the cost of producing one unit of National Health Service Factor VIII concentrate; what is the cost of importing one unit of Factor VIII; and if he will list comparable cost figures over each of the last five years.

"**Mr Moyle:** Detailed costing information in regard to the production of Factor VIII is not available in the form requested, but the department is currently working on costing figures for blood products which will include Factor VIII. It is not the practice to disclose National Health Service contract prices for purchased products.

"**Mr Madden** asked the Secretary of State for Social Services what estimates have been made of balance of payment savings and reduced public expenditure if Great Britain were self-sufficient in the production of Factor VIII concentrate by reducing dependence on expensive commercially produced supplies of Factor VIII."

Go on to the next section please, Paul.

"**Mr Moyle:** In the year ending 1977 to 1978, which is the latest year for which figures are available, the amount of expenditure for the purchase of commercial Factor VIII for England and Wales was approximately £1.18 million. Although the product is

imported by the suppliers, no information is available on the foreign exchange content of the purchase price. Because detailed costings of individual blood products produced within the National Health Service are not readily available, no estimate of a potential reduction in public expenditure has been made."

So those, sir, are the answers that were given. The explanation given in response to the question about whether self-sufficiency was achieved was that the targets that were set were met but that because of new opportunities in the treatment of haemophilia and associated disabilities, further clinical demands were made for Factor VIII.

Of interest from the other answers, the fact that the collective output of BPL and PFL at that time was 15 million international units per annum, and that was said to be them operating at full capacity, but the capacity was being increased, and that's something we'll look at tomorrow.

That's 15 million international units of Factor VIII concentrate. A similar amount of cryoprecipitate was being produced by the National Blood Transfusion Service. That's 30 million international units overall. 45 million international units was the amount consumed, and so a shortfall of

15 million international units was being made up by commercial products. So on that analysis, it's about a third cryoprecipitate, a third domestic concentrate, and a third commercial concentrate.

SIR BRIAN LANGSTAFF: It doesn't deal with the Edinburgh contribution, does it?

MR HILL: He's answering purely for England and Wales because that is his departmental responsible for the DHSS. What is slightly unclear is whether or not these answers cover Northern Ireland as well, but I'm afraid I can't assist on that.

The amount allocated to PFL and BPL in England in 1978 to 1979 was £145,000, and that was said to be allocated to enable them to increase production of blood products, mainly Factor VIII. The amount spent on commercial concentrates in the year 1977 to 1978 was £1.18 million for England and Wales.

It can be seen, sir, from those answers that although the £500,000 investment had achieved the numerical targets that had been set for it, it had not ended the use of imported concentrates in the United Kingdom.

I'm going to move on to a separate topic, sir. I wonder if that would be a good time to pause.

SIR BRIAN LANGSTAFF: Well, probably we'd be better coming

back to that tomorrow, I would think. So we'll take a break now and come back at 10.00 tomorrow. 10.00.

(4.17 pm)

(Adjourned until 10.00 am the following day)

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