1 Tuesday, 6 September 2011
2 (9.30 am)
3 THE CHAIRMAN: Good morning.
4 Mr Di Rollo, what I'm about to say is directed
5 primarily to you but it actually extends right across
6 the whole front and affects everyone.
7 If the report in the Sunday Herald is a fair and
8 accurate reflection of the information provided to the
9 reporter, Judith Duffy, even a moderately cynical person
10 might form the impression that those instructing you --
11 that is Thompsons -- and some of those frequently found
12 behind you are certain undermining the credibility of
13 this Inquiry before the evidence has finished and long
14 before we will have reached the stage of drafting
15 a report.
16 Now, it may be that Mr Patrick McGuire was not
17 guilty of the grammatical infelicity attributed to him
18 and what seems less than comprehensible can be
19 explained. I look forward to hearing that. But on any
20 view, what was published comes over as an attack on
21 Ms Dunlop and her team. They have had a very heavy
22 responsibility in preparing the evidence for
23 presentation to the Inquiry, and that is to
24 Professor James and me as well as the public, because
25 the separation that we have tried to achieve means that

1 I listen, as the public listen, to what is presented,
2 and I have to say that I take it ill that there is that
3 kind of attack on her because I think it is wholly
4 unjustified, and I'll come back to explanations in
5 a moment as to why I think that's so.
6 However, I think that if we look at the report, it's
7 clear that it refers to certain issues that have already
8 been dealt with in correspondence and in particular
9 there is a letter of 8 August that sets out very clearly
10 the background to the issue and analyses Thompson's
11 previous representations in an ordered fashion and seeks
12 to deal with them in turn.
13 It's a polite letter. It was drafted by Mr Tullis
14 not me, and I don't feel quite so constrained. It sets
15 out the reason why certain witnesses have not been
16 available to be called. Some of them are dead. It
17 deals with the Inquiry's views of Lords Jenkin and Owen
18 and it covers civil servants, and finally it sets out
19 what the Inquiry would hope would be the response. It
20 says:
21 "As you are aware, at the hearing on 15 June,
22 Lord Penrose expressed his preference that procedural
23 matters such as this should be dealt with openly rather
24 than by way of correspondence. As the Inquiry is not
25 due to sit again until early September, this exchange of

1 correspondence is expedient, however, if you wish to
2 pursue these applications further in the light of this
3 exchange, it is suggested that you should confirm and
4 arrangements can be made for Lord Penrose to be
5 addressed on them at an open session of the Inquiry."
6 Mr Di Rollo, I did not expect the response to that
7 to be an article in the Sunday Herald. Is seems a quite
8 inappropriate way for a firm of solicitors to behave and
9 I take it ill.
10 I'm going to ask Ms Dunlop to comment on the
11 implication in this letter, that there are material gaps
12 in the evidence collected and to be presented that she
13 knows of that cannot be filled in the areas they are
14 identified.
15 I'm sure she will do her best to tell us.
16 MS DUNLOP: Thank you, sir.
17 I wish to say only two things about the article and
18 the comments in it. Firstly, the article misstates the
19 law. The Department of Health did not run the National
20 Health Service in Scotland before devolution. At that
21 time there was executive devolution. The Secretary of
22 State for Scotland was responsible for the
23 National Health Service in Scotland and that
24 responsibility was discharged by having a Scottish
25 health minister and the Scottish Home and Health

1 Department.

2 The second comment I would make -- and it's perhaps

3 connected to the first -- is that we have not so far

4 come across any issue where it appears the answer lies

5 in the Department of Health and we cannot access it

6 because of limitations on our powers.

7 Thank you, sir.

8 THE CHAIRMAN: Mr Di Rollo, have you any explanation to

9 offer for what has been done?

10 MR DI ROLLO: None whatsoever. I had no knowledge of the

11 article on Sunday. I had nothing to do with its

12 publication. I had no indication that anyone was

13 speaking to the press, and this has got absolutely

14 nothing to do with me or the firm of advocates that are

15 representing the core participants. So I have no

16 explanation whatsoever to offer to you, sir.

17 THE CHAIRMAN: All I can say in answer to that, Mr Di Rollo,

18 is that that means that no explanation is being tendered

19 in the face of the Inquiry.

20 MR DI ROLLO: Well, I don't know whether you want to ask

21 Mr McGuire to give an explanation at some point.

22 THE CHAIRMAN: No. You are the person who speaks for those

23 you represent, Mr Di Rollo. If the times comes that

24 I have to summon Mr McGuire, it will be done formally

25 and I will be taking advice on what my powers are. I'm

1 not doing it just casually.
2 MR DI ROLLO: Very well.
3 THE CHAIRMAN: But I do emphasise that the implications that
4 flow from what you have said are, or include, that no
5 explanation is given in the face of the Inquiry. I will
6 take it very ill if I find that there is an explanation
7 in a newspaper, any newspaper, in substitution for an
8 explanation to me here and now. I hope that those
9 behind you understand that.
10 I have no great faith in the Law Society's
11 disciplinary procedures but anyone who seeks to
12 circumvent the proper process in this respect can expect
13 some reaction.
14 There is another reaction. At the end of the
15 letter, it was made clear that in general I expected
16 matters to be dealt with in open court as it were, and
17 formally. So if the position is to be that there is
18 a request for a witness citation or for the production
19 of documents, amendment of the terms of reference,
20 anything to do with the Inquiry, from now on I insist on
21 that being made in writing, addressed to me for
22 determination, supported by a statement of the reasons
23 for it and the aim intended to be achieved intimated to
24 all parties and presented with an application for
25 a hearing, with a proper citation of the authorities and

1 note of argument where appropriate.
2 I hope that is clear. There is no point in engaging
3 in an informal process when it is liable to be abused in
4 the way the process has been abused to date.
5 I hope, sincerely hope, Mr Di Rollo, that that's the
6 end of this matter and that we can get on with the work
7 of this Inquiry.
8 Mr Anderson, do you have any comment on offer in
9 this matter.
10 MR ANDERSON: I don't, sir. I was unaware until ten minutes
11 ago that the article existed.
12 THE CHAIRMAN: Mr Johnston, do you have any comment.
13 MR JOHNSTON: No, sir, I don't think I can usefully comment
14 either.
15 THE CHAIRMAN: Right. Ms Dunlop, can we get back to what we
16 ought to be doing?
17 MS DUNLOP: Yes, sir.
18 I should explain that in this block we are going to
19 begin by looking at topic B3, which concerns heat
20 treatment of products at the Protein Fractionation
21 Centre. It's therefore largely scientific and
22 technical.
23 We have a number of witnesses coming over the next
24 two weeks to cover the topic with us. We are going to
25 begin with Dr Foster, who plainly is in a better

1 position than anyone else to explain a lot of the
2 matters which crop up.
3 In the course of Dr Foster's evidence, we are
4 also going to look at a short DVD. So I can promise,
5 perhaps, some slight, if not light, relief, in that way.
6 All of our B3 witnesses are coming over the next two
7 weeks, with the exception of one, Dr James Smith, who
8 lives in France. We did attempt to set up a videolink
9 to Dr Smith but for various reasons that hasn't been
10 possible. So Dr Smith is going to come from France and
11 give evidence on one occasion in relation to both B3 and
12 C3, which is the later stage of viral inactivation, and
13 he will be doing that later in the autumn.
14 THE CHAIRMAN: Is this the Dr Smith who was originally in
15 Scotland and went down south?
16 MS DUNLOP: Yes. He went to PFL in England and now lives in
17 France.
18 I hope that gives enough of an introduction to what
19 we are going to do.
20 DR PETER FOSTER (continued)
21 Questions by MS DUNLOP
22 As you can see, sir, we have Dr Foster back with us
23 and Dr Foster has provided a number of different papers,
24 the first of which is a statement in fact on the
25 manufacturing process at the Protein Fractionation

1 Centre.

2 This is something that was alluded to when Dr Foster
3 attended in May. We did say that we would be returning
4 to these more technical issues of how blood product
5 concentrates were actually made at a later stage in the
6 Inquiry and that stage is now. So I intend to begin
7 this morning by taking Dr Foster through his statement
8 on the manufacturing process.

9 However, just before we do that, I wanted to make
10 reference to a short statement which has been sent to
11 the Inquiry by Dr Iain Macdonald. Dr Iain Macdonald is
12 retired but worked in the Scottish Home and Health
13 Department. If we could briefly look at his CV, that is
14 WIT0030295.

15 We can see it's in fact a very short summary CV and
16 that Dr Macdonald graduated in medicine from
17 Glasgow University in 1950. He is a former chief
18 medical officer and in fact, during the period with
19 which the Inquiry is principally concerned, he was
20 a senior medical officer in the Scottish Home and Health
21 Department. That's 1966 to 1973. Then principal
22 medical officer in SHHD 1973 to 1974, and deputy chief
23 medical officer, 1974 to 1985.

24 So he held these positions within the Scottish Home
25 and Health Department. Because of that, he has felt

1 that he wanted to provide a little bit more information
2 about the period when PFC was established.
3 So if we could just look at that. That statement is
4 [PEN0170659]. The position, as you can see, sir, is
5 that Dr Macdonald had provided a statement in relation
6 to topic C2, which we are coming to later in the autumn,
7 but he felt that he wanted to expand those remarks with
8 a little bit more information on, as he says, the steps
9 taken to replace the former blood products unit in the
10 Royal Infirmary of Edinburgh with the free-standing
11 Protein Fractionation Centre at Liberton.
12 In paragraph 2 he refers to the preliminary report
13 and the narrative that the blood products unit was
14 located in the Royal Infirmary of Edinburgh, that the
15 hospital plan for Scotland in 1962 narrated an intention
16 to rebuild Edinburgh Royal Infirmary. At that time it
17 was thought it could be rebuilt in Lauriston Place but
18 I think, as we all know, that didn't happen and it was
19 ultimately rebuilt at Little France. But even with the
20 plan to rebuild at Lauriston Place, Dr Macdonald says,
21 it was obvious that the proposed replacement in the new
22 building would not be satisfactory because of
23 uncertainty about long-term space requirements.
24 He discussed the matter with Dr Cumming, who at that
25 time was the director of Edinburgh and Southeast

1 Scotland Blood Transfusion Service and had been since
2 1948, and their view was that it wasn't appropriate to
3 locate a production unit of this kind in the hospital
4 and that a free-standing building was needed.
5 Then on to the next page.
6 The BPU was deleted from the proposed redevelopment
7 of the Royal Infirmary. A separate site was identified
8 at Liberton. And again, as we know, the site was
9 developed. We can see some reference to the intention
10 which prevailed at that point, to process at PFC, not
11 just material from Scotland but also from the rest of
12 Britain, and that obviously was relevant to what sort of
13 facility was required.
14 Then paragraph 5. Discussions between Dr Cumming
15 and Dr Macdonald and Mr Watt, who was involved by that
16 time too, about introducing a continuous flow method of
17 production, which would provide some flexibility and
18 also, because the facility was to be free-standing,
19 there would be a possibility of expansion in the way of
20 building additional accommodation. Then he goes on to
21 say in paragraph 6 that:
22 "Divergence of views between Scotland and England
23 were influencing our decisions. There was a strong
24 commitment in the Blood Transfusion Service in Scotland
25 to self-sufficiency in blood and blood products and

1 a belief that this could and should be achieved. At
2 that stage, the late 1960s, there was no evidence of
3 such a commitment in England."
4 Lord Owen told Lord Archer's Inquiry that while he
5 was minister of state at DHSS, from 1974 to 1976, there
6 was resistance in the department to going for
7 self-sufficiency. Although he couldn't remember exactly
8 why. This alone would create a difference in the
9 required levels of production of blood products. It was
10 also becoming apparent that the service in Scotland
11 anticipated a higher demand for blood products than was
12 anticipated by some of the colleagues in England.
13 Dr Macdonald goes on to say that he put to senior
14 medical colleagues in SHHD a proposal that the new PFC
15 should be built on the site at Liberton as soon as the
16 necessary capital could be obtained. Then in
17 paragraph 8, the building went ahead on that basis:
18 "It was almost ready to begin production when my
19 involvement with the Blood Transfusion Service ceased in
20 1974. No further advance had been made in furthering
21 the intention to share the Great Britain workload with
22 the English units."
23 THE CHAIRMAN: I think there are some documents that don't
24 square in all respects with Dr Macdonald's recollection
25 but I'm sure he gives us a helpful insight into some

1 aspects of it.

2 MS DUNLOP: Yes, I would simply, as I said, want to draw

3 attention to the fact that the statement has come in and

4 we are grateful to Dr Macdonald for going to the effort

5 of putting his recollections on paper, and we will be

6 able to take it into account if we are writing a section

7 on the history of the PFC.

8 Dr Foster did you want to comment on anything in

9 this statement?

10 A. I would only say that the period that's covered really

11 pre-dates my employment with SNBTA predominantly.

12 However, there is one important detail that might be

13 worth just bearing in mind, that in this period the

14 planning was largely concerned with the supply of

15 albumin, which was what demand was based on, or future

16 predictions were based on, rather than coagulation

17 factors because the plans for treatment of haemophilia

18 were being considered by the MRC working party led by

19 Dr Biggs, and that didn't report until 1973 or 1974.

20 So really this account by Dr Macdonald is really --

21 the planning there pre-dates the report from the Bigg's

22 working party, which then led to the acceptance that

23 factor concentrates were going to be required to treat

24 haemophilia and the projections that came out of that

25 group that then led into further plans that had to be

1 brought and taken into consideration within PFC once the
2 building had been constructed.
3 THE CHAIRMAN: It is quite important for us to understand it
4 because I think in most of the early documents, what we
5 see a references to is PPS as the product.
6 A. That's correct, that's equivalent to albumin.
7 THE CHAIRMAN: That was the albumin, what, slightly less
8 than completely pure that was being produced? And it
9 seems to drift, if one simply looks at production
10 figures, from SPPS into the production of concentrates.
11 At some stage I would like to know a little bit
12 about the production of earlier concentrates at
13 Edinburgh and the antihaemophilic factor, as it was
14 called, Cohn Fraction I. Is that far beyond your time?
15 A. Yes, it was before my time but there are dates when --
16 we know that that type of product was being produced
17 from 1956 until 1972 and there is a publication that
18 describes the method that is available.
19 THE CHAIRMAN: I have found a document that refers to the
20 last date of production of the material. So I think
21 I can cover it but it is always helpful if someone can
22 give flesh to the bones, as it were.
23 A. I can confirm that that product did exist, yes.
24 THE CHAIRMAN: Right. Ms Dunlop.
25 MS DUNLOP: Dr Foster, can we move to the statement you have

1 provided on the manufacturing process. That is
2 [PEN0121852]. It should appear on the screen in front
3 of you. Yes, thank you.
4 The statement begins with a narrative of the letter
5 that was sent in April, asking for such a statement to
6 be provided. That covers the first two pages. If we
7 could then move to page 3, please, the first section of
8 your statement is entitled "Production at the Protein
9 Fractionation Centre". You tell us that by the
10 beginning of 1984 -- which is really the sort of time
11 for which we asked you to provide the statement. We
12 wanted you to describe the process as it would have
13 existed as at the end of 1983:
14 "The amount of human blood plasma that had been
15 donated in Scotland and had been processed annually at
16 PFC was about 60,000 kilogrammes, of which two thirds
17 were suitable for the preparation of coagulation factor
18 concentrates."
19 I just wanted to ask what made the other one third
20 unsuitable?
21 A. It would be called "time-expired plasma". The only
22 plasma that was suitable for coagulation factors was
23 fresh-frozen plasma because the coagulation factors are
24 sensitive and they decay over time. The blood that is
25 being issued to hospitals and which is then returned

1 from which the plasma can then be recovered, has sat
2 around too long, if you like, to be suitable for
3 coagulation factor recovery.
4 Q. Right. Was that material sometimes used for research?
5 A. No, it was used to manufacture albumin and
6 immunoglobulin because those molecules are more
7 resistant and they could be recovered from that material
8 even though it might have sat around for a longer period
9 of time than was suitable for coagulation factors.
10 Q. Thank you. You go on to give us some more statistics.
11 You say that:
12 "In addition to producing about 35,000 vials of
13 Factor VIII concentrate and 4,000 vials of Factor IX
14 concentrate, the annual output from PFC included
15 approximately 55,000 bottles of albumin products and a
16 total of over 25,000 vials of different immunoglobulin
17 preparations."
18 Then you refer to other non-protein products. We
19 then move to section 2, "Product Manufacture". You set
20 out for us the elements involved. Obviously staff and
21 materials, equipment and facilities, processing of
22 plasma, product inspection, application of quality
23 control and quality assurance procedures. Then you say:
24 "A film was made in 1995 which covered all of these
25 activities."

1 You reminded us that you had sent a copy of that to
2 the Inquiry in 2009. It's that film that I intend to
3 show in a little while. But I thought it would perhaps
4 help us if we worked our way through your statement
5 first, so that we knew, when we watched the film, what
6 it was we were looking at rather than watching the film
7 first. So we will come to that. Then you say at (iii)
8 that:
9 "This witness statement concerns only the
10 preparative processes to which the plasma was subjected
11 and in particular processes used in the preparing of
12 concentrates of Factor VIII and Factor IX."
13 You also mention a set of photographs and indeed
14 there is reference to the photographs throughout the
15 statement.
16 If you bear with me a moment, sir, I'll just check
17 the position with the photographs. (Pause)
18 I think, sir, we will distribute some sets of the
19 photographs so that people can have a look at them as
20 well.
21 Most of what's in the photographs is also in the
22 film. I think some of it in fact almost looks like
23 stills from the film. Maybe it was, maybe it wasn't,
24 but the photographs, at least in some respects, don't
25 add a lot to what's in the film.

1 A. I think you are correct. I think when we looked at the
2 film, there were some aspects that we thought would
3 interest the Inquiry that had not been included, so we
4 inserted some still photographs to make that clearer.
5 THE CHAIRMAN: The photographs might help your oral
6 description, of course, as we go along, Dr Foster. They
7 do look quite interesting, I have to say. (Handed)
8 MS DUNLOP: There is also a ground floor plan. Perhaps we
9 will look at it actually, just so that we know what we
10 are talking about. The ground floor plan is in our
11 database, it's [PEN0121694]. This is the ground floor.
12 How many floors were there?
13 A. Two floors.
14 Q. Two floors?
15 A. There was a basement below this which contained a lot of
16 the heavy plant, the refrigeration plant and plant for
17 production of purified water and air conditioning
18 systems.
19 Q. Right. I don't know if we can enlarge this at all.
20 Thank you.
21 I think the difficulty is we are going to lose the
22 clarity of the print if we enlarge it too much but we
23 can see particularly a big room at number 85, the
24 fractionation hall, which is almost exactly on the
25 middle of the screen. Then to the left of that,

1 fractionation laboratory, number 56. Then below that
2 "plasma preparation" and then just really working
3 anti-clock wise from there, "conditioning unit".
4 I think I have the advantage over those who are
5 relying on the screen. That's the small room on the
6 left side, just underneath -- yes, thank you -- being
7 indicated by the cursor. Then next to that, the minus
8 40 degrees centigrade cold room, number 77. Under that
9 the plus 4 degrees centigrade plasma booking, then under
10 that, plasma receipt. Then to the right, the minus
11 40 degrees plasma deep freeze.
12 So are these the main areas of the activity with
13 which we are concerned today?
14 A. I would say probably, yes. But we should bear in mind
15 that this plan is a relatively recent floor plan and it
16 does, I think, fit with the film that you are going to
17 watch, which was made in 1995. And there were changes
18 between the early 80s and 1995, so this plan doesn't
19 reflect exactly how it was in the period that you want
20 to look at in more detail. But in terms of the
21 fractionation hall and the plasma conditioning area,
22 plasma preparation, that is essentially the same.
23 Q. Right. Obviously, if we had had a film from the 1980s,
24 we would watch that but I take it this is the only film
25 that there is?

1 A. That's the only one we have, yes.
2 THE CHAIRMAN: Can you take us through the sort of process
3 relationship between these buildings. There is plasma
4 receipt at the bottom, 79. Is that where the stuff came
5 in?
6 A. That's correct. If you look at what is room number 1,
7 which is at the bottom left, that is really the entrance
8 where the plasma would be unloaded from the van and then
9 it would be put into cold storage, pending processing at
10 some point in the future. So you see the minus 40
11 plasma deep freeze. Then, once the plasma is taken from
12 there, you try to follow the circular route, beginning
13 with the thawing of the plasma and then the mainstream
14 fractionation in room 85.
15 THE CHAIRMAN: I think it's the relationship before that
16 that I'm not immediately clear about. I can see the
17 stuff coming in through the main door, going along the
18 corridor into receipt, and then booking, I take it, is
19 some sort of administrative procedure?
20 A. That's correct.
21 THE CHAIRMAN: Does it then go to the cold room or to the
22 deep freeze?
23 A. It would go to the deep freeze and that would be stored
24 there for -- it could be weeks, could be months, before
25 it is then removed for processing and then it would go

1 to the --

2 THE CHAIRMAN: The cold room?

3 A. No, I didn't actually work in production so I'm having

4 to stretch my memory a bit here, but the cold room might

5 have been used for the storage of intermediate

6 materials, the minus 40 cold room.

7 THE CHAIRMAN: I'm sure that some people will remember --

8 A. Because once you have carried out the first

9 fractionation stages, those materials are then stored at

10 minus 40. So that room 77 is for the storage of

11 intermediate materials at minus 40, not for the storage

12 of plasma.

13 THE CHAIRMAN: What happens is it comes in in the boxes of

14 12 units of plasma and goes into deep freeze in that

15 form?

16 A. That's correct.

17 THE CHAIRMAN: And then they are withdrawn as boxes of 12

18 and moved towards a first stage of fractionation.

19 I think I didn't myself understand that until I started

20 reworking some of the evidence earlier, that there was

21 an initial stage which produced an intermediate

22 fractionation of material.

23 A. That's correct.

24 THE CHAIRMAN: Is that a way to put it?

25 A. That is a good way to put it, yes.

1 THE CHAIRMAN: Then it's from this that one part of the
2 intermediate fractionation material is taken on to
3 produce concentrates?
4 A. Yes. If we are talking about Factor VIII, then the
5 intermediate material is cryoprecipitate.
6 THE CHAIRMAN: So that happens in number 85, the
7 fractionation hall, or its equivalent at the time.
8 A. It was the same at the time, yes.
9 THE CHAIRMAN: Does it come out of the fractionation hall at
10 that stage, if it's going to become Factor VIII --
11 A. Yes.
12 THE CHAIRMAN: -- and into 77, the cold room?
13 A. With the Factor VIII, the cryoprecipitate at that time
14 was processed fresh, so we didn't actually store that,
15 we carried on processing within the same working day.
16 So the cryoprecipitate would be collected in room 85.
17 Then it would be taken to a separate laboratory area,
18 which is actually probably off the top of the diagram
19 here, and it would be -- in this diagram it was actually
20 room 28, I think, where the further processing was
21 carried out in specialist laboratories.
22 THE CHAIRMAN: Right.
23 A. But in the 1983 period that laboratory was located in
24 a different place here but it was re-arranged later.
25 THE CHAIRMAN: I think I'm going to fail in what I was

1 hoping, which was to get a nice easy roadmap, as it
2 were.
3 A. I don't think that there is. The whole production
4 operation is so complicated, it is very difficult to get
5 a simple route.
6 THE CHAIRMAN: Ms Dunlop, I'll try and restrain myself and
7 let you get on with it.
8 MS DUNLOP: I hope that it will become clear by the end,
9 sir, and certainly, a film, like a picture, is worth
10 a thousand words.
11 The other thing you have most helpfully provided for
12 us is a glossary. That's in section 7. Could we go
13 back to the statement? This is [PEN0121852] at
14 page 1855. Just looking at (v), there is a reference to
15 the glossary.
16 Then section 3, you detail the overall process
17 scheme and you tell us that you have given a schematic
18 illustration and a simplified process flow sheet, which
19 is figure 1. Perhaps we could look at figure 1 at this
20 point. This is at the end of the statement and it's
21 page 33 of [PEN0121852]. You do explain this as well,
22 so i'll keep this statement in front of me while people
23 are looking at the flowchart. You say:
24 "Processes are shown for the preparation of six
25 different types of plasma product."

1 We can see this if we look at the column on the
2 right-hand side headed "Final Product". It's actually
3 in bold text. We can see Factor VIII concentrate,
4 Factor IX concentrate, immunoglobulin for intramuscular
5 administration, immunoglobulin for intravenous
6 administration, and then SPPS, to which reference has
7 already been made, and albumin. Then you say that:
8 "For all of these products, three different process
9 stages can be identified: a mainstream process then
10 leading to intermediate -- sorry, if we can just keep
11 figure 1. I'm reading along the top of the figure. So
12 that people can see it on the chart.
13 There is a mainstream process, in which plasma was
14 processed in sequential steps to obtain intermediate
15 products. We can see those intermediate products listed
16 in the second column working from the left. Then from
17 the intermediate products further processing is carried
18 out to produce final products.
19 Just looking at this chart, Dr Foster, to make sure
20 that I'm following the way it's organised, if we take
21 the first step in the left-most column, so frozen plasma
22 is thawed, as I understand it, at that point, looking at
23 the chart, you could either turn right and you could say
24 from the thawing there emerges cryoprecipitate. Then
25 you would follow the train horizontally and gain an

1 understanding of what happens, that leads in the end to
2 Factor VIII concentrate, or you could follow what is
3 done with the supernatant and work your way down
4 vertically. Is that correct?
5 A. Yes, that's correct.
6 Q. Yes. So, just taking that very simple step, because I'm
7 trying to keep it simple for my own sake, after the
8 thawing, which is that first box, you are going to have
9 the solid part, the cryoprecipitate, and the fluid
10 that's left, the supernatant, and the supernatant is
11 then subjected to further processes, ion exchange,
12 elution, and that process is used to make Factor IX
13 concentrate from what was the supernatant, after the
14 thawing of the frozen plasma. Is that correct?
15 A. I think the simple way to perhaps think about this is,
16 in the mainstream process at this stage, what remains is
17 the fluid or the supernatant, and that's what proceeds
18 down the mainstream process. One of the outcomes at
19 each of the steps is a solid, in one case an ion-exchange
20 eluate, which forms the intermediate of the stream that
21 is being taken off.
22 Q. So everything in the vertical column, the lefthand
23 column, is really depleted plasma, as it were?
24 A. Yes, that's correct.
25 Q. That second row, as it were, the ion exchange adsorption

1 and the process needed to get Factor IX, that's actually
2 a process with which we are perhaps slightly less
3 familiar, but in a nutshell this is the addition of
4 charged particles, which then causes something else to
5 emerge from the plasma, or from the supernatant, and
6 with that something else you can make Factor IX
7 eventually?
8 A. The particles are in such a state that the Factor IX
9 sticks to the particle, along with some other proteins,
10 and then can be separated from the plasma in that way.
11 Q. Yes. And we have referred to this before, but our main
12 interest is obviously with Factor VIII and Factor IX and
13 when plasma is thawed, they don't go the same way. The
14 Factor VIII is in the cryoprecipitate and the Factor IX
15 is in the supernatant?
16 A. That is correct.
17 Q. Right. Can we go back then, please, to the statement.
18 We are now at page 6 of [PEN0121852]. Just looking from
19 the top, you say:
20 "Further processing of each intermediate product
21 would then be carried out via a series of sequential
22 steps designed to produce a specified final product.
23 These steps typically involved further purification and
24 formulation of the protein solution to make it suitable
25 for clinical administration, filtration of the

1 formulated product, for clarification and to remove any
2 bacteria ..."
3 And then obviously dispensing into sterile glass
4 vials.
5 Then with the concentrates there would be
6 a freeze-drying step before the vials were stoppered and
7 sealed. So in most cases, with the solution depleted,
8 as it becomes, one is either trying to extract what you
9 want or forcing out what you don't want. That's a very
10 crude summary but that is, as I understand it, the
11 overall theme of what's going on.
12 A. Yes, I think that's a good way to describe it.
13 Q. Right. Thank you.
14 We move now to section 4, the preparation of
15 Factor VIII concentrates. Firstly you are going to talk
16 about unheated Factor VIII concentrate, which was known
17 as NY. We established before that the "NY" is New York,
18 and that that in fact reflects your connection with Alan
19 Johnson of New York. Is that correct?
20 A. That's correct, yes.
21 Q. He is a name that we will be hearing quite on a bit
22 today because he recurs throughout the story.
23 You are saying that the aim -- and I think this is
24 perhaps uncontroversial -- is to provide a specified
25 amount of Factor VIII activity per vial so that

1 a patient could use it at home. Obviously you had to
2 comply with the British Pharmacopeia specification.
3 You then mention Alan Johnson by telling us that the
4 procedures used were based on the method of Newman and
5 Johnson and he refers to an article. We will just
6 glance at that. That's [SGF0011913].
7 This is an article from the British Journal of
8 Haematology in 1971. Perhaps if we just look at the
9 summary. What the article is describing is a method of
10 preparing both intermediate and high purity Factor VIII
11 by cryoethanol precipitation. The extraction of the
12 precipitate with Tris Buffer and fractionation with
13 polyethylene glycol. So that reference to cryoethanol
14 precipitation, when we talk about cryoprecipitate, would
15 it really be correct to think of that as cryoethanol
16 precipitate?
17 A. No. In this paper the use of ethanol was described but
18 that was eventually discarded because it gave a product
19 that was too impure.
20 Q. I see.
21 A. So it was just the cryoprecipitate. The ethanol was
22 left out.
23 THE CHAIRMAN: The other problem of terminology is that
24 there is a reference in the fourth line to "intermediate
25 material". I don't think that's quite the same as we

1 have been talking about as intermediate material so far.

2 A. We tend to talk about intermediate purity products, and

3 I think that's the type of product he is talking about.

4 But Johnson goes on to develop what he called a "high

5 purity product" as well, and in the period that you are

6 talking about, we didn't take that extra step because

7 the work that was done -- and this was done by

8 Dr Smith -- found that the yield was so low that we

9 couldn't really accommodate that extra step.

10 THE CHAIRMAN: Purely in terminology, I think that when you

11 were talking about "intermediate materials" earlier,

12 they were intermediates in the process step.

13 A. I see, yes, sorry.

14 THE CHAIRMAN: But here "intermediate" refers to the purity,

15 in effect, of the product.

16 A. Yes, you are quite right.

17 MS DUNLOP: Can we look then back at the statement and at

18 figure 2, which again is at the back. That's the

19 statement, [PEN0121852] at 1885.

20 If we look at the left-most column, we can see that

21 you have tabulated your process as between 1980 and

22 1984. This is column A. You have, at that point, 17

23 steps, culminating with freeze-drying and then obviously

24 at the end of 1984 there is an 18th step, which is the

25 dry heating, two hours at 68 degrees centigrade.

1 If we look at that, we can see, obviously, a very
2 bald summary of what was done. You go on in the text of
3 your statement to elaborate a little bit about what each
4 of these steps involved. So if we could return then
5 to the text at 1857. Step A01, the plasma was warmed to
6 minus 10 degrees centigrade. You go on to tell us, on
7 the next page, that this was really done as a precursor
8 to processing. So it was necessary to raise the
9 temperature from minus 40 to within the range of minus
10 15 to minus 10. There were two reasons. The first was
11 to assist in the removal of the plastic bag, something
12 that was very difficult to achieve at temperatures
13 colder than minus 15, and then the second reason was to
14 avoid damage that could occur to proteins if frozen
15 plasma was held at temperatures warmer than minus 10.
16 When we come to see the film we will see this, I think,
17 the warming of the frozen plasma in the shape of the
18 bags being laid out on shelves.
19 A. That's correct.
20 Q. Yes. Then you say, (iv), that this process was termed
21 "plasma conditioning" and it took place overnight and
22 then obviously it follows that the plastic bags had to
23 be removed. You tell us that:
24 "Each frozen donation was cut in half using
25 a specialised bandsaw."

1 This too is in the film. We can see that very
2 clearly at the start. Then:
3 "Each piece of frozen plasma was squeezed out into a
4 holding container."
5 Then step 3, the crushing and thawing of the plasma.
6 Then on to the next page, please:
7 "The objective at this step was to prepare
8 cryoprecipitate with a high yield of Factor VIII
9 activity."
10 You say:
11 "It was necessary to thaw the plasma as quickly as
12 possible whilst preventing newly formed particles of
13 cryoprecipitate being dissolved due to an increase in
14 temperature. This objective was best achieved using a
15 process of continuous rather than batch thawing."
16 You go on to deal with that in more detail later in
17 the evidence you have provided.
18 Then, in the next paragraph:
19 "Pieces of plasma were reduced in size from lumps of
20 about 150 grammes with the consistency of finely crushed
21 ice using a hammer mill that was designed to break up
22 frozen materials. The hammer mill was fed continuously
23 with lumps of frozen plasma and the resultant particles
24 were discharged continuously into a specially designed
25 thawing vessel in which controlled melting of the plasma

1 ice took place, the melting point of plasma being minus
2 0.5 degrees centigrade."
3 There is a lot of water in plasma, isn't there?
4 A. I think so, yes.
5 Q. I have to warn you, Dr Foster, that at various points
6 today, and no doubt tomorrow, we will come to bits that
7 I have looked up and you must correct me if the
8 information I have obtained is wrong, but actually,
9 according to some of the sources I looked at, with
10 plasma, as much as about 92 or 93 per cent is water?
11 A. Yes, I hadn't looked that up but I will accept your
12 figure.
13 Q. Right. It is not that surprising then that it would
14 have a melting point around about the same as water or
15 ice?
16 A. Yes.
17 Q. Right. Then you say:
18 "The hammer mill can be seen ..."
19 And we can look at a photograph, but is the hammer
20 mill sometimes called "the crusher"?
21 A. It is, yes.
22 Q. Perhaps we can then look at our photographs. We need to
23 turn to page 3. I'm holding my breath here but that
24 must be it then, is it?
25 A. Sorry, I can't see it.

1 Q. Sorry, it's the top left-hand corner.

2 A. I haven't got it.

3 THE CHAIRMAN: Dr Foster must have one.

4 I think the point that Ms Dunlop made about

5 correcting us, applies to everybody. We have been here

6 a long time now, Dr Foster, and some of us have the

7 conceit that we understand some of it, but if you notice

8 that things are going wrong, please do tell us. It's

9 what you tell us that's going to matter at the end of

10 the day.

11 MS DUNLOP: I'm being told that we do have the photos in our

12 system so that's my fault. I even looked for the word

13 photographs and I couldn't find them. Anyway they are

14 [PEN0121695]. Here they come. Even better.

15 So we need to go to page 3. There it is, yes. The

16 hammer mill. You say:

17 "The hammer blades are arranged in a screw

18 formation."

19 I think we can all see that.

20 THE CHAIRMAN: It looks like a large-scale mincer.

21 MS DUNLOP: It certainly looks like something you wouldn't

22 want to have your arm in.

23 A. You can see in photograph 4 the whole thing assembled,

24 so the blades -- when it is being used it is not open.

25 It is enclosed in a casing in photograph 4.

1 MS DUNLOP: Yes. So there is a kind of shaft at the top of
2 photograph 4, which must be the entry point, is it?
3 A. Yes, that is sited above the blades.
4 Q. Right. Then photograph 5 shows the particles of plasma
5 ice going into the thawing vessel, looking very
6 slightly, I suppose, like a Slush Puppy or something
7 like that, that sort of texture, I guess?
8 A. Yes.
9 Q. Then you tell us that the thawing vessel was a tubular
10 container. I don't think we see the thawing vessel on
11 this page.
12 THE CHAIRMAN: Photograph 2.
13 MS DUNLOP: Oh, yes, sorry, right. Yes. It was a tubular
14 container. It had a hollow jacket through which heated
15 water was pumped. The contents of the vessel were mixed
16 using a double helical ribbon impellor, which I think we
17 can see right there. That's the impellor:
18 "Which was designed to sweep the vessel wall and to
19 continually mix thawed plasma with particles of plasma
20 ice to prevent the melted plasma from overheating."
21 So the point of this vessel, you tell us:
22 "... was to retain the plasma ice and also to allow
23 melted plasma containing particles of cryoprecipitate to
24 drain out continuously by gravity into a small holding
25 vessel, from which it was pumped continuously into a

1 refrigerated large-scale flow-through centrifuge."
2 You explain all of this. You say:
3 "This can be seen in photograph 2 and the assembled
4 vessel with stirrer motor, cables for temperature
5 monitoring, the small holding vessel and the centrifuge
6 feed pump are all shown in photograph 3."
7 You point out that of course these are more recent
8 photographs but again the essential design was the same
9 in 1983. Is that correct?
10 A. That's correct, yes.
11 Q. Perhaps we can go back to the text. We are now on
12 page 1860. The system for continuous thawing was
13 introduced routinely in August 1979 and replaced
14 a previous batch tank process:
15 "Continuous thawing process was first operating at
16 a thawing rate of 70 litres of plasma per hour using
17 pilot scale equipment. That was replaced with a larger
18 scale unit in January 1981, and that could thaw 200
19 litres of plasma per hour."
20 We asked you, Dr Foster, just so we were clear,
21 what's meant by "pilot scale", and you explain that to
22 us in a supplementary statement, which we don't need to
23 go to at the moment, but you said that by "pilot scale"
24 is meant preparation of small batches at a volume of
25 production representative of full-scale manufacture

1 without using large volumes of plasma.
2 A. In the context of this particular sentence here, the
3 definition is slightly different.
4 Q. Right.
5 A. Here "pilot scale" was using a piece of equipment that
6 was really a small production unit, that could process
7 the whole production batch, but it would take longer
8 because it was a small unit.
9 Q. Right. The concept of pilot scale in general, though,
10 as I understand it, is it's something in between the
11 person at the lab bench with a flask and the full
12 industrial process?
13 A. Yes, that's correct.
14 Q. Right. So it has got to be big enough to give reliable
15 results but not so big that you are wasting material.
16 Is that correct?
17 A. That's correct, and of course what you find in the
18 research laboratory is that the equipment that you use
19 bears little resemblance to industrial equipment and so
20 you have to test out the methods with something that
21 will behave in the same way as industrial equipment but
22 perhaps with the smallest scale that you can get away
23 with, so that you don't waste valuable material.
24 Q. Right. This question of using continuous thawing rather
25 than batch thawing, I take it that the advantage of that

1 must have been to cut out a kind of stop/start element
2 that there would be. So instead of putting everything
3 you want to work with in a tank and then thawing it and
4 carrying out the additional steps sequentially, you are
5 always topping up the material, but I think it might be
6 helpful for us if you could summarise why continuous
7 thawing worked better than batch thawing?
8 A. Continuous processing in general allows you to have
9 uniform conditions. In a batch process the conditions
10 are changing from start to finish, and if you are
11 dealing with material that's very sensitive, then for
12 a period of the time that a batch process takes place,
13 you might be beyond the area where the material is going
14 to be stable and so you find you have more losses, more
15 danger.
16 In a continuous process you aim to have the key
17 parameters held in a -- at least a kind of uniform level
18 of what's called a steady state, so that you are not
19 exposing the material to harmful conditions. And that
20 was the basic ideas of trying to use continuous thawing,
21 to hold the plasma at this critical point at
22 a temperature where it would be a uniform temperature
23 that wouldn't be causing harm. It wouldn't be causing
24 the cryoprecipitate to redissolve. If you look at the
25 temperatures inside a batch tank, once the plasma is

1 thawed, the temperature starts to rise, certainly at the
2 wall where the heat is coming from, and you are starting
3 to lose Factor VIII, redissolving back into solution,
4 because the temperature is too high at the wall. With
5 a continuous process, where the thawed plasma is removed
6 as soon as it melts, then you avoid that implication.
7 THE CHAIRMAN: That was quite a lot to take in. You have
8 written quite a lot about the development of the
9 continuous thaw process. I seem to have seen quite
10 a lot of presentations by you and your colleagues on
11 this. Is that right?
12 A. That's correct, yes.
13 THE CHAIRMAN: It is quite complex. What's the really
14 critical point? We have the material going into the
15 thawing vessel with its impellor and all the rest of it,
16 and planters or equipment is circulating around within
17 it, trying to maintain the temperature by mixing ice
18 into it in some way?
19 A. No, no. Well, yes, there is an element of that but
20 basically the idea is to expose the plasma to heat for
21 as short a time as possible and as soon as an element of
22 plasma melts, we avoid that overheating because it's
23 still in contact with ice particles as it drains from
24 the tank.
25 THE CHAIRMAN: Right, that step, the material going in from

1 the crusher, and then you are achieving a situation in
2 which it drips out the bottom and is ready to go on to
3 the centrifuge.
4 A. It kind of flows continuously --
5 THE CHAIRMAN: It's flowing continuously.
6 A. -- by gravity.
7 THE CHAIRMAN: What's happening?
8 MS DUNLOP: Yes, Dr Foster, I just wanted to clarify,
9 because we will go on to see later in your statement the
10 use of the word "batch", so in one sense there is
11 a batch, if you like, because you say later that at the
12 end of 1983 you would be working with about 4,000
13 donations per batch, so --
14 A. There is a defined quantity of plasma that is processed
15 to collect the cryoprecipitate, which is collected in
16 one centrifuge. So although the thawing is done
17 continuously, you are starting with a defined quantity
18 of plasma as individual donations and you are ending
19 with a defined quantity of cryoprecipitate that has been
20 derived from all of that plasma which constitutes the
21 batch.
22 Q. Yes, so at some point with your 4,000 donations, there
23 obviously must be a starting point and a stopping point
24 for the 4,000 donations, so although the processing is
25 continuous, it must be continuous within the 4,000

1 donations?
2 A. That's correct, yes.
3 Q. Right. It's not that the whole assembly ran 24 hours
4 a day, seven days a week, 52 weeks a year?
5 A. No, a defined quantity of plasma would be taken out of
6 cold storage, would be conditioned, the plastic would be
7 removed, and then it would be fed in this continuous
8 manner until all of cryoprecipitate from that defined
9 quantity of plasma was collected in the centrifuge, and
10 the whole arrangement would be sized so that you
11 wouldn't have too little cryoprecipitate or too much
12 cryoprecipitate in the centrifuge, so you have to size
13 it to fit the centrifuge.
14 Q. So when we see references to a batch, we should
15 understand by that the total of, say, 4,000 donations
16 that is, as it were, processed together. Is that right?
17 A. That's correct, yes.
18 Q. Right. Just to go back to the statement, you say:
19 "The temperature was maintained close to zero at all
20 times."
21 That's obviously, as you have described, because of
22 the maintenance within the tank of particles of ice?
23 A. That's correct.
24 Q. So although there is melting going on, there is still
25 ice to keep the melted material cool. You say that

1 enabled plasma throughput to be increased relatively
2 easily. Reading from (viii):
3 "Each particle of plasma ice was held in the system
4 for only about 15 minutes, thereby minimising the time
5 during which Factor VIII activity was most vulnerable to
6 damage."
7 Then turning over, we can see that there was
8 a spectacular improvement in yield when you introduced
9 this change. Is that correct?
10 A. That's correct.
11 Q. Yes. Appendices C and D are in fact articles concerning
12 continuous thawing. So if further study is required,
13 these are both articles to which Dr Foster contributed,
14 about large scale plasma thawing, and they are listed.
15 We don't need to go to it but they are listed on
16 page 1879.
17 Then step 4, you are collecting the cryoprecipitate,
18 and this is melted plasma containing fine particles of
19 cryoprecipitate pumped directly into a multichamber
20 centrifuge. This is all happening in a cold processing
21 area, maintained at about 4 degrees centigrade, so the
22 plasma is, as it were, only just melted, it is not
23 heated up enormously beyond its melting point?
24 A. No, it's close to zero degrees as it flows into the
25 centrifuge.

1 Q. Right. You detail further steps in the collection of
2 the cryoprecipitate. You are trying, in the centrifuge,
3 to keep the contents at about 2 degrees. Then the
4 melted plasma with the particles of cryoprecipitate in
5 it is fed into the rotating bowl and the centrifugal
6 force causes the cryoprecipitate to settle on the
7 vertical walls of two cylindrical chambers within the
8 bowl and be retained in the machine.
9 We can actually see in the film -- and it is not,
10 I don't think, cryoprecipitate -- someone scraping white
11 material from the side of a centrifuge bowl. So we can
12 understand, in general terms, that process, that
13 obviously the physics of it are that the particles are
14 adhering to the side of the bowl and is needs to be
15 scraped out.
16 A. It needs to be scraped out, yes. It's a manual process
17 at that point, yes.
18 Q. Yes. Then you say in (iv):
19 "The centrifuge is run down at the end of the
20 thawing process and the bowl is removed."
21 Perhaps we can just look quickly back at the
22 photographs. I must say, in the film it looks as though
23 all of this is very heavy material. It's machine
24 lifted, it is not manually lifted.
25 A. Yes, it's too heavy to be manually lifted, yes.

1 Q. Yes, right. This is page 7, so if we can go back to the
2 photographs, that's [PEN0121695]. The next page, after
3 that one, please. We can see the bowl being lifted with
4 some sort of pulley device. If we go down one, please.
5 Yes, thank you. In fact, the next photograph is good
6 too because we can see -- I just want to say "stuff",
7 obviously it is not stuff. There is a much more
8 accurate description than that but we can see that after
9 the bowl is removed, there was material adhering to the
10 side.
11 A. In that photograph, that's one of the ethanol fractions
12 that has been recovered, it is not cryoprecipitate.
13 Q. Yes. It looked to have a more lardy consistency than
14 the cryoprecipitate.
15 You will have to forgive me, Dr Foster. I keep
16 reaching for cooking analogies because I understand that
17 better.
18 Anyway, we have got the bowl out and if we can go
19 back to the text, please, at 1862. You say that the
20 cryoprecipitate is collected in a single mass of about
21 10 kilogrammes of solids for further processing. So
22 that 10 kilogrammes of cryoprecipitate, that is roughly
23 what you would get from the 4,000 donations, is it?
24 A. That's correct.
25 Q. Right. What's the rough weight of the 4,000 donations?

1 A. It would be approximately 1,000 kilogrammes, 800 to
2 1,000.
3 Q. Right.
4 THE CHAIRMAN: It has come a long way from Pool and
5 Shannon.
6 A. I think it has.
7 MS DUNLOP: Yes. Then we see the reference to the 4,000
8 donations in the next paragraph and you talk, in (vi),
9 about further processing of the cryoprecipitate in
10 a separate process area.
11 At this point, if we all remember what figure 1
12 looked like and the possibility of travelling
13 horizontally or vertically -- I think in the film we
14 actually travel vertically a bit because we work our way
15 down the first column, whereas in your statement you
16 have gone horizontally and you continue to tell us about
17 cryoprecipitate.
18 A. That's correct.
19 Q. I'm sure we can cope with that but just to flag that up
20 for us all when we are watching the film.
21 So staying with cryoprecipitate and its fate, we
22 come to step 5. It's rinsed with ethanol and then step
23 6, rinsed cryoprecipitate is suspended in a specially
24 formulated buffer solution, and you tell us in the
25 glossary that a buffer solution is designed to regulate

1 the pH of what you are working with. So it is designed
2 to keep whatever material you are working with at a
3 reasonably stable pH. Is that correct?
4 A. If you think of a buffer, obviously with a train, it's
5 absorbing shock, and it's the same here, it's the
6 chemical shock. This buffer absorbs the shock so that
7 you can make changes in a gentle way instead of causing
8 sharp changes that might damage the proteins. So it's
9 a chemical buffer.
10 Q. A chemical buffer? That's how it gets its name, yes,
11 thank you.
12 On to the next page. You tell us that the pH is
13 controlled. It is brought to neutrality by the slow
14 addition of hydrochloric acid. This pH is optimal for
15 the recovery of Factor VIII. Then step 8, adsorption
16 with aluminium hydroxide. Adsorption I understand to be
17 a process where molecules will collect on the surface of
18 another substance but will not mix with it. Is
19 that reasonable?
20 A. Yes, basically what's happening here is that some of the
21 proteins that we want to remove stick to the aluminium
22 hydroxide, which is a solid fine particle, which can
23 then be removed by centrifugation and taken away from
24 the main solution.
25 Q. Right. This is because the thawing process has not been

1 100 per cent perfect. So, as you say, some plasma
2 remains within the cryoprecipitate mass?
3 A. Yes, within any of these precipitates -- these are not
4 pure proteins, it is still what is called the "mother
5 liquor", which was the original plasma, quite a bit of
6 that is retained inside all of these precipitates. So
7 if you like, these impurities have to be removed because
8 they could damage the Factor VIII.
9 Q. Right. After that you have to take the aluminium
10 hydroxide out again, and that's step 9. You say that's
11 done by a further use of a centrifuge, 4,000 revs per
12 minute for 15 minutes at 20 degrees, and then the
13 supernatant was decanted into a sterile pressure vessel.
14 Then on to the next page. The solution was then further
15 clarified by filtration through a series of membrane
16 cartridge filters. The last filter in the series having
17 a mean membrane pore diameter of 0.45 micrometres?
18 A. That's correct.
19 Q. The chairman will correct me if I'm wrong, but this is
20 1 millionth of a metre -- is that right? -- 10 to the
21 minus 6 of a metre. Is that right?
22 A. It sounds right, yes.
23 Q. Good enough. Then step 12, you are adding citrate,
24 which is an anticoagulant, trisodium citrate. Step 13,
25 further adjustment of the pH, and then more filtration,

1 step 14. 0.22 micrometre filter at this point. What's
2 the magic about 0.22?
3 A. As it says here, this is the standard in the
4 pharmaceutical industry that's required to ensure you
5 can remove all bacteria that might be present.
6 Q. So it must be something to do with empiricism --
7 A. Yes, it is.
8 Q. -- that this is the measurement that works best?
9 A. It is, yes.
10 Q. Then you say:
11 "The sterile line to a sterile receiving vessel in
12 an aseptic dispensing suite, with filtrate Factor VIII
13 passed directly into receiving vessels."
14 Then step 5, you dispense aseptically. The idea of
15 this, I understand, to be that the Factor VIII is put
16 into a bottle which is a little bit bigger, so there is
17 room in the bottle, so that the patient can add
18 distilled water to reconstitute it. Is that right?
19 A. That's correct, yes.
20 Q. I like this bit because I didn't know this before: each
21 vial was fitted with a raised stopper especially
22 designed for freeze-dried products and the point of the
23 raised stopper is that the stopper has holes in the side
24 so that the water vapour can come out during the
25 freeze-drying. Is that right?

1 A. Yes, the stopper has a little ridge and it can sit on
2 top of the bottle and have, as you say, these small
3 grooves in the side that allow the moisture to come out
4 during freeze-drying. Then it can be pushed home
5 automatically to seal the vial.
6 Q. Yes. Then 16, the product was frozen to minus
7 50 degrees centigrade in order to ensure that all
8 constituents were in the solid state prior to
9 freeze-drying. Then you had freeze dryers with a number
10 of shelves.
11 THE CHAIRMAN: Before you go on to freeze-drying, I think,
12 Professor James and I would like to go back just
13 a little bit.
14 I mentioned Pool and Shannon, and as I understood,
15 the early descriptions of that which were said to be
16 capable of being carried out in any transfusion centre
17 or hospital, it involved centrifugation and then
18 freezing of the individual plastic containers to enable
19 the cryoprecipitate to be separated from the supernatant
20 that's then taken off. Clearly, what you are doing is
21 a much more sophisticated product but is the
22 cryoprecipitate the same or has it changed in some way?
23 A. It would be the same type of material and
24 cryoprecipitate itself can vary according to how it's
25 manufactured. A wide range of results can be obtained

1 depending on how well the process is controlled, and
2 I think in the hospital blood bank people do this in
3 a water bath, which I would say was less well controlled
4 than the process that we were providing.
5 THE CHAIRMAN: I would understand that. I think the
6 critical piece of information that we would like to
7 have, you may not be able to give. We know that at
8 Law Hospital in the West of Scotland, there was a great
9 deal of production of cryoprecipitate, and at certain
10 stages they tried to freeze-dry it and sorts of things.
11 Do you know whether they used the industrial process
12 that you have described to us or a more basic process,
13 using very small numbers of individual bags?
14 A. It would be the latter, and this would be typical of all
15 of the regional transfusion centres, Edinburgh, Law and
16 I think even possibly other regional transfusion
17 centres, they all prepared cryoprecipitate from single
18 donations using a water bath method with these single
19 donations, and then they might pool some of the single
20 donations to get a larger quantity, but basically that
21 was the scale that they operated.
22 THE CHAIRMAN: I think that's what we wanted; simply to get
23 a feel for what was happening around Scotland and really
24 PFC was where this large-scale continuous flow method
25 was being used.

1 A. Yes, that is the only place where that took place in
2 Scotland.
3 MS DUNLOP: Thank you.
4 I just wanted to look at the photograph of the
5 freeze dryer, Dr Foster. It's rather a psychedelic
6 picture. It's on page 17. Unfortunately I don't have
7 the signature references on my photographs but if we can
8 find page 17.
9 Aseptic loading onto the freeze dryer. We can see
10 a masked person carrying that out. And then there is
11 the unloading in the other picture. So obviously the
12 door is closed and then the shelves are refrigerated to
13 minus 50 degrees and the product is left overnight. Can
14 we go back to page 1856, please?
15 You then take us through freeze-drying, the
16 essential process is sublimation, so removal of water by
17 heating the material under a vacuum. Then (ii), two
18 drying stages: primary drying and secondary drying. In
19 secondary drying the shelf temperature is increased to
20 reduce the residual moisture to less than 2 per cent by
21 weight. So you are aiming for something that has very
22 little water in it.
23 A. That's correct.
24 Q. Then you go on to tell us in detail what the conditions
25 were for primary and secondary drying at the end of

1 1983, and then what happened at the end of secondary
2 drying. The chamber was raised to atmospheric pressure.
3 Then the stoppers are firmly closed rather than sitting
4 on top of the bottles and the stoppered vials are removed.
5 On to the next page. You say:
6 "This completed the processing of unheated
7 Factor VIII to about one week, having been required to
8 progress from frozen plasma to the freeze-dried
9 product."
10 Then:
11 "Three to four months are required to complete
12 inspection, labelling, packaging, quality control
13 testing, quality assurance procedures and batch
14 release."
15 You then tell us, because we are talking about
16 a timeframe, where heat-treated Factor VIII is going to
17 arrive. You say that when heat treatment began, the
18 process was as described except that dry heat treatment
19 at 68 degrees was applied to the final product. For so
20 long as the product could take it really, and initially
21 that was two hours and fairly swiftly in the early
22 months of 1985, increased to 24 hours. We will
23 obviously look at that in more detail.
24 You narrate that as step A18. We will remember from
25 figure 1 that that was the step that we saw that had

1 been added at the bottom of the left-hand column.
2 Then section 4.3, if we could look at the next page,
3 that's the 24-hour heated material, and you say that was
4 implemented routinely from 20 January 1985 and in
5 essence, if we look at the next page, what I understand
6 to have happened at that point is that you discovered
7 that adding a little bit of plain, ordinary sugar
8 really, because that's sucrose, isn't it, it's the white
9 stuff?
10 A. Exactly.
11 Q. That adding a bit of sucrose enabled the product to take
12 heat at 68 degrees for a longer period and that enabled
13 you to increase it from two hours to 24 hours. I think,
14 before you had added the sucrose, if you had increased
15 it to 24 hours, there would have been a loss of
16 solubility, is that right?
17 A. The product would not have been soluble.
18 Q. So adding the sugar meant that you could heat it for
19 much longer and it was still soluble?
20 A. That's correct.
21 Q. Right. Mid 1985, you tell us that you actually got
22 a bespoke oven, which had been specifically designed and
23 manufactured for the dry heat treatment of coagulation
24 factor concentrates, and those documents, which we are
25 not going to look at, are correspondence in relation to

1 the oven, the initial specifics for it and then the
2 final technical specification of the actual oven.
3 So for anyone who wants to do some extra reading,
4 those are the references to those particular documents.
5 Then the next part is heat treatment as it carried
6 on beyond 1985, which we are going to deal with in topic
7 C3, so I'm not going to go through this. I'm just going
8 to look at page 1873.
9 Perhaps, sir, if we can maybe finish this before we
10 break. I'm hoping we can carry on a little bit because
11 we started slightly later.
12 If we look at 1873, we see the preparation of
13 Factor IX concentrates being discussed, the same idea,
14 specified amount of Factor IX, activity per vial, to
15 comply with the British Pharmacopeia. You say the
16 method was based on the ion exchange purification method
17 of Middleton, Bennett and Smith. That's Dr Jim Smith
18 who has been mentioned already, I think. You actually
19 give us a definition of ion exchange purification. You
20 say:
21 "Ion exchange is a process used to separate or
22 purify proteins in which selected proteins are bound to
23 a solid matrix and then removed."
24 I think you explained that earlier. It makes use of
25 the charge in the particle because an ion is a charged

1 particle?

2 A. That's correct.

3 Q. Then A01 to A04 is the same as for Factor VIII, but

4 obviously at this point, because we are dealing with

5 Factor IX, we have to go one step down in the vertical

6 column and then travel along horizontally in the row

7 that leads to Factor IX?

8 A. That's correct.

9 Q. Yes. You tell us what was done to achieve that. Again,

10 formulation of the supernatant and then adjusting of the

11 pH. Then the ion exchange adsorption, special gel, and

12 then the gel removed again, A08. Then suspending the

13 gel in a buffer solution, and we have talked about

14 buffer solutions, and then chromatography. This is A10.

15 Sorry, this is page 1875. Thank you.

16 10, you add the gel to a chromatography column.

17 I think it would be fair to say, Dr Foster, at this

18 point, it's getting really quite technical but you then

19 tell us what happens after the chromatography. Then in

20 step 12, Factor IX is removed with an elution buffer,

21 and this is all to do what sounds like a swap, that the

22 chloride ion attaches preferentially to the ion exchange

23 gel, exchanging places with the protein that was bound

24 at a lower concentration of chloride ion. So the

25 protein is displaced.

1 A. That's correct.

2 Q. This is (iii). You can tell that the coagulation
3 factors are beginning to emerge from the column because
4 there is a sharp rise in, presumably, the electrical
5 conductivity of the solution?

6 A. That's true.

7 Q. Then you collect the Factor VIII eluates, six different
8 fractions, and then they are frozen and stored and then
9 thawed, pooled, diluted to the targeted potency and then
10 filtered. And this is back to a 0.22 micrometre filter.
11 And then aseptic dispensing, freezing, freeze-drying,
12 and then lastly you narrate the process for
13 heat-treating Factor IX?

14 A. I should say that not all of those fractions would be
15 used. They would be tested and then the ones that were
16 appropriate would be selected, and if one or more of the
17 eluates was inappropriate, it wouldn't be used. So
18 a selection process takes place there.

19 Q. By "appropriate" do you mean in terms of potency?

20 A. It could be potency, and there were a number of tests to
21 assess whether the material might be thrombogenic, it
22 might cause a thrombosis in a patient. If there was any
23 possibility of that, that eluate would not be used.

24 THE CHAIRMAN: Can you test that quickly.

25 A. There were some laboratory tests that could be done.

1 THE CHAIRMAN: To give an indication.
2 A. To give an indication. It was never certain how precise
3 they were but they were the best guidance we had at the
4 time.
5 THE CHAIRMAN: Again, I had the impression that there were
6 fairly large-scale thrombogenicity tests carried out
7 from time to time.
8 A. There were. This was something we could do routinely.
9 It was a simple laboratory test that was devised under
10 Professor Cash.
11 MS DUNLOP: Yes. We will look at that in your main paper
12 because there is an article -- particularly in which
13 Professor Cash was one of the writers -- about the
14 thrombogenicity of DEFIX. Did you call it "DEFIX".
15 A. Yes, it's called DEFIX.
16 Q. Right. In fact here you tell us that there was
17 a concern about the possible thrombogenicity of
18 heat-treated Factor IX and that you and Dr Feldman at
19 PFL discovered that adding another human protein,
20 antithrombin 3, corrected the potential defect, so that
21 step was incorporated into the method for producing
22 dry-heated Factor IX. Then, as from the autumn of 1985,
23 I think, the dry-heated Factor IX that was issued was in
24 fact dry-heated for 72 hours at 80 degrees, using the
25 oven that we have just mentioned.

1 Is Factor IX a simpler protein than Factor VIII?
2 A. Yes, very much so.
3 Q. Yes. According to my limited references, Factor VIII is
4 made of something like 2,350 amino acids; does that
5 sound about right?
6 A. I haven't looked that up recently but it's a very
7 different molecule. It's much larger than Factor IX.
8 Q. Sir, that would be a convenient point at which to break
9 and then when we come back, we can watch the film.
10 THE CHAIRMAN: Very well.
11 (11.04 am)
12 (Short break)
13 (11.29 am)
14 MS DUNLOP: I think, if we may, we will just go straight to
15 the film.
16 THE CHAIRMAN: Yes, right.
17 (film shown)
18 THE CHAIRMAN: The date that have, just to get it into the
19 notes.
20 MS DUNLOP: 1995.
21 A. Although the film that was made in 1995 was basically
22 a home movie that was made by individual members of
23 staff. It had no sound track. And the script was
24 written by myself a couple of years ago to add to the
25 pictures to help to understand them.

1 Q. Thank you.
2 THE CHAIRMAN: Were you the narrator?
3 A. No, I was not.
4 THE CHAIRMAN: Anyway, the baseline is 1995.
5 A. It is, yes.
6 MS DUNLOP: Can we just have a look at the floor plan again,
7 please? That's [PEN0121694]. This is something
8 I should have asked you earlier, Dr Foster. This
9 drawing is dated 8 March 1996. If we had come to PFC
10 then, where would we have found you?
11 A. I wouldn't be on this drawing.
12 Q. Where would you have been?
13 A. Well, part of this area -- in fact I'm wrong. I would.
14 I would be in the office at the top left-hand corner,
15 and the research and development laboratories are in the
16 far left of this drawing.
17 If you can see this building, the building on the
18 left is really the administration and laboratory
19 building, which is, in a sense, a separate building to
20 the production building, although the two are joined by
21 a corridor, a vertical corridor here. So I wouldn't
22 normally spend time in the production building, unless
23 I wanted to go and look at something specific; I would
24 be working more in the administration and the laboratory
25 area.

1 Q. Right. So this whole area on the far left of the
2 diagram is the building you are talking about, and
3 that's the building in which you would have been
4 working?
5 A. Yes, that includes the research laboratory and the
6 quality control laboratories, and that's essentially the
7 area I would spend most of my time in.
8 Q. Right. Would the same have been true in the 1980s? Was
9 the layout much the same then?
10 A. Yes, this would be.
11 Q. Right, thank you.
12 Dr Foster, I want to go to the paper that you have
13 prepared, which is [PEN0131309], and we can see that
14 this is a briefing paper, prepared by you and concerning
15 the development of heat treatment of coagulation
16 factors, dated November 2010, and it begins with
17 a glossary, which is very helpful. It has a contents
18 list and then a sort of executive summary, but we are
19 going to go straight to the meat rather than looking at
20 the executive summary.
21 So could we go, please, to 1319? This section is
22 entitled "Historical Background Worldwide", firstly,
23 dealing with the pasteurisation of albumin.
24 You explain a little bit first of all about the
25 effect of heat on proteins and you give us the example,

1 which I think is often used, about the effect of heat on
2 an egg. So you say, for example, cooked against
3 uncooked egg white is an example of the denaturing of
4 protein, and I suppose our own experience with eggs has
5 taught us that there is also a contribution made by the
6 length of time for which the protein has been heated.
7 So, for example, the difference between a soft boiled
8 egg and a hard boiled egg is a question of heating for
9 a longer period of time.
10 A. Yes.
11 Q. Yes. So it is not just a question of temperature, it's
12 a question of the duration of the heating as well?
13 A. Yes, it's both.
14 Q. Yes, and you say that albumin is one of the most stable
15 to heat and Factor VIII is one of the least stable,
16 because of that albumin was the first plasma product to
17 be subjected to a heat treatment process. Then you
18 mention Dr Cohn, and we learned, I think, in block 2
19 that in Cohn fractionation, Fraction I is where
20 Factor VIII would be found. Is that correct?
21 A. It would, yes.
22 Q. Yes, and for those who want to do some further reading
23 on the work of Edwin Cohn, it is dealt with in
24 Douglas Starr's book, and no doubt numerous other places
25 as well, but in Douglas Starr's book, chapter 7, the

1 process is described.

2 You then explain to us that successful treatment of
3 casualties at Pearl Harbor led to the large-scale
4 production of human albumin, but obviously the albumin
5 had to remain usable. You give us the example that it
6 had to be treated so that it could withstand storage in
7 a tank in Tobruk, and then the happily named Dr J Murray
8 Luck discovered chemicals which could enhance the heat
9 stability of albumin:

10 "So profound was the effect that it was suggested
11 that albumin might tolerate pasteurisation which could
12 be used to destroy bacterial contaminants instead of
13 using a mercury preservative. So a modified product
14 that had been heated in solution and pasteurised for ten
15 hours at 60 degrees was introduced in the United States
16 from June 1945."

17 Just pausing briefly to mention Pasteur himself, not
18 least because we have already talked about Robert Koch,
19 so it seemed only right to talk a little bit about
20 Pasteur. As far as I could discover, he was initially
21 approached to see if he could offer anything to solve
22 the problem of wine and beer becoming sour and it was in
23 that context that he developed his process in the 1860s.
24 It's also interesting to note that he met Robert Koch in
25 London in 1881, interesting perhaps.

1 THE CHAIRMAN: Just thinking of the Koch-Pasteur hypothesis.
2 There must have been something come out of it.
3 MS DUNLOP: What is the defining characteristic of
4 pasteurisation?
5 A. The defining characteristic is that the heating is
6 carried out with the protein when it is dissolved. So
7 it's actually in solution. It's a liquid. And heating
8 can take place at whatever temperature and time is
9 appropriate but the key thing is that it's the liquid
10 that is being heated, and the objective here was to
11 destroy bacteria, as it was with Louis Pasteur in the
12 original process, and when you pasteurise milk also.
13 Q. Yes. What about the cooling aspect of pasteurisation?
14 Is there an expectation that in a pasteurisation process
15 the product will be cooled quite rapidly, or not
16 necessarily?
17 A. It depends how the pasteurisation is carried out. In
18 some cases it can be carried out in a large bulk vessel
19 and that would take a long time a cool down. In other
20 cases, as in the film that you have just seen, it is
21 done in individual bottles and they cool down more
22 quickly, and you may be able to cool the bottle. If it
23 is done in the bottle like that, you can add cold water
24 to cool it down, just to prevent any damage to the
25 protein, because it is a fine line between inactivating

1 the bacteria, or in our case the virus, and destroying
2 protein. So you don't want to have it sitting around
3 for a long time at, say, 55 degrees. You just want to
4 do the ten hours at 60 degrees and have that defined and
5 bring the temperature down relatively quickly, but it is
6 a difficult problem.
7 For example, in our case we designed -- what you saw
8 were spray cabinets, where the material would cool down
9 quite quickly, whereas at the same time I think at BPL
10 they used a hot air oven for their albumin
11 pasteurisation, and that took longer to heat up and to
12 cool down. So there were these nuances, if you like.
13 Q. Right, but it is not a key feature?
14 A. It is not a key feature, no.
15 Q. That it has to cool rapidly, it really depends on
16 whatever you are pasturising?
17 A. The key thing is that you meet the defined conditions.
18 If we say ten hours at 60 degrees, then we can be sure
19 we have achieved that in every bottle.
20 Q. Can we move to the next page, please, and see you
21 dealing with human immunoglobulin. An equivalent method
22 for stabilising immunoglobulins could not be found and
23 the project was abandoned. Then we move to hepatitis,
24 serum hepatitis, so at that point what we are really
25 talking about is Hepatitis B. Is that right?

1 A. Yes.
2 Q. Yes. Dr Cohn --
3 A. It is difficult to distinguish because there may have
4 been cases of serum hepatitis that we would now regard
5 as Hepatitis C but at that time we just don't know.
6 Q. I appreciate the difference.
7 So Dr Cohn was suggesting studies to determine what
8 would be needed by way of heating to destroy the
9 infective agent responsible for hepatitis, and it's
10 interesting to note that the American National Institute
11 of Health financed studies using prison volunteers as
12 subjects. Obviously those experiments were successful
13 in that none of the recipients of the albumin that had
14 been heat-treated developed jaundice.
15 Then you go on to explain some of the other
16 scientific work in the early days and really leading to
17 the conclusion that pasteurisation of albumin was
18 a successful inactivation step. But then you note, in
19 the penultimate paragraph on that page, that
20 pasteurisation was less successful in eliminating
21 Hepatitis B and that that could be demonstrated once
22 a test was available for Hepatitis B. Retrospective
23 testing could be carried out and it was discovered that
24 pasteurisation had been less successful in eliminating
25 Hepatitis B.

1 A. That was pasteurisation of plasma, which had not been
2 fractionated.
3 Q. Right. Then you say that cold ethanol fractionation
4 became the recommended procedure for the manufacture of
5 albumin and immunoglobulin products with albumin being
6 pasteurised for ten hours at 60 degrees.
7 A. Yes, the key thing here is that some of the virus was
8 being removed by the fractionation process as well as by
9 pasteurisation. So it was the combination of the two
10 that was fully effective.
11 Q. Yes. We have had some evidence about the pasteurisation
12 process in connection with albumin in the context of our
13 enquiry into Mr Tamburrini's situation, and on the next
14 page you refer to an incident in the United States
15 whereby hepatitis was transmitted by a number of batches
16 of PPF. I think that was an article by Pattison. You
17 mentioned that article which we looked at in that
18 context. You weren't here then, I don't think?
19 A. No.
20 Q. But we have obviously had some evidence about that.
21 Then 1.2, you deal with attempts to treat
22 coagulation factors to destroy viruses. You quote from
23 a textbook by Webb, that albumin could be pasteurised at
24 60 degrees for 10 hours but the other fractions are heat
25 labile, in other words, heat changeable. So will be

1 changed by heat. Is that right?

2 A. It means destroyed by heat.

3 Q. Yes. That's a book dating from 1964. So a prevailing

4 view then. Just to give the reference without looking

5 at it because what you have supplied says what you say

6 it says. That's [PEN0121484].

7 Then you list a number of different methods which

8 were tried, which I think could broadly be summarised

9 under three headings, that people tried firstly adding

10 chemicals, secondly, the effects of radiation, and

11 thirdly, heat. Is that a reasonable summary --

12 A. Yes, I think that's fair enough.

13 Q. -- of what was going on?

14 One that was interesting is the third bullet,

15 "Pasteurisation of plasma for four hours at 60 degrees",

16 and I suppose what jumps out at us about that one is

17 that the time is much shorter, the four hours, and also

18 the fact that it was the plasma in its entirety which

19 was being pasteurised and presumably without the

20 addition of any stabilisers?

21 A. Certainly not the stabilisers that Edwin Cohn was using,

22 no.

23 Q. Yes, and then we notice in the fourth bullet that:

24 "Storage of plasma for six months at 30 to 32

25 degrees centigrade ..."

1 And the "Allen" mentioned there as in fact
2 Garrot Allen whom we have heard of already, and we are
3 going to see him cropping up today later as well.
4 Various other attempts. Nitrogen mustard, I had never
5 heard of before. I don't imagine it's anything like
6 Colemans?
7 A. It's better known as mustard gas.
8 Q. Then you say:
9 "None of these procedures successfully eliminated
10 infectivity from Factor VIII concentrates without
11 causing unacceptable damage to the product."
12 A. Can I just make one comment here and that is that
13 I don't know that this list is definitive because, of
14 course, in many cases investigators don't publish
15 negative results.
16 Q. I see. Can we look at the next page, please?
17 You describe for us attempts physically to remove
18 viruses from coagulation factors, and we can see the
19 word "adsorption" cropping up there too. So that would
20 be an attempt to get the virus to bind to silicic acid.
21 That would be the first bullet, I guess. And various
22 other attempts, but again you say none of those was
23 applied successfully to the routine manufacture of
24 plasma products and research was generally superseded by
25 the research of the 1980s.

1 So having looked at these sections, 1.2 and 1.3, one
2 can see that between 1944 and 1983 there were a lot of
3 attempts made, trying various different techniques, but
4 nothing you have listed here was successful in achieving
5 the aim of dealing with the virus.
6 A. Yes, that's my understanding.
7 Q. Right. Then in section 2, "Development of heat
8 treatment of coagulation factors worldwide", you say:
9 "A number of methods were devised in the early
10 1980s, with the objective of inactivating the agent
11 responsible for non-A non-B hepatitis. These methods
12 involved heating the coagulation factor either dissolved
13 in solution (pasteurisation) or in the form of
14 freeze-dried powder."
15 People were basically trying to apply as much heat
16 as they could before the product was damaged. You say:
17 "Pasteurisation was undertaken for ten hours at
18 60 degrees with dry heat treatment methods ranging from
19 [that] up to 72 hours at 68 degrees."
20 You give us a benchmark about the respective
21 temperatures, which is certainly interesting when one
22 considers that we are talking about these temperatures
23 well above normal human body temperature, with
24 presumably anticipated effects on proteins which are
25 normally in the human body.

1 A. Yes, I think it is quite interesting to look at it from
2 that point of view.
3 Q. Then you list some of the early heat treatment
4 procedures, and these are summarised in an article by
5 Kasper, which we can just, I think, glance at briefly
6 because it's an article we have looked at before. It's
7 [SGH0021947]. It is a very useful summary of the
8 preparation of clotting factor concentrates and attempts
9 to inactivate viruses. The first bullet that you record
10 on page 1323 is "pasteurisation":
11 "Heating a solution for ten hours at 60 degrees ..."
12 Can we look at 1952 in the article, please? We can
13 see in fact the descriptions of the various different
14 concentrates, marketed by the different manufacturers,
15 beginning there. This is Armour, which is the first
16 manufacturer dealt with in the article. It's quite
17 interesting to see in their virus inactivation column,
18 dry heat and pasteurisation listed, and an interesting
19 footnote there that Humate -- and you say this,
20 obviously. You say this in your paper. Humate, if we
21 look at the key, that product, although marketed by
22 Armour, was something manufactured by Behringwerke, and
23 as we will come on to see, it was Behring who really
24 made the dramatic announcement in the early 1980s about
25 their apparent success in pasturising Factor VIII. Is

1 that correct?

2 A. That's true.

3 Q. Can we look at 1954 as well, please, so two pages

4 further on? If we go down to Cutter. We have come

5 across before the fact of these companies being referred

6 to by different trading names, which can be a bit

7 confusing. Cutter, sometimes linked with Bayer, they

8 also have Koate. We can see the first heat-treated

9 Koate is HT, licensed in February 1984, that's a dry

10 heat-treated product, but then HS, which is

11 a pasteurised product. That was licensed at least by

12 the FDA from April 1986, and I think these are the two

13 companies, or the two different products, that you are

14 referring to in your paper. Is that right?

15 A. That's correct.

16 Q. Then can we go back to the paper, dry heat treatment.

17 You list various different formulations of that. I just

18 wanted to ask you about the second bullet:

19 "Heat treatment of freeze-dried powder of

20 Factor VIII for 24 hours at 60 degrees in the presence

21 of the organic solvent n-heptane."

22 Why is that not pasteurisation, if there is

23 a solvent involved?

24 A. I regard it as a dry heat process, because the

25 Factor VIII is in the state of a dried product. It's

1 the dried powder that is suspended in the organic
2 solvent, and the purpose of the organic solvent is to
3 increase the heat transfer, if you like, throughout the
4 dried material, but the Factor VIII itself is still in
5 the dried form.
6 Q. I see.
7 A. It's sometimes referred to as "wet heat". You will find
8 it in publications described as "wet heat", which
9 personally I think is incorrect.
10 Q. Right, for our purposes perhaps all we need to know is
11 that the Factor VIII is suspended in the heptane but not
12 dissolved in it?
13 A. That's correct, yes.
14 Q. Right, thank you. You say:
15 "The dry-heated products were approved in the
16 United States in 1983 but weren't widely used because
17 they weren't proven to be effective in destroying
18 viruses. There was concern patients might be harmed and
19 they were more expensive. Commercial dry-heated
20 concentrates were not licensed for use in Britain
21 until February 1985 for similar reasons."
22 Then you tell us some of the obstacles that lay in
23 the path of those trying to develop the heat treatment
24 of coagulation factors. Firstly, the sensitivity of
25 Factor VIII and related proteins to heat, the difficulty

1 of manufacturing Factor VIII and the lower yields which
2 resulted. Then on the next page, a long list of
3 difficulties. And when I read this, I was reminded of
4 your evidence in May when we spoke about what it was
5 like in the early 1980s, trying to produce enough
6 Factor VIII concentrate, that it was a kind of race,
7 trying to catch a runner in front who was always just
8 disappearing over the horizon and you felt you were
9 running uphill as well. Do you remember our discussion?
10 A. Yes.
11 Q. Yes. I think we see some of the points being made here,
12 that it was really very difficult, if not impossible, to
13 satisfy all the different requirements.
14 A. It was very difficult, yes.
15 Q. Because as soon as you start introducing another process
16 step, there is likely to be a yield penalty, and a yield
17 penalty is the last thing you want because you are
18 trying to satisfy not just a high demand but
19 a constantly increasing demand. Is that a reasonable
20 way of putting it?
21 A. That's correct. I wouldn't say the yield penalty was
22 the last thing we wanted but it was certainly
23 undesirable.
24 Q. Yes, and so you were trying really to develop these
25 methods of viral inactivation at a point where demand

1 was increasing. Then another interesting bullet in this
2 list is the penultimate one, about the failure of the
3 chimpanzee model in predicting the effectiveness of heat
4 treatment procedures, and I'm going to make reference to
5 this more than once but if we could go back to the
6 article from Transfusion, that's [SGH0021947]. Can we
7 go to page 1950 in that, please? We can find a little
8 bit more information about the failure of the chimpanzee
9 model. If we look, I think, on the left-hand side.
10 I think it's about eight lines into the last paragraph:
11 "The first dry-heated Factor VIII licensed in 1983
12 proved capable of transmitting Hepatitis B to
13 chimpanzees but didn't appear to transmit non-A non-B to
14 those animals."
15 This is the Hyland product. This is Hemofil. Is
16 that right?
17 A. I think so, yes.
18 Q. Then it says:
19 "However, in a later study in humans, this product
20 transmitted non-A non-B hepatitis to 84 per cent of
21 infants and children who were treated exclusively with
22 it."
23 So as I understand it, this particular episode,
24 involving chimpanzees, the chimpanzees got Hepatitis B,
25 or some of them got Hepatitis B, but not non-A non-B

1 hepatitis and then there was a sort of mirror image with
2 the humans, a very large number of whom got non-A non-B
3 hepatitis?
4 A. It's important to emphasise that in the studies with
5 chimpanzees, the product had virus deliberately added to
6 it and then heated to see if that amount of virus could
7 be destroyed by the heat treatment process, whereas in
8 the human studies, of course, no virus was added
9 deliberately, that was just the normal plasma pool that
10 was used.
11 Q. Right. Actually, Mannucci -- I'm not sure if he is
12 Professor Mannucci or Dr Mannucci. I'm not sure what
13 title to use for him. He also comments on this in one
14 of his articles, if we could have a look at that,
15 please. That's [LIT0010369]. Can we go to page 0371,
16 please? This is in fact the article from 1985, which
17 records quite long lasting monitoring of patients given
18 this particular product. If we look on the right-hand
19 side of this section, which is the discussion section,
20 and we go further down, please, we can see there the
21 author's comment. This is about the middle, I think.
22 The sentence:
23 "The high prevalence of non-A non-B hepatitis and
24 the absence of Hepatitis B transmission in our subjects
25 are in contrast with the Hepatitis B transmission and

1 the absence of non-A non-B hepatitis in chimpanzees
2 given the same heated concentrate. These differences
3 indicate that the animal model is not reliable for non-A
4 non-B hepatitis transmission studies."
5 So you would agree with that, I take it? I think
6 that's the point you are making --
7 A. That was the point I was making, yes.
8 Q. -- about the unreliability of the chimpanzee model.
9 I have also seen, Dr Foster, references to viral
10 interference. Is that a phenomenon that one encounters?
11 A. I'm not a virologist.
12 Q. Right.
13 A. But I have seen similar discussions as to perhaps there
14 could be interactions and interference between the
15 different viruses. I don't really know how to interpret
16 that.
17 Q. We certainly don't. It's just the term was not too
18 difficult to understand, because I suppose one can
19 envisage that if the two different viruses are present,
20 one may affect the other or they may affect each other
21 in some kind of way?
22 A. I think in some of these animal studies there's a lot of
23 speculation as to what might be happening and why the
24 results came out the way they did, and I would be
25 nervous about over interpreting what people meant at the

1 time.

2 Q. I think all we need to take from it is that you can't

3 just extrapolate from whatever happens to the

4 chimpanzee?

5 A. No, I think the chimpanzee was seen, certainly in the

6 United States, as a first step, and if your products

7 appear to be safe in the chimpanzee then the technique

8 might be effective and it was worth then going to

9 studies in monitoring patients. And also I think the

10 chimpanzee data were when the FDA used to award these

11 licences. And of course, when the same companies came

12 to apply for licences in the UK, they were rejected

13 because by then the UK authorities were aware that the

14 patients were being infected.

15 Q. Right. The next section, if we can go back to your

16 paper, please. The next section, which begins on

17 page 17 of [PEN0131309], does deal with AIDS and events

18 towards the end of 1984. So I want to leave this section

19 for the moment because I would like to try and come to

20 that later. So we can simply note that we have looked at

21 the dry-heated product, Hemofil, the Hyland product, which

22 emerged in 1983 and its failure to prevent non-A non-B

23 hepatitis and now I would like to skip on, if I could,

24 to page 23 of [PEN0131309], where you deal with what

25 are called "platform technologies", and "platform

1 technology" I understand to mean the creation of
2 products or processes to support present or future
3 development. Is that a reasonable working definition?
4 A. Yes, that would be fair enough.
5 Q. Right. Thank you. Here we find, 3.1:
6 "Improved cryoprecipitate by continuous thawing of
7 plasma."
8 We have obviously already mentioned this and I think
9 the article that you refer to at the end of the third
10 paragraph there, "Foster et al, 1982", is one of those
11 that was appended to your manufacturing process
12 statement. Is that right?
13 A. That's correct.
14 Q. I may have juxtaposed digits here - not juxtaposed,
15 reversed - but we will try it and see, [LIT0010790].
16 That's you discussing the large-scale plasma thawing
17 and we see the point made there that you alluded to
18 earlier, about the introduction of a process of
19 continuous plasma thawing having generated an increase
20 in both yield and purity of over 50 per cent. Then can
21 we go back to the paper, please, back to page 1331?
22 Obviously, when you found that this was a successful
23 step, you moved as swiftly as you could to replace your
24 established process of batch thawing by continuous
25 thawing and that happened, I think, in the summer of

1 1979. We noticed in the earlier paper that you replaced
2 a processing rate, as it were, of 70 litres per hour
3 with one of 200 litres per hour. Is that the same step?
4 A. Yes, this is the process and in July 1979 it was
5 70 litres an hour and it stayed at that level
6 until January 1981, when it was increased to 200 litres
7 an hour.
8 Q. Right. Then can we move on to the next page, please?
9 It was this very product, in fact, that was able to
10 withstand dry heating for two hours at 68 degrees. You
11 didn't have to do anything more to the product?
12 A. No, the two hours at 68 degrees was defined because that
13 was what would work with that product. We didn't say,
14 "We are going to heat it to this temperature at this
15 time and will it work?" It was the other way round. It
16 was, "What will work with this product?"
17 Q. I see. You say that essentially what you were able to
18 do at that point was to do a kind of swap. So not only
19 were you able to begin heat-treating product, and you
20 were able to heat-treat your stock of product, but you
21 were also able to recall unheated stocks and this all
22 happened at the turn of the year 1984/1985?
23 A. And there was quite a large inventory of material that
24 has to be dealt with and this gave us the ability to do
25 that very quickly.

1 THE CHAIRMAN: Dr Foster, were you involved in the recall
2 process?
3 A. No, I wasn't.
4 THE CHAIRMAN: I have an interest in whether it extended to
5 the regional centres and hospitals or whether it went so
6 far as to capture individual stocks of particular
7 patients in their own homes, for example.
8 A. My understanding is that from our perspective the
9 intention was to go right into the patients' home.
10 THE CHAIRMAN: To take everything?
11 A. You would need to discuss that with Dr Perry, I think.
12 THE CHAIRMAN: Thank you.
13 MS DUNLOP: The next platform technology that you deal with
14 is the use of zinc, and I think in fact if we were to go
15 back to your processing statement we would see zinc
16 being added as a new step. I think it is in the middle
17 column? I don't want to go back to it but in column C
18 we see the zinc precipitation being added as a step
19 between 1986 and 1991. Is that right?
20 A. That's correct.
21 Q. Yes. And this was thanks to a visit by Dr Milan Bier.
22 Is that correct?
23 A. That pronunciation is correct.
24 Q. Thank you. All of this, of course, the use of the zinc
25 precipitation, was taking place in the context of

1 pasteurisation work which you were carrying out. Is
2 that right?
3 A. That's right.
4 Q. Yes. On the next page you say that not only were you
5 trying to reduce the fibrinogen to support the
6 pasteurisation but also the haemophilia directors had
7 advised that a reduction in the fibrinogen content of
8 Factor VIII was desirable clinically and that reference
9 is to a meeting in March 1981. If we just have a look
10 at the minutes of that. That's [SNB0015064].
11 I wondered, it doesn't seem to be dealt with explicitly,
12 Dr Foster. Is it really just all within the context of
13 the discussion in paragraph 11? Can we go to the page
14 that shows paragraph 11, please? I think it might be
15 two pages in.
16 It looks as though there has been quite
17 a wide-ranging discussion of the clinical role of the
18 products, and would it be in that context that the
19 doctors would be saying that they wanted something of
20 greater purity?
21 A. My memory of this is quite clear because at this meeting
22 I remember asking the doctors present what they wanted
23 us to do, and the only answer I got at that time was
24 from Dr Ludlam and he explained that the reduction in
25 the fibrinogen content would be very helpful because he

1 thought that wasn't clinically desirable because people
2 with haemophilia have a normal fibrinogen level, so we
3 were giving excess fibrinogen which he thought wasn't
4 clinically desirable. So I took that away from the
5 meeting that he really wanted that from a clinical
6 perspective to have a lower fibrinogen content. And of
7 course, from our point of view and trying to develop
8 pasteurisation, we also wanted to achieve that from
9 a processing point of view.
10 Q. Right. So everybody was on the same side?
11 A. Yes.
12 Q. Yes.
13 THE CHAIRMAN: Can I just ask a question? It really relates
14 to a later period. Is the concentration of fibrinogen
15 the same as purity. I am sure it is not totally the
16 same as purity but when one is talking about "purity",
17 does it relate to the presence of other proteins,
18 including fibrinogen?
19 A. It does.
20 THE CHAIRMAN: So a high level of fibrinogen would mean
21 a reduced level of purity?
22 A. It would mean an increased purity. A high level of
23 fibrinogen is a reduced purity and a low fibrinogen is
24 a higher purity. In the intermediate purity product, 50
25 to 60 per cent of that material was fibrinogen.

1 THE CHAIRMAN: So Dr Ludlam is pressing for higher purity in
2 effect, at this stage in 1981?
3 A. Yes.
4 THE CHAIRMAN: Thank you.
5 MS DUNLOP: Yes. So higher purity, specifically less
6 fibrinogen?
7 A. Yes.
8 Q. Yes. Can we go back, please to the paper? We are now
9 at page 25 of [PEN0131309]. There is a passage in italics
10 and this is really, I think, taking us beyond where we need
11 to go at the moment, but you say that:
12 "Whilst studying the use of the SNBTS zinc heparin
13 precipitation process, scientists at PFL discovered an
14 alternative method for the precipitation of fibrinogen
15 and fibronectin using a much higher concentration of
16 heparin."
17 According to Dr Smith, that was actually a mistake.
18 Is that your understanding?
19 A. Yes, that's my understanding.
20 Q. Yes. So the technician made a calculation error and
21 added far too much heparin?
22 A. Yes, the heparin that we used was clinical product and
23 it was highly concentrated. Large amounts of heparin in
24 a small volume. And in order to provide the amount that
25 we were using, we had to dilute it quite considerably

1 and it was a mistake in that calculation led to the
2 discovery at Oxford.
3 Q. Right. When that happened, that mistake happened at
4 Oxford, did anyone tell you?
5 A. Yes, we were aware -- and I think this was probably my
6 colleague, Dr McIntosh, who learned this talking to
7 Mrs Winkelman who worked with Dr Smith, that that was
8 what had happened. I can't say exactly when we knew
9 that but we did learn of that.
10 THE CHAIRMAN: Sorry, the timing fascinates me, I have to
11 say. When it was discovered that there had been this
12 overuse, as it were, of heparin.
13 A. Dr Smith did write to me to say that he had made a -- he
14 said he had literally stumbled on something and there
15 was a letter in --
16 THE CHAIRMAN: I have seen --
17 A. Which I think is May 1984, something like that.
18 THE CHAIRMAN: Before or after the Winkelman patent?
19 A. Much before. This was the beginning of the process that
20 led to the Winkelman patent. The Winkelman patent was
21 a year further on because they had to refine the process
22 and procedure.
23 MS DUNLOP: Dr Smith does explain this, sir, and I'm
24 certainly intending to ask him a bit about it when he
25 comes.

1 THE CHAIRMAN: Just reading things, I had a question in my
2 mind about the utility of the Winkelman patent, if it
3 depended upon an error, as to the concentration to be
4 used --
5 A. I would call it serendipity, and it happens quite a lot
6 in science, and the key thing here is that the
7 investigator recognised what was happening. You could
8 apply that to the discovery of penicillin.
9 THE CHAIRMAN: Serendipity is great at the start but if it
10 persists after you put in your specification, it tends
11 to undermine the validity of your patent. That's the
12 point I'm interested in.
13 MS DUNLOP: The third technology you discuss is the
14 stabilisation of Factor VIII with calcium. As
15 I understand that, what seems to have been happening was
16 that the addition of sodium citrate was thought to have
17 been responsible for the removal of calcium from the
18 Factor VIII. Is that right? And that removal of
19 calcium -- and this is reading on from the next page --
20 was thought to be destabilising the Factor VIII.
21 A. Yes, I mean, we now know that calcium is an important
22 molecule in the structure of Factor VIII and it helps to
23 hold the molecule together, and that wasn't known at
24 this time and so my observations were purely empirical,
25 and I observed that the Factor VIII activity was falling

1 away with time and that seemed to coincide with the
2 addition of this citrate and it was from that that
3 I developed the idea of adding calcium to retain the
4 stability of the Factor VIII.
5 Q. You go on to tell us that you used that technology and
6 you shared this information with BPL and they used it in
7 their preparation of 8Y. You say it was also one of the
8 changes made by Behringwerke in their modified version
9 of pasteurised Factor VIII, Hemate. I actually looked
10 for Hemate, was that a successor to Humate?
11 A. It would be the same thing. I think in America they
12 just gave it a different name.
13 Q. The terminology is confusing sometimes. Then you say:
14 "The addition of calcium has since become virtually
15 universal in the preparation of Factor VIII
16 concentrates, both from plasma and by recombinant
17 technology."
18 That is something that you personally discovered?
19 A. I had a role in it, yes.
20 Q. Right, thank you. Then 3.4. We have spoken about sugar
21 before but essentially what's summarised here is the
22 discovery that adding a little bit of sugar was what
23 enabled you to increase the heating time from two hours
24 to 24 hours in the early part of 1985. Is that right?
25 A. That's correct.

1 Q. Then lastly here, the addition of sodium chloride. So
2 you discovered that a coagulant activity of Factor VIII
3 in solution was lost when the concentration of sodium
4 chloride fell below a critical level, and obviously
5 redressing that was an improvement too, but again
6 I think time-wise we are kind of going beyond the period
7 on which we are mainly focusing at the moment, because
8 I think that belongs in the 1986 to 1991 category. Is
9 that right?
10 A. That's correct.
11 Q. Thank you. Then section 4, "SNBTS development of
12 heat-treated Factor VIII". You have set out firstly for
13 us management processes, which I think we can probably
14 take as read, Dr Foster. First of all, you describe
15 national management. We know that there were meetings
16 between SNBTS and the haemophilia directors and SHHD.
17 Then SNBTS management structures and PFC, and then in
18 4.2 you address communications between SNBTS and the
19 English fractionation arm, as it were, which is BPL,
20 Blood Products Laboratory. I think later known as
21 "Bioproducts Laboratory". Is that right?
22 A. That's correct, yes.
23 Q. A bit like UKHCDO. If you keep the same initial letter,
24 you can change the word. Then PFL, which was their
25 fractionation laboratory.

1 A. That was in Oxford. That was the plasma fractionation
2 laboratory and that dealt only with coagulation factors.
3 Q. Yes. So BPL was at Elstree, I understand?
4 A. That's correct, yes.
5 Q. And PFL was at Oxford, and actually PFL, I think, was
6 situated right next door to the Oxford haemophilia
7 centre?
8 A. Yes, it was the Churchill Hospital in Oxford.
9 Q. Yes. Did you ever feel that you lost something by not
10 being right next door to the clinicians?
11 A. No, I didn't feel that. We had very close contact with
12 clinicians whenever it was required.
13 Q. Right. Then you have described the links that there
14 were between Scottish personnel and the English
15 personnel and national directors, and then heads of
16 research and development, and we know that Dr Smith, who
17 was the chief scientist responsible for developments at
18 PFL, was ex-PFC anyway, which presumably got the
19 communications off to a good start?
20 A. Yes, we knew each other very well from that time.
21 Q. And then research and development scientists were in
22 contact as well. Heads of quality.
23 Then, on to the next page, you discuss some joint
24 development projects, two in particular, one which again
25 is slightly beyond our current time period, "Virus

1 Inactivation Studies of 8Y". I think one could call it
2 the severely dry-heated English product. Is that right?
3 A. That is correct.
4 Q. Yes. That's 80 degrees for 72 hours?
5 A. Yes.
6 Q. Yes. And then, secondly, studies on the thrombogenicity
7 of heat-treated Factor IX. We have alluded to this
8 already, that, because of a risk of thrombosis, clot
9 formation, with heat-treated Factor IX, some extra steps
10 were required before it could be introduced for
11 patients. Is that right?
12 A. A study was required to be sure that the product would
13 be safe.
14 Q. Yes, and that involves dogs?
15 A. That's correct, yes.
16 Q. Quite a lot of reference to dogs actually and I think we
17 will come back to dogs later.
18 Then, 4.3, you are talking about background, and
19 this is background to your development of heat-treated
20 Factor VIII. Dr Johnson crops up here and you tell us
21 that initially, when you started preparing intermediate
22 purity Factor VIII in 1975, you were losing some
23 Factor VIII activity at the filtration stage and there
24 was a temperature solution to this problem. Is that
25 right?

1 A. That was Dr Johnson's advice, yes.
2 Q. Yes. But in fact the change that you made on
3 Dr Johnson's advice rather pointed in the other
4 direction?
5 A. It did, yes.
6 Q. Yes. So I think, as I understood it, Dr Foster, your
7 point, in referring to this, is that you, acting on the
8 advice of Dr Johnson, raised the temperature at which
9 the filtration was being carried out from 20 degrees to
10 30 degrees and, because of a loss of Factor VIII
11 activity in that simple 10-degree increase, that was
12 another reason for thinking that any further heating of
13 Factor VIII would be damaging to the product. Is that
14 right?
15 A. Yes, it's an illustration of the sensitivity of
16 Factor VIII to heat, in terms of the knowledge that we
17 had at that time.
18 Q. Why were you doing it at 20 degrees in the first place?
19 A. You have to ask Dr Smith. He designed that process.
20 But that's what he chose to do.
21 Q. Fine. I don't imagine it matters.
22 Then we can read on to the following page and you
23 explain the logic of the point I have just put to you,
24 that just that small, 10-degree, increase had a adverse
25 effect on Factor VIII activity and you say:

1 "It seemed inconceivable that Factor VIII could be
2 treated at a temperature high enough to eliminate the
3 risk of hepatitis transmission."
4 Then, another interesting piece of the story,
5 a collaboration with Dr Johnson on research into the
6 adsorption of Factor VIII to solid phase polyelectrolytes.
7 You were using reagents that came from Monsanto but for
8 essentially selfish commercial reasons Monsanto drew the
9 line at allowing commercial exploitation of this. Is
10 that right?
11 A. That's my understanding.
12 Q. Yes. Perhaps one should say "self-interested", rather
13 than "selfish". Then further research was carried out
14 but using reagents that were commercially available.
15 A. I ought to say, just for completeness, that this
16 polyelectrolyte process, these reagents, were allowed to
17 be used by Monsanto for a company called Speywood. It
18 was based in the UK. But they were manufacturing
19 Factor VIII from porcine plasma, from pig plasma, and it
20 was specifically to treat patients with inhibitors, who
21 would react to human Factor VIII, but I don't think it
22 ever went into production of human Factor VIII.
23 Q. So a much more limited application?
24 A. Yes.
25 Q. Yes. At this point I would like to move to the actual

1 statement that you have provided, Dr Foster, which is
2 [PEN0121438]. That statement, actually, should be read
3 with a schedule, which was the set of questions sent to
4 you, and this is [PEN0121531]. I think we are probably
5 going to dot between those documents, so it is as well
6 to keep them both open, if we could, please.
7 So, trying to pick up the thread here of what was
8 happening in the early days of such research at PFC --
9 yes, we have the schedule. You were asked about
10 research in the 1970s and I think we may have thought
11 that there were two different projects -- but I think
12 there probably was only one -- in relation to the
13 removal of Hepatitis B from Factor IX. Is that right?
14 A. There was one from Factor IX, and the other one that we
15 have just mentioned, which was the polyelectrolyte
16 method, is actually noted in one of the documents here,
17 which was a report that had John Watt's name on it.
18 I think it was dated 1973 and he does talk about
19 polyelectrolytes. So that work was actually underway at
20 that time but there were no publications at that time.
21 Q. Right. We asked you firstly about a report. We thought
22 it had been prepared by Mr Watt in December 1973.
23 I think we will just look at that, if we could, please:
24 [SNB0016903]. Dr Smith has actually said he thinks
25 he -- he uses the word "assembled" this report.

1 I suppose what he means is he wrote it. But it has
2 a front sheet giving Mr Watt's' name. I don't suppose
3 you are in a position to comment on who wrote it?
4 A. No, I'm not in a position to comment on that.
5 Q. Right. This I understand to be essentially a summary of
6 the products that were available at the time of writing.
7 Perhaps we could just look through it.
8 "Development of Factor VIII concentrates". This is,
9 I think, quite a technical description of the story so
10 far in terms of the preparation of Factor VIII, but
11 I don't think there is any mention of viral inactivation
12 in this.
13 A. Oh, no, there wouldn't be.
14 Q. Right. Then the other document that we referred you to,
15 could we just pass on and look at that? That's
16 [SNB0104779]. This is the report of research and
17 development from 1975 and by that time you were at PFC;
18 is that right?
19 A. I joined in January 1973.
20 Q. Yes. Sorry, so you were there at the time of the
21 earlier report too.
22 This does mention viral inactivation research and
23 I think, if we could look at what is our page 11 in the
24 document, we can see at 2.2 -- this is the reference
25 that's in the question -- that there had been a paper

1 presented at the Congress of the International Society
2 of Thrombosis and Haemostasis in Vienna, and the paper
3 concerned the removal of Hepatitis B antigen from
4 coagulation Factor II, VII, IX and X concentrates. What
5 we should understand from that description, Dr Foster,
6 is that this is one product with all these factors in
7 it. Is that right?
8 A. This would be DEFIX.
9 Q. Yes. I think it's possible --
10 A. Actually, no, I'm wrong because DEFIX didn't have
11 Factor VII. This is an earlier product. I'm sorry
12 about that.
13 Q. I think the only point I was going to make is that
14 sometimes, when one reads information about these
15 concentrates for the treatment of Haemophilia B, it can
16 be a bit confusing because you don't realise you are
17 dealing with the sort of amalgam of the different
18 factors.
19 A. Yes, I ought to explain there were two types of
20 Factor IX concentrate, one of which contained
21 three factors and one of which contained four factors.
22 In Johnson's work he was looking at both types of
23 product because he had samples from companies that
24 manufactured the four factor style of product, and
25 that's what's mentioned in this title.

1 Q. Right. Could we go back, please, to page 5, our page 5,
2 of this document. Look at section 2.1. This is
3 a description of ongoing work:
4 "Preparation of a Factor IX concentrate with reduced
5 Hepatitis B antigen activity."
6 And this is:
7 " ... optimisation of Factor IX recovery and removal
8 of HBAg from DEFIX by manipulation of the pH ..."
9 Et cetera. The participants in that are shown as
10 Dr Smith and Mrs Middleton and it had begun in 1971 and
11 had about 18 months left to run. So this was as at
12 1975.
13 So, Dr Foster, what's the connection between that
14 project and the paper that had been delivered in Vienna?
15 A. It's the same project.
16 Q. The same? Right, good. Thank you.
17 Can we look at your answer, please, if we could go
18 back to your statement? That's [PEN0121438] at the
19 second page. You give us a great deal more information
20 about this period. You tell us in writing what you have
21 told us today, that there was research in relation to
22 removal of Hepatitis B from Factor IX and also from
23 Factor VIII concentrates and both projects were
24 collaborations with Dr Johnson at New York University.
25 Both projects concerned removal of Hepatitis B because

1 it was the only virus known to be transmissible via
2 plasma products at that time, and also you had a marker
3 so you could track what was happening to it, which must
4 improve any project of this nature, I imagine?
5 A. Yes, I should point out it was Dr Johnson who was
6 actually doing the work with hepatitis. We were
7 refining the process parameters, looking at where the
8 Factor IX would distribute and what would happen to the
9 process, and he was making the measurements on
10 hepatitis.
11 Q. Right. I reminded myself of how Dr Johnson came to
12 collaborate with PFC by looking at your evidence from
13 10 May. You said that there had been a chance meeting
14 between Mr Watt and Alan Johnson in Australia in 1966
15 and that you personally became good friends with
16 Dr Johnson and that Dr Johnson became, probably, one of
17 the world's leading experts in the development of
18 Factor VIII concentrates. So that's the Dr Johnson we
19 should have in mind when we find him referred to in
20 these papers?
21 A. That's correct. I think by 1966 he was regarded as
22 a world expert in this area.
23 Q. So it was really very fortunate that PFC was able to
24 have his assistance, and no doubt it worked in both
25 directions?

1 A. It was very helpful, yes.
2 Q. Can we read on to the next page, please? This is you
3 talking about the Factor IX project and you say that you
4 had studied PEG precipitation during your PhD, "PEG"
5 standing for "polyethylene glycol". Is that right?
6 A. That's correct.
7 Q. In fact it is the "PEG" of "pegylated interferon"?
8 A. Yes, it probably is.
9 Q. My understanding of its function there -- and
10 Professor James will correct me if this is wrong -- is
11 that it enables the interferon to remain in the body for
12 longer than it otherwise would?
13 A. It makes the molecule bigger so it isn't lost so quickly
14 from the body.
15 Q. Right. Thank you. Then you say -- and this is looking
16 at paragraph (f):
17 "Factor IX, prepared experimentally in the USA by
18 this procedure, was tested by Dr Johnson in chimpanzees
19 but the chimpanzees developed Hepatitis B, demonstrating
20 that Hepatitis B infectivity had not been fully
21 removed."
22 So it wasn't an magic bullet, this methodology?
23 A. By no means. I think Dr Johnson was doing the best that
24 he could with whatever he could think of to try and deal
25 with this problem.

1 Q. Right. Another issue, as you go on to explain, was not
2 just that it didn't solve the problem, there was also
3 concern that it might actively harm recipients. That's
4 the thrombosis problem, is it?
5 A. Yes, it was Dr Cash who actually discovered this because
6 in the study that's mentioned here he was administering
7 different Factor IX concentrates to these animals and he
8 had a higher degree of thrombogenic reaction associated
9 what we had called a Supernine product, which was the
10 PEG precipitated product, than he had with DEFIX and
11 that caused him to think that this might actually have
12 been made more thrombogenic.
13 But one of the difficulties is that the dose of the
14 product was much higher than DEFIX. The Supernine sample
15 that was given to the animals was much higher. That
16 might have been the reason for that reaction rather than
17 any intrinsic reduction in the safety of the product.
18 Q. Can we just have a quick look at that article? That's
19 [LIT0010959]. We can see names we recognise: Dr Cash,
20 Mrs Middleton, Dr Smith. Is the Kasper referred to
21 there -- that's Kasper writing in 1973. Is he the same
22 Kasper that wrote the article on transfusion?
23 A. She is, yes.
24 Q. Sorry, that's a dreadful mistake. Thank you.
25 In this summary, at the start, there is a narrative

1 of the preparation of, firstly, PPSB and then DEFIX,
2 1971:
3 "Further protein fractionation developments led to
4 the introduction of DEFIX."
5 As you have said, that was a concentrate that
6 contained Factors II, IX and X, and we can see for
7 ourselves that a further product, known as "Pegix",
8 I guess -- and that was Supernine really, was it?
9 A. Yes, that's what I would have referred to it as. I
10 hadn't realised that John had called it "PEG IX".
11 Q. Yes, I suppose, if it is PEG IX, you can't really call
12 it "Pegix".
13 Anyway, PEG IX had been developed but there was
14 a concern about possible thrombogenicity, so dog studies
15 were carried out. Can we look firstly at page 5 of this
16 article, please?
17 THE CHAIRMAN: What is a "collio" dog? The first page.
18 MS DUNLOP: We had better go back to the first page.
19 PROFESSOR JAMES: It is a collie dog.
20 MS DUNLOP: I think it is "collie".
21 THE CHAIRMAN: Oh, I see, it is "collie".
22 MS DUNLOP: Sorry, can we go back to page 5, please? There
23 we see that we are talking about PEG IX and that in the
24 dogs there was disseminated intravascular coagulation.
25 Is that what "DIC" stands for?

1 A. It does.

2 Q. So that means lots of little clots forming in the blood

3 vessels?

4 A. Yes.

5 Q. Right. Then can we go on to 6, please? I suppose we

6 should note also that the dogs had severe oliguria,

7 which means they weren't producing any urine, or not

8 enough urine. I'm not sure if that's connected.

9 PROFESSOR JAMES: It is.

10 MS DUNLOP: It is? Right.

11 PROFESSOR JAMES: It means the kidneys were blocked off with

12 the clots, the blood supply to the kidneys.

13 MS DUNLOP: Thank you.

14 Then on page 6 there is the discussion:

15 "In very high doses the particular batches of PPSB

16 and PEG IX were associated with low-grade and extensive

17 DIC respectively."

18 This is just what you have been describing,

19 Dr Foster, that that would obviously be a concerning

20 finding and one could speculate that it might be to do

21 with the particular doses administered but it would

22 still be something that would require further analysis.

23 Is that correct?

24 A. That's correct.

25 Q. Yes. Then can we look at page 7, please? And that's

1 really said there. We see that the resume, the little
2 resume, is also in French and German, but the bit that's
3 in English makes the point that you have made about the
4 need for further research.
5 So I suppose what we need to take from this is that
6 there has been for some time this concern about the
7 thrombogenic potential of Factor IX concentrates
8 generally and then that recurs when one comes to look at
9 heat-treated Factor IX. Is that right?
10 A. Yes, this concern of thrombogenicity did arise in this
11 period, 1974/1975, and, I think, in the United States,
12 even with the standard products, there were some serious
13 problems seen in some patients. So it was really quite
14 an issue of great concern.
15 Q. Right. Perhaps we could just finish this section before
16 we stop.
17 Could we go back to the statement, [PEN0121438] at
18 1441? You yourself became involved in work on this
19 Factor IX. Is that right?
20 A. Yes.
21 Q. You tell us that Dr Smith led the project at first and
22 then he went to PFL and you led further research.
23 Obviously, you must have thought that it was worth
24 pursuing, even though there were some apparent
25 downsides, because there were some obviously desirable

1 aspects of the product, and you developed a mark 2
2 procedure?
3 A. It was Dr Johnson who developed the mark 2 procedure.
4 I can't claim any credit for that.
5 Q. Okay.
6 A. The purpose of that was to deal with this issue of
7 infectivity. He revised the procedure, to try and get
8 a greater degree of removal of the virus than he had
9 achieved previously, which had caused infection in
10 chimpanzees, and of course it was the mark 1 procedure
11 that had been tested in John Cash's dog model. So the
12 mark 2 product was a revised version of the product.
13 Q. And you actually published on this. That's
14 [LIT0010208]. It's not a terribly good copy but we can
15 see it's something that was sent in in June 1979 and
16 this is essentially dealing with that project. Is that
17 right?
18 A. It deals with the aspect of thrombogenicity.
19 Q. Actually it is not really dealing with Supernine, is it?
20 It's dealing with DEFIX.
21 A. No, it is the Supernine material that I was looking at.
22 But what we were doing was taking eluates from the DEFIX
23 process that would be rejected because of a high
24 thrombogenic potential in the tests that were done then
25 and then carrying out the Supernine process on those --

1 not producing a clinical product, just for research --
2 and then seeing what happened to that. What we found
3 was that the polyethylene glycol processing actually
4 made it less thrombogenic, not more thrombogenic,
5 according to these tests.
6 Q. I see. Just to conclude this section, going back to the
7 statement, 1441, Supernine actually never became
8 a product administered to patients?
9 A. It did actually go into some clinical evaluations --
10 I think that's in the preliminary report -- but we
11 reached a point where we were having to decide, kind of,
12 which horse to back, if you like, and heat treatment was
13 seen to be much more likely to be effective than this
14 procedure in obtaining a safe product.
15 So Supernine was shelved and we concentrated on heat
16 treatment, and I think there was an issue about
17 licensing because the licensing authority didn't want us
18 to have two Factor IX concentrates and the clinicians
19 preferred to keep the one that they knew worked well.
20 I think we had that conversation earlier.
21 Q. Yes. Sir, that would be an appropriate point at which
22 to stop?
23 THE CHAIRMAN: Thank you.
24 (1.09 pm)
25 (The short adjournment)

1 (2.00 pm)

2 THE CHAIRMAN: Yes, Ms Dunlop?

3 MS DUNLOP: Thank you, sir.

4 Dr Foster, I would like to go back to where we were

5 just before lunch, which is in your statement. That is

6 the document [PEN0121438] and go to 1442. We can see

7 there a heading "Factor VIII", and you say that:

8 "PEG precipitation ..."

9 Dr Johnson's method:

10 "... was not applicable to Factor VIII, separations

11 using PEG being based on the difference in size of the

12 macro molecules to be separated."

13 Would I be right in thinking that a virus is a macro

14 molecule?

15 A. That's what I have called it, yes.

16 Q. I thought this was implicit but just to spell that out.

17 I found the note that I was remembering before lunch,

18 about Factor VIII being made of 2,351 amino acids, but

19 is it right to say that understanding the structure of

20 Factor VIII was a process that really took quite a long

21 time and continued into the 1980s at least?

22 A. Yes, at least, and of course at this time we talked

23 about the Factor VIII, you will see I have called it the

24 Factor VIII complex, and today we would understand that

25 as being the Factor VIII molecule and the von Willebrand

1 factor protein combined, because that is how they were
2 presented at that time and it wasn't understood that the
3 von Willebrand factor and the Factor VIII were actually
4 combined. It was unclear. We had this very large macro
5 molecular substance which we now know to be two proteins
6 which were combined.
7 Q. Just so that we can get our terminology correct, would
8 it be wrong to think of the combination of the
9 von Willebrand factor and the Factor VIII as one macro
10 molecule or are they two macro molecules?
11 A. They would be regarded as one. You would have to treat
12 them to separate them. So in terms of the natural
13 process, the natural circulation in the body and the
14 plasma, they would be considered as one macro molecule.
15 Q. So then you weren't preparing Factor VIII concentrate,
16 you were essentially preparing a concentrate of
17 Factor VIII and von Willebrand factor?
18 A. Yes, the two molecules were combined.
19 Q. Yes, right.
20 A. But we didn't know that at the time.
21 Q. I see. Just to go back to that report from 1973, that's
22 [SNB0016903]. This would be written at the time when
23 PFC was still based at Edinburgh Royal Infirmary and
24 indeed we can see that from the address on the front,
25 Protein Fractionation Centre, Royal Infirmary,

1 Edinburgh. We can actually see within this document the
2 same old tension between purity and yield. So if we
3 look, for example, at page 5 -- it is actually labelled
4 "page "2 but it's our page 5. Mr Watt or Dr Smith, or
5 whoever wrote this, is talking about a target potency
6 which he is actually taking from the commercial product,
7 ie Hemofil, so the PFC preparation -- and this is about
8 the middle of the big paragraph that we can see -- had
9 a potency of between eight and 16 units per millilitre
10 compared with 20 units per millilitre for Hemofil.
11 Hemofil is not a high potency preparation, so it's
12 interesting that the target was to try to match what
13 could be achieved with a commercial concentrate. But
14 then if we look at page 7, we can see that again there
15 is concern about yield. Can we go a little bit further
16 down?
17 Under the heading "Future high potency concentrates"
18 the author is saying that achieving a new concentrate
19 with a higher potency, that is 20 units per millilitre,
20 that could assist, because he says:
21 "It is not disputed all haemophiliacs would prefer
22 low volume injections."
23 I suppose the logic of that is the more potent the
24 concentrate the less of it you are needing to inject?
25 A. That's correct.

1 Q. But he says that a 50 per cent penalty in yield couldn't
2 be ignored. So even in 1973 it was not really possible
3 to take your eye off questions of yield because of the
4 aim of trying to produce as much of the national
5 requirement as possible?
6 A. Yes, I think Mr Watt understood this very well.
7 Q. Yes. Just before we leave this document, Dr Foster,
8 I did notice on the previous page, page 5, a reference
9 to the product being hypertonic. I don't understand
10 what that would mean in this context?
11 A. It's essentially about the salt content. Isotonic being
12 what you would expect in a normal blood stream and you
13 can add reagents to make them either have more or less
14 salt and that's what he is talking about.
15 Q. Right. Okay. Can we leave that document, please, and
16 go back to the statement? That's 1442, the page we were
17 on. You have extracted from that report Mr Watt's
18 suggestion of using specific polyelectrolytes, and then
19 you go on in subparagraph (n) to say that:
20 "PFC scientists worked with Dr Johnson on this in
21 the early 1970s."
22 And I think this is something to which we have
23 already made reference, because you go on to talk about
24 Monsanto. Just to note that that is what you dealt with
25 at page 32 of your longer paper, which we were looking

1 at earlier.

2 Then you say, if we can go on to the next page, that

3 Mrs Middleton went to Speywood and worked on the

4 production of porcine Factor VIII, which was called

5 Hyate, that's paragraph (q), further treatment of

6 patients with inhibitors.

7 Then reading on to the next page, subparagraph (t),

8 there is a reference to an improved purification

9 process, which I think we come back to because that

10 recurs, and then a description of other initiatives in

11 the 1970s, one of which we picked up with you and it's

12 the one that's in subparagraph (v), a reference to the

13 University of Bristol, where you tell us that your

14 suggestion of research to discover a means of

15 eliminating the risk of hepatitis from Factor VIII seems

16 to have received a bit of a dusty answer. Can we have

17 a look at the additional statement because we asked you

18 to elaborate a little bit on that. It's [PEN0121797].

19 It's at page 2, please.

20 We asked you about that and I think we can all read

21 for ourselves what you think underlay the less than

22 enthusiastic reception that you received and if you were

23 asked to choose which you think was the most likely, you

24 think it was (iv), that it was perhaps less of an

25 interest in the sort of applied research that you were

1 considering.
2 A. That was my sense at the time as to why they reacted
3 that way.
4 Q. Then can we go back --
5 THE CHAIRMAN: Sorry, who was the director at Bristol at
6 that time?
7 A. The head of department was a man called John Holbrook.
8 I did not have the conversation with him. It was
9 members of staff in his department, and I have to say
10 I forget their names.
11 MS DUNLOP: So people didn't want to collaborate with you on
12 your suggested project?
13 A. No, that wasn't taken up.
14 Q. Yes. Then can we go back to the statement, please, at
15 1445? You mention a bit about Dr Feldman, and we saw
16 his name earlier today. Dr Feldman who was a research
17 student who worked, I think, both at Bristol and with
18 you?
19 A. He did his PhD at Bristol and we part-sponsored that PhD
20 project, and part of the conditions of the project was
21 that he should spend some time with the industrial
22 sponsor. So he came to PFC for a few months to fulfil
23 the obligation of the research award.
24 Q. You say he is currently working at BPL?
25 A. I think he is still there.

1 Q. Right. Finally in this section you talk about another
2 initiative that PFC looked at in the late 1970s and
3 that's to do with getting Factor VIII from human cell
4 culture rather than from blood donors, which seems
5 perhaps to chime with what we read about different
6 research on cell culture nowadays. But you say that
7 this was superseded by the development of recombinant
8 technology, in which human Factor VIII was produced in
9 animal cells, but that was something that was considered
10 to be too complex and expensive for PFC to pursue.
11 So that is really, I suppose, a quick run through
12 some initiatives of the 1970s and a look at some of what
13 was ongoing at that point. Your next section really
14 still deals with research in the 1970s and you go back
15 to talking about the Hepatitis B Factor IX project, and
16 that being essentially an attempt to separate the virus
17 from Factor IX physically rather than by heating. You
18 say in subparagraph (c) on the next page that that's
19 essentially the situation which pertains today
20 concerning VCJD. So it wouldn't be possible to do
21 something by way of heat, presumably, to a plasma
22 product which would destroy -- well, it's the prions you
23 were attempting to --
24 A. That's correct. The prion agents are very resistant to
25 heat and the only means of eliminating them from plasma

1 products are by means of separation rather than
2 inactivation.
3 Q. Right. Can we go back to the questions document, which
4 is [PEN0121531] but not lose the answers. Can we just
5 look at the next question? We don't need to ask you if
6 Dr McClelland had attended this working party meeting
7 because he has told us he did. Can we look at number 3,
8 please, over the page?
9 This is the minutes of the meeting of the MRC
10 working party on post-transfusion hepatitis. This is
11 14 February 1980. Can we just look at that quickly?
12 That's [DHF0024845]. I think this was a fairly
13 short-lived working party in fact, but if you look at
14 paragraph 3.3 of these minutes, please, we can see that
15 they did discuss methods of inactivation of hepatitis
16 viruses and there is a reference to Bayer, which you
17 think should actually be "biotest", that that's
18 a mistake?
19 A. That's what I would say.
20 Q. Yes, I think from reading around it that looks almost
21 certain to be the case but this was research using beta
22 propiolactone. That's the addition of a chemical to
23 attempt to destroy the virus. Is that right?
24 A. Yes, it's actually beta propiolactone combined with UV
25 radiation and it was unsuccessful with Factor VIII, as

1 it turns out.

2 Q. You say, and I think we can now go back to your answers
3 document, 1446, that this approach would have been
4 unlikely to have been pursued in the UK anyway because
5 beta propiolactone was known to be a carcinogen, which
6 is actually mentioned in the minutes as well.

7 Then if we turn over to 1447. I should have pointed
8 out too that in paragraph 3.4 of the minutes of that
9 meeting, there is a reference to work in the
10 United States on the removal of viruses concerning the
11 polyelectrolyte method of Dr Johnson, with which the PFC
12 was already familiar. Although you weren't aware of
13 this meeting until you read our preliminary report, you
14 don't think there is anything in the minutes that would
15 have altered your strategy at the time, had you been
16 more aware of it then?

17 A. No, I think I was already aware of the points in the
18 minutes, even though I didn't know about this meeting or
19 the minute.

20 Q. Right. The next question concerns the work of Behring
21 and Dr Cash becoming aware of what Behring were doing
22 in October 1980. Can we look at your answer? You say
23 that the symposium in Bonn that was attended by Dr Cash,
24 which is discussed in our preliminary report, was the
25 first public disclosure of the work of Behring on the

1 pasteurisation of Factor VIII and I understand the
2 symposium in Bonn to have been the first international
3 haemophilia conference, I think. Does that sound right?
4 A. Something like that, yes.
5 Q. Yes. I think we should just look at Dr Cash's letter
6 because it perhaps conveys the startling quality of the
7 news, [SNB0072646]. Dr Cash writes to Mr Watt on
8 27 October 1980. We can just see Dr Cash's brief
9 narrative of what he had heard. He says to Mr Watt:
10 "Sounds unbelievable. Thought you might be
11 interested."
12 So there is then a number of different documents.
13 I think, because the Behring work is quite important,
14 I would like, if I may, just to run through what the
15 different Behring articles and papers were because
16 I think it has not been always straightforward for us to
17 establish who saw what when. You mention an abstract of
18 the presentation -- in other words, some sort of written
19 note of the talk -- being published in 1981. If we
20 could look at that, that's [SNB0073300], and that's
21 a simple, one-page abstract.
22 From a journal, "Haemostasis". It looks to have
23 been a supplement to the journal "Haemostasis". It's
24 from 1981 and it simply tells us that Behring -- well,
25 it doesn't actually mention Behring, I don't think -- it

1 may do at the bottom. It tells us that there has been
2 discovered a method to produce a highly purified
3 Factor VIII concentrate heated in solution.
4 Trying to follow the thread here. This is an
5 abstract which is published in 1981 but there was
6 a paper which dates from 1980, and if we look at that,
7 that's [SNB0045880], this comes from Die gelben Hefte.
8 Please correct me if your German is better than mine,
9 which wouldn't be difficult, but I think it translates
10 roughly as "the golden booklet" or something of that
11 sort, and was an internal Behring journal.
12 A. My understanding is that it was a company internal
13 document, yes.
14 Q. Yes. This document, which is describing the same work,
15 mentions, as you point out to us, the presentation in
16 Bonn. So it has been written after the conference in
17 Bonn, which was attended by Dr Cash but is an internal
18 journal. Then the next piece of writing on this, if we
19 could move back -- just look at page 2 of this, just to
20 let ourselves see what's being said in this, we can see
21 that Dr Heimburger and Dr Schwinn and Dr Mauler are
22 quoted and they, I think, have featured also in the
23 abstract that we looked at but they are describing the
24 same research work, I think, essentially. Then can we
25 go back to your statement, please, to page 1451? As

1 I understand it, although that golden booklet article
2 dates from 1980, you first got a version of that when
3 you were in Budapest in 1982 at a conference in
4 Budapest. Is that right?
5 A. That's my best guess, yes.
6 Q. Yes. That is [SNF0010929].
7 This is all rather puzzling, I'm sure, sir. It
8 doesn't particularly matter but that is essentially the
9 same document as the published version in the golden
10 notebook, but this is obviously a much more informal,
11 typewritten version, but it seems to be the same text.
12 And that, I think, Dr Foster, is the paper that you
13 received in Budapest?
14 A. Yes.
15 Q. Yes. Right. Then meanwhile there was another paper,
16 which was written in German, in 1981 -- and we are going
17 to look at that as well -- and that's [SNB0086794].
18 This seems to have come from a publication called "Drug
19 Research", and we can see there is a small English
20 summary on the right-hand side:
21 "Factor VIII concentrate, highly purified and heated
22 in solution."
23 This looks possibly to have been the full version of
24 the abstract, the 1981 abstract. So this is the paper
25 that seems to go with the 1981 abstract and it features

1 all the same people with the addition of a Herr or
2 Dr Luben. Then finally there is another article from
3 1982, which is [SNF0010921], and this comes from
4 a publication called, I think, "Medical World", and also
5 concerns the work of Behring on the pasteurisation of
6 Factor VIII. We can see Behring referred to there and
7 the director of the research at Behring seems to have
8 been Heimburger, who features in most of these
9 publications.
10 So there seem to have been a number of different
11 accounts of the research and it seems to have been
12 publicised in different places at different times but
13 that, I think, is a summary of the different papers that
14 were around and we will look at them --
15 A. I'm not sure this final paper actually deals with
16 pasteurisation. I think it might be more just the
17 composition of the different products.
18 PROFESSOR JAMES: Yes.
19 MS DUNLOP: Yes, I see that.
20 To look in more detail at what Behring had done, can
21 we go back to your statement and go to page 1447? You
22 say you were told by Dr Cash; were you startled?
23 A. Yes, I was completely gobsmacked.
24 Q. Right. You say you were quite shocked on the next page.
25 You say:

1 "I was quite shocked when I heard of this claim."

2 As the notion was inconceivable to you. One of the

3 things that may have been in your mind at the time when

4 you heard the news is the standing of Behring, and

5 without going to it but just to read you what Dr Smith

6 says, he says:

7 "Behringwerke was a well respected company. If they

8 said a process was feasible, it was worth pursuing, even

9 if one remained sceptical about yield and about proof

10 that viruses were sufficiently inactivated."

11 Of course, one of the problems that is evident from

12 all this recital of the publications is that the yield

13 was very low. I think about 8 per cent. Is that right?

14 A. That's what they quoted, yes.

15 Q. Do you agree what Dr Smith said about news from Behring

16 being worth listening to?

17 A. Oh, definitely, yes.

18 Q. Right. You give us a bit more explanation for why you

19 were so shocked and you refer to the Webb book, which

20 was mentioned earlier, in your paper. Just to say en

21 passant that that reference, PEN0121480, the actual

22 part of that, which is the Webb extract, is [PEN0121484].

23 Then you say that in your PhD you had learned that

24 proteins could be easily damaged by heat and you make

25 another reference to a publication of Dr Cohn, which we

1 also have, although I don't think we need to go to it.
2 Then on to the next page, you say:
3 "Factor VIII from human plasma was considerably more
4 sensitive and more difficult to work with than any other
5 proteins I had encountered, making it an implausible
6 candidate for research on heat treatment."
7 Then you go back to saying that what you were doing
8 at that time in PFC was based on the method of Newman
9 and Johnson, and we looked at that article earlier, and
10 you make the same point about the logic that you had
11 discovered that even a 10-degree rise in temperature,
12 when working with Factor VIII, caused a loss of yield.
13 So intuitively it had seemed to you that treating
14 Factor VIII at something like 60 degrees just wouldn't
15 work?
16 A. I can't admit that I ever considered that. It was just
17 so -- literally inconceivable. I didn't sit down and
18 say, "Would this work or would it not work?" it was
19 something I didn't even consider, it was inconceivable.
20 Q. Right. I think as another mark of how surprising this
21 news was, you tell us about Dr Garrott Allen, and I said
22 this morning we would be coming back to him. If we look
23 at subparagraph (k), by the time you had done a bit of
24 research of your own and had published in the Lancet,
25 that news surprised Dr Allen so much that he wrote to

1 PFC about it. Can we look at your publication? That's
2 [LIT0013924].
3 Can we just go back to the top of that, please.
4 This is the Lancet of 19 November 1983. So we have
5 obviously gone on a bit to just stay with the order of
6 your statement, but to look at what you had said in the
7 Lancet, which is that letter that's in the right-hand
8 column, about inactivation of viruses, and this is
9 actually in the context of immunoglobulin. Can we turn
10 to the next page, please? This team, of which you are
11 one, and we see Dr Welch and Dr Cuthbertson,
12 Dr McIntosh as well. That first full paragraph:
13 "Pasteurisation at 60 degrees centigrade for ten
14 hours has been used for the inactivation of hepatitis
15 viruses in albumin solutions for over 30 years and has
16 recently been applied to a Factor VIII concentrate, with
17 carbohydrates used to stabilise the protein."
18 So you are reporting what you have found in
19 connection with the pasteurisation process and that
20 elicited the response from Garrott Allen, which is
21 [SNB0074036]. So he is writing in some surprise as
22 well. Is that right?
23 A. That's correct.
24 Q. Yes. He refers to his own previous research, which I'm
25 sure everyone will remember. We highlighted as one of

1 the bullets in the early part of your paper, in your
2 list of previous unsuccessful attempts, this particular
3 piece of research features as well. He is writing and
4 saying, "Well, I couldn't do it and I'm really
5 interested to hear how you can". Is that fair?
6 A. Yes, that's fair.
7 Q. He says that all he was able to do was eradicate the
8 activity of the viruses but also inactivate the clotting
9 factors at the same time, so not a successful project,
10 and wondering how can you do the one but not the other.
11 Then you replied -- and that's [SNB0074287] -- and gave
12 him some information about your work up until that
13 point.
14 In a nutshell, were you saying to him that you had
15 discovered ways of stabilising the proteins more than
16 stabilising the viruses? In other words that the
17 proteins were being preferentially stabilised, which
18 meant that the viruses could be attacked more than the
19 clotting factors?
20 A. Yes, that's what was being discovered.
21 Q. So that's what you are explaining to him really. Then
22 just to go back to your statement at page 1450, you
23 quoted for us a view from leading individuals speaking
24 on behalf of the FDA in America.
25 That's actually going back to 1974.

1 Just, as we say, for completeness, if we look at
2 Mannucci's review of the time, which is [LIT0011101],
3 this is his retrospective, "AIDS, hepatitis and
4 haemophilia in the 1980s: memoirs from an insider". He
5 also records his scepticism on hearing of the Behring
6 news. If we could look at the second page, please, and
7 then the bottom of the right-hand column.
8 The first paragraph under that subheading, "Heat
9 treatment and other viricidal methods," that's actually
10 dealing with the biotest research, is that right? That
11 mentions beta propiolactone?
12 A. That's correct.
13 Q. Then in the second paragraph, what he is talking about
14 is the Behring work. There we see:
15 "The first information appeared in 1980 in a house
16 journal of the company. I, like other clinicians, was
17 unimpressed with the claim because clinical evidence was
18 meagre and the design of the study retrospective and
19 poor."
20 So rather a negative comment on the whole Behring
21 episode but certainly, as far as you were concerned, it
22 was a trigger for your own research?
23 A. Yes, I mean, it seemed to us worthwhile to pursue.
24 Q. Yes. So really that's the sort of mindset that Dr Smith
25 is encapsulating about, "Well, if Behring are doing it,

1 it's worth paying attention to". If we go back to your
2 statement, we can see you have told us what happened in
3 response to this news from Germany. So if we go back to
4 1450, you tell us that the research which then began at
5 PFC was a direct response to the information obtained
6 concerning the procedures used by Behring.
7 Then, because we had been using the expression
8 "developments in the rest of Europe", I think you
9 thought we were suggesting that everybody else in Europe
10 was working on this, but that wasn't the intention.
11 I think it was just an attempt to replace the wording we
12 originally had, which was "on the continent". It was an
13 attempt to use a form of words which was slightly more
14 modern. That's all it is. I don't think we were ever
15 under the impression that anybody other than Behring was
16 pasturising Factor VIII at this point?
17 A. I see.
18 Q. Then you tell us the objective of the time, obviously to
19 inactivate agents responsible for hepatitis transmission
20 including the transmission of non-A non-B.
21 Then a bit more information, which we have looked
22 at, about how you obtained information on what Behring
23 were doing. The article we looked at, which was written
24 in German, you tell us that you had a copy of that from
25 a Behring trade stand or Behring stand at a trade

1 exhibition in Cambridge. I think we misunderstood and
2 thought perhaps Behring had been presenting at that but
3 in your supplementary statement you explain they weren't
4 presenting but they had a stall, as it were?
5 A. That's correct.
6 Q. You obtained this paper in German and Dr MacLeod passed
7 it to Dr Zolg, who was a German post-doctoral researcher
8 at Edinburgh University, and he translated it?
9 A. That's correct.
10 Q. Right. Then you say that you were then absent from work
11 for a period of illness.
12 THE CHAIRMAN: Just before you go on. Dr Zolg, was he
13 a scientist?
14 A. Yes, he was doing research at Edinburgh University and
15 he was collaborating with us on a different project
16 altogether.
17 THE CHAIRMAN: I just wondered at one stage whether he was
18 simply a languages person who had translated it for you,
19 but he was actually a scientist?
20 A. He was a scientist but the primary interest was his
21 ability to understand German.
22 MS DUNLOP: And probably scientific German at that.
23 A. That helped.
24 Q. In your absence on sick leave, Dr MacLeod had taken the
25 initiative to see if he could reproduce the findings of

1 Behring, and you tell us about this:

2 "According to his laboratory notebook, he began his

3 experimental work on pasteurisation on 2 September

4 1981."

5 And you were delighted to discover that that had

6 happened?

7 A. That's true.

8 Q. He did it off his own bat?

9 A. Exactly.

10 Q. Yes. Then following on, I think in our snapshots and

11 landmarks, 6 and 7, we asked about the early research.

12 It obviously began in the autumn of 1981 and then the

13 establishment by Dr Cash of the Factor VIII study group

14 in 1982, and you have given us a lot of detail about

15 that, snapshots and landmarks, 6 and 7?

16 THE CHAIRMAN: You make a comment in paragraph (c) that

17 interests me, because having read and indeed reproduced

18 the whole terms of the summary of what was known at the

19 time, it occurred to us, I think, earlier on, that there

20 was no reflection of an understanding on the part of

21 Dr Cash and his team at that stage of work on

22 pasteurisation. You don't know whether he knew about it

23 or not?

24 A. It is very hard for me to answer that because it was

25 such a long time ago. I'm fairly sure he was aware of

1 it but I can't be absolutely certain.
2 THE CHAIRMAN: Yes.
3 MS DUNLOP: Right. Yes. We asked that specific question.
4 We said:
5 "The report of the first meeting does not describe
6 ..."
7 And that was at the end of January 1982:
8 "... any work on the viral inactivation of
9 Factor VIII."
10 A. If you go to the minute of that meeting I think you will
11 find a comment by Dr Prowse where he does refer to
12 pasteurisation. So I think the knowledge was there.
13 This was beginning to be looked at but it was maybe
14 a bit too early to make it a big item on the agenda.
15 Q. Right. What Dr MacLeod was trying to do, I suppose, as
16 a first step, was to see if he could reproduce what
17 Behring had achieved. Is that right?
18 A. Yes, in science that's the first step you do. You see
19 something published. Can it be reproduced or is there
20 something wrong with this and it doesn't work? And
21 really Dr MacLeod was beginning this at a very simple
22 level to see if he could just recover Factor VIII
23 activity in that kind of stabilising mixture that
24 Behringwerke had used.
25 Q. Reading on down through this answer, you make the point

1 that the first meeting was taking place two weeks before
2 Dr MacLeod had completed his preliminary evaluation. So
3 still very early days?
4 A. That's right.
5 Q. You think Dr Cash was aware of the work. And then
6 similarly the meeting of the safety action group, that
7 was one of the subgroups of the study group, I think,
8 preceded Dr MacLeod's first report.
9 As you point out, by this time you had the abstract
10 of the 1980 Bonn presentation. That's the one-page
11 document we looked at earlier. This abstract gave the
12 yield of Factor VIII at 8 per cent. So when you read
13 that, you must have seen that as a really serious
14 drawback?
15 A. Yes, it was a major point.
16 Q. Yes. You say:
17 "It was less than one third of the yield then being
18 obtained at PFC."
19 So you had two different tasks. You wanted to
20 devise a pasteurisation process, if you possibly could,
21 but also increase the yield because 8 per cent really
22 would not have been satisfactory?
23 A. It didn't seem to us to be a viable process for our
24 purposes.
25 Q. Right. Perhaps if we look at question 8, which is on

1 page 2 of [PEN0121531]. That's the second page of the
2 schedule. We mentioned in our questions the conference
3 in Budapest in July 1982 and that you were able to get
4 another copy of a Behring paper and a typewritten paper
5 on the process, and that's the one that seems to be the
6 version of the golden notebook text?
7 A. My guess is that the typewritten version was probably
8 what was produced in 1980 for the in-house journal and
9 it was only later that they turned it into a printed,
10 colour piece of commercial literature.
11 Q. Right. Thank you.
12 I was puzzled as to the sequence of events because
13 the typewritten version doesn't look properly finished
14 and the tables have been filled in in handwriting, so it
15 must logically have preceded the much glossier -- I'm
16 not sure if it was glossy, but the much more
17 professional looking golden notebook publication. But
18 that explanation would fit the facts. Perhaps when they
19 realised how much interest there was, do you think?
20 A. Yes, I think, as they progressed, they decided to turn
21 their initial typewritten document into a proper
22 brochure almost, that they could hand out to potential
23 customers.
24 Q. Right. Can we go back to the statement? That's at
25 1453, please. You mention, picking up the paperwork in

1 Budapest and also you wrote a report about your trip to
2 Budapest, which I think we should look at. It's
3 [SNB0104452]. I think this is a 30-page report of your
4 visit to the conference, so obviously something that you
5 felt you wanted to report on in considerable detail?
6 A. There was a lot of interesting material, yes.
7 Q. So it was definitely worth going to?
8 A. Very much so.
9 Q. Yes. You have told us that it wasn't just conversation
10 about Behring, obviously, at that conference, but that
11 you also learned of other research and I think beta
12 propiolactone is mentioned. Can we look at page 4
13 there, please? 2.3.2, biotest presented on beta
14 propiolactone and ultraviolet treatment. But then also,
15 interestingly, if we look down to the bottom of that
16 page, please. I think these are your own personal
17 comments, are they?
18 A. That's correct.
19 Q. Yes. You have obviously subjected the beta
20 propiolactone methodology to a bit of analysis. Can we
21 go on to the next page, please? You say:
22 "The mechanisms of viral inactivation are difficult
23 to discern."
24 Then a number of comments about that presentation
25 but if we scroll down the page, the next one, the next

1 section, 2.5.2, is actually about dry heat treatment.
2 Is that right?
3 A. That's correct.
4 Q. Yes. Who was Rubenstein?
5 A. He was an American researcher. I don't think he worked
6 for any companies. I think it was Rubenstein and
7 Rubenstein. I think they were two brothers in New York.
8 Q. I just wondered whether it was connected to Hyland but
9 maybe Hyland obtained information from him, or was his
10 work separate from Hyland?
11 A. I don't know the answer to that.
12 Q. It doesn't matter. On the last paragraph on that
13 passage you say:
14 "The Hyland product is perhaps the most interesting.
15 If the yield indication is confirmed it is probably
16 higher than the present method of manufacture for
17 Hemofil."
18 That would be surprising because that seems to
19 suggest that what Hyland were talking about was some
20 form of heat treatment that they were using that also
21 achieved a higher yield?
22 A. Well, it's conceivable if they had some kind of
23 stabilisation that was used earlier in the process, that
24 might protect the Factor VIII. At this stage we didn't
25 know really what they were talking about. They just

1 made this announcement that they were using
2 a heat-treated product and this was the yield they were
3 getting, and this is my comment on it. This is the
4 product that you talked about earlier, with the Mannucci
5 trial and the patients that continued to transmit
6 hepatitis. It's the Hemofil T product.
7 Q. Yes.
8 A. We later found that out. At this point in time we
9 didn't know that.
10 Q. Yes, it probably, at this point, looked more promising
11 than it ultimately turned out to be. Is that fair?
12 A. Well, it was a heat-treated product that gave no
13 indication as to whether it might deal with viruses or
14 not and as we see, it didn't deal with non-A non-B. So
15 the questions were still waiting to be answered.
16 Q. A bit tantalising?
17 A. Certainly tantalising. That the major plasma
18 fractionation company in the world was announcing
19 a heat-treated product.
20 Q. Right. Can we look on to the next page, please?
21 I think we need to go to the bottom of the page. I have
22 missed the reference I want. Can we scroll back up,
23 please? Go back to the previous page. Sorry.
24 Can we go back down to the bottom again? Thank you.
25 Yes. I'm not seeing it at the moment but I think

1 there is a reference to pasteurisation but if there is,
2 that turned out to be wrong because the Hyland process
3 was definitely a dry heat process?
4 A. Yes, at the time I didn't know what it was and it was
5 only later that we discovered it was a dry heat process.
6 Q. Yes. Can we go back, please, to the schedule, the
7 questions? This is 1982, and by this time you know
8 about the Behring work on pasteurisation and you are
9 working on that yourselves at PFC, and you have also
10 heard that there is a dry heat-treated product around,
11 devised by an American company. And then
12 in October 1982 the Factor VIII study group met and we
13 asked a question, firstly about the reference in the
14 minutes of that meeting to heat treatment now being the
15 first option of the group, and then we also asked about
16 whether the pasteurisation work you were carrying out in
17 some way had been developed from or come from the
18 pasteurisation of albumin, to which I think your answer
19 is a fairly firm "no", but superficially there is some
20 similarity.
21 I quite accept that the technology is different and
22 that albumin is much easier to work with but at least
23 the actual heat treatment protocol was the same, the ten
24 hours at 60 degrees.
25 A. Yes, of course, you are dealing with heating in solution

1 and the same time and the same temperature, so in all of
2 those respects it is the same. What is different is the
3 way in which the material is stabilised in order to
4 protect the protein.
5 Q. So we should look at your full answer number 9, which we
6 can find on page 17 of [PEN0121438]. Actually this is not
7 in any sense splitting hairs but the minute says that
8 heat treatment is the first option of the group, not
9 specifically pasteurisation but I suppose for you in PFC
10 at that time the only heat treatment you were
11 investigating was pasteurisation?
12 A. It was, and I think at the time the minute was written
13 I doubt if we even knew that Hyland were doing dry heat
14 treatment. I think Dr Prowse discovered that possibly
15 later than that date.
16 Q. Okay. So just to look through that answer, you are
17 giving three principal reasons why pasteurisation or
18 heat treatment was the first option of the group, and
19 the first was the news from Behring and then the second
20 is to do with the zinc precipitation, which we mentioned
21 this morning. So am I correct in seeing this as the
22 step which facilitated the removal of fibrinogen and
23 therefore gave you something which -- well, you say
24 yourself -- could be pasteurised with little loss of
25 yield? So the pasteurisation was more efficient once

1 you had got rid of more of the fibrinogen?
2 A. If you pasteurised in the presence of fibrinogen, you
3 get a lot of insoluble material forming and Factor VIII
4 is removed with that. So you really have to remove this
5 labile fibrinogen first, which is what Behringwerke had
6 done, but their method also had quite a yield penalty
7 whereas the method with zinc had a much lower yield
8 penalty.
9 Q. Right. Then the third reason, which is on the next
10 page, was that Dr MacLeod had obtained promising results
11 using sorbitol instead of sucrose to stabilise
12 Factor VIII during pasteurisation. Is sorbitol another
13 carbohydrate?
14 A. I think it was Duncan Pepper who obtained a publication
15 and passed it through to us. And it was very much
16 a theoretical paper but from the thermodynamic
17 properties which were given for the different
18 carbohydrates, it looked as though sorbitol might have a
19 stronger effect that sucrose. So that was what we moved
20 to. By coincidence it turns out that's what Bayer
21 were working on in the United States at that time.
22 Q. Right. Then you go on to remind us about some of the
23 details of the process for pasteurisation of albumin,
24 and really any opportunity to mention the fortuitous
25 Dr J Murray Luck shouldn't be passed up. So here he is

1 again at Stanford, discovering how to stabilise albumin.
2 Then you say, well, that's all very well but the
3 chemicals that were used to stabilise albumin just
4 didn't have the same effect with other plasma proteins
5 including coagulation factors.
6 I wonder, sir, given that this is quite heavy going
7 if we could perhaps have our afternoon break and have
8 another session about the same --
9 THE CHAIRMAN: Ms Dunlop, I was enjoying it, but we will
10 have the break.
11 (3.00 pm)
12 (Short break)
13 (3.25 pm)
14 MS DUNLOP: Thank you, sir.
15 Just to backtrack slightly, this was something
16 I wanted to check, and I have checked in the break, that
17 in your report of the Budapest conference, Dr Foster, it
18 does looks as though you may have gained the impression
19 that Hyland were using a pasteurisation process. Can we
20 just go back to [SNB0104452], please? Could we go to
21 our page 5 in that? It's that section there, "Hyland
22 concentrate," 2.1.2:
23 "This topic was not listed in the programme but
24 Dr Dolan ..."
25 Who is presumably from Hyland:

1 "... was invited to present a report of the work,
2 following an earlier piece by Dr Prince. The method was
3 said to involve pasteurisation ..."
4 So it does look as though --
5 A. It's conceivable that he said "heat treatment", and my
6 interpretation at that time was pasteurisation because
7 that was the only process that I was aware of.
8 Q. It's really just to make the point, perhaps with
9 slightly more force than you put it in your statement,
10 that you didn't really know what Hyland were doing at
11 all and you certainly when you returned from Budapest,
12 you didn't return with an understanding that they were
13 following a dry heat protocol?
14 A. No, I didn't know that at all.
15 Q. Right, thank you.
16 We were in answer 9. Can we go back to the
17 statement? That's [PEN0121438] at 1456? You have
18 actually given us a little bit more detail about what
19 had happened at Behring and it looks as though some of
20 the credit belongs exclusively to Dr Schwinn. Is that
21 right?
22 A. Yes, I think you would call him the inventor.
23 Q. Right. But everybody always thinks of Heimburger
24 because he was the director of the unit concerned. Was
25 that right?

1 A. He was the first name on the publications but I think
2 Schwinn was the inventor.
3 PROFESSOR JAMES: That was the traditional German method and
4 remains so to this day.
5 MS DUNLOP: Right. Well, we can read for ourselves that he
6 was originally asked to discover a means of reducing the
7 fibrinogen content of Factor VIII and then he tried a
8 heat shock. What's that? Short sharp heating?
9 A. Yes, that's right.
10 Q. Right. And to prevent the Factor VIII being denatured
11 he tried out various additives, and from that the
12 Behring pasteurisation process seems to have been
13 developed?
14 THE CHAIRMAN: Dr Foster, I wonder what the reality might
15 have been. At this stage Behring would still be
16 interested in setting up or protecting patent rights,
17 I imagine, for any process that was being developed or
18 under development. Are pharmaceutical companies given
19 to prior publication of the essential characteristics of
20 processes before the patent is granted?
21 A. Absolutely not.
22 THE CHAIRMAN: Because prior publication can undermine your
23 claim?
24 A. It would certainly undermine the claim, yes.
25 THE CHAIRMAN: So it wouldn't be a surprise if the

1 information given at the conference was rather less than
2 specific as to methodology?
3 A. That would apply to any commercial company, yes.
4 THE CHAIRMAN: I'm not being critical of Behring. I'm just
5 trying to get the feel for a situation in which you
6 might put your own interpretation on what you were
7 hearing that might not in fact reflect precisely what
8 was going on.
9 A. I think that comment applied to Hyland rather than
10 Behring but it probably applies equally --
11 THE CHAIRMAN: To Behring.
12 MS DUNLOP: As I read your statement, you are only really
13 able to tell us this section at all because of
14 a deposition that Dr Schwinn gave in an American
15 litigation in 1996.
16 A. That's correct.
17 Q. At a point when it was safe for him to spill the beans?
18 A. Yes, you could say that.
19 Q. Can we move on then, please, and look at question 10.
20 We should do that by going back to the questions
21 schedule, [PEN0121531] at 1533. We asked a bit about
22 correspondence between PFC and BPL in the autumn of 1982
23 and a specific letter in which Dr Smith said that BPL
24 were doing a little on heating Factor VIII. We are
25 going to ask Dr Smith specifically about that

1 correspondence and he has explained what he meant and to
2 what he was referring in the letter, but we also asked
3 you to characterise the cooperation at this point and
4 what the position was in England. Your answer, which is
5 on page 20 of [PEN0121438], in your statement, describes
6 the working relationship that you had with Dr Smith,
7 or the collaborative relationship that you had with Dr
8 Smith, and we can see that really you enjoyed a very
9 cooperative relationship with him?
10 A. Very much so.
11 Q. Yes. In fact he had visited you at UCL when you were
12 doing your PhD. How did that come about?
13 A. In 1970 Mr Watt had given a lecture at
14 University College London about the work that was going
15 on in Edinburgh, and in the same set of lecture courses
16 I was giving a lecture too, and that interested Mr Watt
17 sufficiently to suggest to Dr Smith he should come and
18 discuss my research with me.
19 Q. So you were spotted?
20 A. I suppose so.
21 Q. Yes. You explain in subparagraph (c) about a certain
22 economy of man hours, if you like, whereby the two of
23 you tended to share reports from conferences, so if
24 one of you could go and the other one couldn't, you
25 would exchange information afterwards?

1 A. Yes, we came to that informal agreement between
2 ourselves to do that because there were so many
3 conferences you couldn't possibly get to all of them and
4 even if you wanted to, you probably couldn't get enough
5 money to go to all of them. So it made sense to share
6 our reports.
7 Q. Right. And indeed one of reports that you sent to him
8 was that report that we were looking at of the
9 conference in Budapest because you were there and he
10 wasn't?
11 A. That's correct.
12 Q. Is that right? Obviously the timing of that may help to
13 explain why not very much may have been happening in
14 England at that point because the conference had only
15 been in the summer of 1982. So you suggest that that
16 might be why only a little research was going on,
17 although in fact, I think, Dr Smith will explain that
18 they weren't really researching heat treatment at all;
19 they were still trying to precipitate fibrinogen and
20 that was what he was describing in this letter.
21 Then question 11, I think there was
22 a misunderstanding, certainly on my part, about the
23 reference in a letter you wrote to your experiences with
24 freeze-drying, and we just asked about what the status
25 of freeze drying was at that point and everyone has

1 explained to us that obviously freeze-drying had been
2 part of the whole process since the beginning. So it
3 wasn't that something particularly remarkable was
4 happening with freeze-drying around that time.
5 Question 12. We asked you about a particular
6 meeting and I think we should look at the question.
7 Thank you, there it is on the screen.
8 There is a bit of correspondence, which postdates
9 this meeting. The subject matter seems to have been the
10 imminent arrival of commercial heat-treated concentrates
11 and whether the pharmaceutical companies would be able
12 to trial these products in the United Kingdom, and in so
13 doing possibly harm the chances of the NHS fractionators
14 for trialing their own products in due course. Is that
15 a reasonable summary?
16 A. I think it is, yes.
17 Q. Right. It is also plain, I think, from the
18 correspondence, that feelings were running high and we
19 did ask you about a particular comment that was made in
20 a letter by Professor Cash. Just to let everyone have
21 a look at the reference which we asked you about, the
22 description of the contact between yourself and Dr Smith
23 as "furtive". If we go to your answer, which is on
24 page 21 of [PEN0121438], you tell us that you weren't aware
25 of the meeting, nor the subsequent correspondence from

1 Dr Cash, in which your contact with Dr Smith was described
2 as "furtive".
3 Dr Foster, if we turn on to the next page, you have
4 given us your thoughts on this particular question and
5 that little series of letters. Dr Smith has commented
6 in response to this same question that you remained
7 serene, his word, but I suppose if you didn't know about
8 it, that was perhaps the happiest position in which to
9 be. I don't want to take up any particular time with
10 this at all, save to note -- and I'm sure you have seen
11 this yourself -- that Dr Cash feels that an apology is
12 due. Have you seen that in his statement?
13 A. I have, yes.
14 Q. Yes. We will hear from Professor Cash on this but
15 I think perhaps simply the wrong word was used but it
16 may be, as you suggest, that the point is really whether
17 one is going to have formal, organised liaison or kind
18 of spontaneous interactions whenever someone has
19 something to impart.
20 A. Yes. At this time Dr Cash had been heading up the
21 situation in Scotland, where he had created the
22 Factor VIII study group, which was a relatively formal
23 arrangement with different groups reporting, and he was
24 chairing the meetings and we had minutes and reports,
25 and of course that kind of level of formality didn't

1 exist in the communications with Dr Smith and myself.
2 So although Dr Cash was, I'm sure, well aware of the
3 communications, that was perhaps a difference in
4 emphasis that he was perhaps a little bit -- thinking
5 about and maybe would have preferred to have something
6 that was more formal from his perspective.
7 Q. Yes. Just, I think, if we can read on for ourselves to
8 the conclusion of that answer, perhaps scroll down and
9 on to the next page in due course. (Pause)
10 I think, Dr Foster, you have had experience of both
11 the formal and the informal, and in relation to this
12 particular contact -- that is your regular contacts with
13 Dr Smith -- your view, even looking in retrospect, was
14 that informal worked just fine?
15 A. Certainly when you are dealing with scientists who are
16 getting on with dealing with the same problems, then
17 talking face-to-face is the best way to proceed in terms
18 of communications.
19 Q. Over the phone, presumably, as well?
20 A. Over the phone and having meetings, yes, and obviously
21 correspondence, some of which you have seen.
22 Q. Yes. There is actually quite a few references in your
23 timeline to Dr Smith coming to visit as well. I think
24 he maybe called in at PFC when he was in Edinburgh?
25 A. That's exactly what happened. He would visit Edinburgh

1 quite frequently and he would always drop in to see us
2 and to have a chat.
3 Q. Can we go back to the questions document, please,
4 [PEN0121531] at 1534? Still in the same area, as
5 a theme. We are attempting to narrate events in the
6 first part of 1983, to summarise some themes that seemed
7 to us to be evident, and then we asked if the reporting
8 to England was reciprocal, and you have said to the best
9 of your knowledge it was, except when precluded by
10 a requirement for confidentiality. So can we go back
11 and just look at that answer, page 24 of [PEN0121438]
12 I would like now, if I may, to go back to your
13 paper, which you prepared for us. That is the document
14 [PEN0131309]. If we go to 1340, this is to take
15 forwards the story of your development of heat-treated
16 coagulation factors. There is a table and we can see
17 "ZHT", which was really the pasteurised product,
18 pasteurised Factor VIII. Is that right?
19 A. That's correct, it's an SNBTS version of pasteurised
20 Factor VIII.
21 Q. Yes. Then NYHT1 and NYHT2, which I think differ only in
22 the length of time for which the product was heated, the
23 first being the two-hour heating and the second being
24 the 24-hour heating. Is that right?
25 A. That's correct.

1 Q. Right, and then Z8. Mr Mackenzie is going to be dealing
2 with that when we come to do topic C3. Then the
3 heat-treated Factor IX product, HT DEFIX, which is on to
4 the next page.
5 Then can we just scroll down. I think, much of this
6 we have already covered. Just scroll down that section
7 headed "1981 to 1983". We know that you began your
8 research on the heat treatment of coagulation factors in
9 1981 as a response to the news from Germany. Then work
10 on stabilisers and then on to the next page, please.
11 You tell us that pilot preparations of ZHT were prepared
12 in 1983. You were also working on trying to pasteurise
13 Factor IX and then you refer to the risk, which I think
14 was always in the minds, particularly of the haemophilia
15 clinicians, of harmful neoantigens being formed by heat
16 treatment. In other words, heat treatment might do
17 something to the coagulation factor concentrate that
18 would actually cause harm to the patients. Is that
19 right?
20 A. That's correct.
21 Q. Yes. We will look, in particular, at an episode
22 involving Dr Ludlam further on.
23 Then you say:
24 "Experiments were also performed using the technique
25 of dry heat treatment, after this method had been

1 reported and it was discovered that Baxter were
2 developing a product of this type."
3 Which you think was possibly information obtained by
4 Dr Prowse?
5 A. That's my memory. Dr Prowse was reasonably close
6 friends with the medical director of Hyland and managed
7 to get him to tell him that it was dry heat treatment.
8 Q. Right. In fact you went on -- "you" being PFC -- and
9 did some dry heat experiments of your own and these were
10 actually conducted, I think, by Dr Cuthbertson. Is that
11 right?
12 A. It was Dr Cuthbertson and Dr Pepper.
13 Q. We have Dr Cuthbertson coming, so we can ask him about
14 that. But we know that the Hyland product turned out to
15 be a bit of a disappointment and I think we should just
16 remind ourselves and go back to that review article by
17 Mannucci, because he talks about this. That's
18 [LIT0011101].
19 Dr Foster, this is another little part of the story
20 where it's a little bit difficult to work out who knew
21 what, when and from whom. So it's rather like the
22 Behring part but I think the bottom line is that it did
23 become known eventually that this Hyland product had not
24 been a hepatitis-safe product, despite initial
25 advertising or perhaps claims for it from the company.

1 But if we look at page 3 of this article, and we can see
2 on the left-hand side he describes how in June 1983,
3 during the Stockholm Congress of the World Federation of
4 Haemophilia, the manufacturer of coagulation factor
5 concentrate previously evaluated only in chimpanzees --
6 now that reference 17 does appear to be to the Hyland
7 work:
8 "... summoned a group of haemophilia treaters and
9 proposed a study to evaluate whether or not the
10 Factor VIII concentrate heated in the lyophilised state
11 at 60 degrees for 72 hours transmitted hepatitis."
12 He enrolled a relatively large number of patients.
13 I think it's Milan, isn't it? Mannucci is Milan?
14 A. I think so.
15 Q. Yes. He says:
16 "From the follow-up of the first few enrolled
17 patients it was clear that the viricidal procedure was
18 ineffective because practically all patients developed
19 non-A non-B hepatitis. The study continued to enrol
20 more patients. It was only in July 1985 that with
21 Colombo, we published the data of the first study. The
22 results showed that the concentrate transmitted non-A
23 non-B hepatitis to as many as 11 of the 13 patients."
24 That article referred to, I don't think this is in
25 my list but it's SNB0045835. No, sorry, that is

1 reference 17. I included that just to show the
2 description of the work that was carried out by the
3 company, which led them to make the claims they made.
4 And we can see from that it is Hyland which is the
5 company involved.
6 So that was the background to the claims that were
7 being made for the product at that time and then we
8 talked this morning about what, to a layperson at least,
9 are rather confusing results about whether the
10 chimpanzees got Hepatitis B but not non-A non-B, and
11 then the patients got non-A non-B but not Hepatitis B,
12 but it certainly seems that even in the summer of 1983,
13 people had doubts about this product.
14 If we look at [DHF0025668], we do actually have
15 Dr Gunson's letter, but not to take up time looking at
16 his letter to Dr Walford. This is a letter from
17 Dr Walford back to Dr Gunson and the important part of
18 it is that she is saying that she has also heard that
19 three chimpanzees which received the Hyland heat-treated
20 Factor VIII had developed hepatitis, and I think from
21 knowing all we know about the surrounding circumstances,
22 she must be meaning Hepatitis B.
23 A. That must be the case, yes.
24 Q. Yes. So even though the Mannucci/Colombo research
25 wasn't published until 1985, the word on the street

1 seems to have been that there were these problem with
2 the product, even in 1983 people knew that?
3 A. I think in one of his memoirs, Professor Mannucci does
4 say that he announced the findings later in 1983, in one
5 of the conferences.
6 Q. I think it is September?
7 A. I think if you look at the SNBTS papers in January 1984,
8 in one of the notes of one of the meetings, it records
9 that the Hyland product had transmitted to patients. So
10 we were aware of it by January 1984.
11 Q. Yes. It is perhaps slightly difficult to explain that
12 if Dr Gunson and Dr Walford knew by the end of June that
13 there was a problem with the product and yet the
14 congress at which clinicians were being asked to enrol
15 patients in the study was also in June 1983, there is
16 really a very short window of time --
17 A. There were two things happening here.
18 One, this letter here concerns the chimpanzee study
19 and that might have been running in parallel with the
20 patient monitoring and, as I said earlier, the
21 chimpanzee study would have received product that had
22 had virus deliberately added to it whereas the patient
23 study was just normal product that would be heated in
24 the same way. But the chimpanzees would be monitored
25 and the patients monitored in parallel, and I think

1 these chimpanzee results must have come out ahead of
2 Dr Mannucci having evidence that the patients were then
3 developing hepatitis in the parallel study that was only
4 set up really after this, I think, because it followed
5 the congress in Stockholm. So they couldn't really have
6 got going until a few weeks after this.
7 Q. Yes. I suppose, as a layperson I would wonder if it
8 wouldn't perhaps sap the faith of the clinicians as they
9 enrolled their patients in the study, hearing that the
10 chimp results were not especially encouraging?
11 A. I think the differentiation between Hepatitis B and
12 non-A non-B might be important, because by this time
13 there was a vaccine against Hepatitis B, so patients
14 would be vaccinated against that. So even if that
15 treatment wasn't effective against B, it was more
16 important that it was effective against non-A non-B
17 because there was no vaccine for that because the virus
18 hadn't been discovered. And there still isn't today.
19 PROFESSOR JAMES: And all the donors were being screened for
20 Hepatitis B.
21 Could I just comment very briefly, Mr Chairman. The
22 Mannucci studies obviously started in 1982 and from what
23 Mannucci said and from what you have already referred
24 to, their abstract in 1983, they must have been very
25 quickly dismayed at the number of their patients who

1 showed evidence of possible non-A non-B hepatitis during
2 their study but, as is the nature of these studies, they
3 had presumably undertaken that they would study
4 a certain number of patients and so they didn't complete
5 the publication of this until they had completed the
6 formal study, which was in 1985, I would imagine. But
7 already we know -- and from what you have said
8 already -- they were actually intimating to the world by
9 the end of 1983 that this stuff didn't work.
10 MS DUNLOP: Yes.
11 PROFESSOR JAMES: I think that's probably the explanation.
12 A. Yes, I mean, you get the bad results very soon but good
13 results take a very long time to get.
14 PROFESSOR JAMES: Well, precisely.
15 MS DUNLOP: Right, thank you.
16 At this point can we return to your statement,
17 please, having looked at that part of the paper. Can we
18 go back to the statement at page 1461, which is where we
19 were?
20 THE CHAIRMAN: Before you go on, Ms Dunlop, going back to
21 Mannucci, I'm not at all clear at the moment whether he
22 and others went on enrolling new patients for the study,
23 after the first 11 out of 13 were found to have been
24 infected. Do you know?
25 A. I have no idea.

1 PROFESSOR JAMES: As I said to you, Chairman, I would guess
2 that I very much misspoke then. That actually they
3 didn't enrol any additional patients but they almost
4 certainly had an agreement that these patients had to be
5 followed up for, for example, a year or two years, you
6 know, after the start of the study, and therefore that's
7 why the report was delayed for 18 months or whatever it
8 is, to finish the follow-up. But I suspect they just
9 stopped enrolling patients when they saw what bad things
10 were happening to them.
11 THE CHAIRMAN: It would be irresponsible to tell the
12 interested world that it was a bad product. It might be
13 irresponsible to go on proving again and again that it
14 was a bad product.
15 A. Perhaps I can just qualify this. I wouldn't say it was
16 a bad product but it was -- it wasn't better than the
17 current products --
18 THE CHAIRMAN: A good product that transmitted disease.
19 A. It was comparable to the existing products.
20 THE CHAIRMAN: Right.
21 MS DUNLOP: Yes. I think his research is spelt out in more
22 detail, sir, in his 1985 article, that Colombo, Mannucci
23 et cetera article, which is [LIT0010369]. That provides
24 more information about the study in the patients.
25 Going back and looking at number 15 in your

1 statement, and perhaps we should look at the question as
2 well. Actually this is in response to question 17, so
3 if we can see question 17. We highlighted a memo which
4 you wrote, dated 3 May 1983. Actually, before I ask you
5 about that, even going slightly before that,
6 to March 1983, if we look at a document [SNB0073503],
7 this looks to be the notes of a presentation that you
8 gave to the haematology department in the
9 Royal Infirmary in March 1983. Is that right?
10 A. That's correct.
11 Q. I noticed that even there you were making some reference
12 to AIDS, if we look on page 5. We should note that the
13 title of your talk is "Methods for preparing
14 non-infective blood products". So if we look at page 5,
15 you are talking about the hepatitis problem, plainly,
16 and that was the problem which had motivated our
17 research up until this point but you do list, under
18 a heading "Problems", in number 4, you do list other
19 infectious agents, admittedly with a question mark, but
20 you instance CMV and AIDS. So it does look as though
21 in the spring of 1983 your mind was at least beginning
22 to entertain the prospect that the research on viral
23 inactivation was not going to be focusing exclusively on
24 hepatitis. Is that a reasonable way of putting it?
25 A. Yes, I was beginning to think that AIDS might be caused

1 by an infectious agent and we would have to take that
2 into consideration.
3 Q. Yes. Then can we go back to the question? We will see
4 that that's 1534. Question 17 is referring to that memo
5 of 3 May, which we should have before us. It's
6 [SNB0073635]. This is obviously an internal PFC
7 memorandum. Is that fair?
8 A. That's correct.
9 Q. Right. You are writing to Mr Watt and to other heads of
10 department.
11 A. That's correct.
12 Q. Right. The subject matter is "Heat treatment of
13 Factor VIII: a strategy". You say:
14 "Until very recently the objective of our heat
15 treatment programme was to cope with the hepatitis
16 problem in haemophiliacs."
17 You then sketch the thinking and I think it's
18 reasonably self-evident that what has been anticipated
19 as the likely demand, if you like, at least in the early
20 years, is in relation to mild and moderate
21 haemophiliacs. So patients with mild or moderate
22 haemophilia were the main target group in the context of
23 research to inactivate hepatitis.
24 A. The severe haemophiliacs were by this time, it was
25 generally known, probably almost certainly infected and

1 therefore the patients who would benefit most were those
2 who were not infected who would fall in the category of
3 mild and moderate, and therefore as a strategy, at least
4 our initial target was to try and make enough material
5 to at least provide safe product for those particular
6 patients. Professor Cash estimated that that would
7 require 30 per cent of our production to do that.
8 I think what he is taking into consideration here is
9 the inventory that you need because you don't know when
10 a patient is going to present or where, so you have to
11 have an inventory all around so that the product is
12 available. But that was the strategy in the early
13 1980s, at least to start off with, to see if we could
14 provide at least 30 per cent of the production as
15 heat-treated, pasteurised material for these patients.
16 And of course the possibility that AIDS might be an
17 infectious agent, completely reversed the situation
18 because there it is the patients who receive the most
19 treatment who are at most risk.
20 Q. Yes. Taking it step by step, Dr Foster -- and
21 I apologise for the fact that this is, in a sense,
22 obvious, but just to make the point that the patients
23 with severe haemophilia would not have been ignored
24 under the previous strategy, it is just that
25 pragmatically, because at that point they would be

1 assumed to be infected, the priority would have been the
2 patients with mild or moderate haemophilia and
3 presumably previously untreated patients?
4 A. Yes, it's a question of what can be achieved, and given
5 the yield penalty that pasteurisation would introduce,
6 even with the improvements we could make, it didn't seem
7 possible that you could heat all of the Factor VIII, at
8 least not immediately, and therefore the strategy was to
9 target those patients who would benefit most.
10 Q. Yes. You have answered this already. The arrival on
11 the scene of what appeared to be another infectious
12 agent and a more serious one, namely AIDS, was
13 suggesting to you that that strategy might have to be
14 rethought?
15 A. That's correct.
16 Q. You have already said that the difference, the key
17 difference, was that the people most at risk in the new
18 scenario -- that is the AIDS infection -- were patients
19 with severe haemophilia, and I think you should probably
20 just spell out for us why that is?
21 A. Because they received much more treatment.
22 Q. Yes. This is a terribly crude analogy but it has been
23 used before. There is a sort of Russian roulette
24 phenomenon that if you are receiving a lot of product
25 that finally somebody may get a product which has the

1 virus in it. Is that really the thinking?

2 A. Yes, the risk is related to the prevalence in the

3 population and the more exposure you have to blood

4 donations, then the greater the probability that you

5 might come across one that's infected.

6 Q. Yes. So your suggestion in this memorandum -- albeit,

7 as you say, there isn't any hard data -- is that:

8 "Heat treatment of everything looks at the moment to

9 be the most likely possibility that we have to face up

10 to. If this is so, we will have to plan to pasteurise

11 all of the Factor VIII rather than 30 per cent and we

12 may also want to review the timescales noted above."

13 The timescales, we can see, had been four to six

14 pilot scale lots in 1983 and then 30 per cent production

15 for 1984 to 1985 at the earliest.

16 You explain your reasoning on timing by saying that:

17 "It may become crucial for a number of reasons.

18 Firstly that there may be a long incubation period."

19 So I take it that means that there may be something

20 already destined to happen, which, because of the long

21 incubation period won't become apparent for some time

22 yet.

23 A. That's correct.

24 Q. You say also:

25 "There are some who would find a move back to cryo

1 attractive and if this gathers momentum, it would only
2 need one suspected case from NHS Factor VIII and we
3 could see our fresh-frozen plasma disappear overnight.
4 In other words ..."
5 I think we have seen this elsewhere, the panic
6 recourse to cryoprecipitate. If everybody suddenly
7 said, "We want cryoprecipitate", you wouldn't have any
8 raw material from which to make your concentrates?
9 A. No, we would not.
10 Q. Yes. Then looking at the second page of this
11 memorandum, you say:
12 "There may therefore be case for accelerating our
13 heat treatment programme."
14 What you are suggesting is an intermediate stage,
15 still using the pasteurisation cabinets, and you say:
16 "We will probably have most of the equipment to
17 allow us to do this already."
18 You then do, I suppose, a worked example, a worked
19 example with 1,000 kilogramme pool of fresh-frozen
20 plasma. Is that right?
21 A. That's correct.
22 Q. Yes. You give a tentative programme for how it would
23 run in practice. So five days and you would end up,
24 I think we can see from step (iii), that the full-scale
25 Factor VIII batch could result in 225 100 ml bottles.

1 So that's from your 1,000 kilogramme pool, is it?
2 A. That's correct.
3 Q. Your caveat at the end is that:
4 "Of course, the in vivo recovery and Factor VIII
5 yield would have to be adequate and information on this
6 should be generated as quickly as possible."
7 The next document which follows logically from this
8 is [SNB0073638]. This is Mr Watt. This is two days
9 later. So 5 May 1983. Mr Watt writing to Dr Cash. He
10 doesn't actually mention your memorandum but it does
11 looks as though the letter has been triggered by your
12 memorandum because he is really writing on more or less
13 the same topic. Is that right?
14 A. Well, it's the same topic. It's possible that he has
15 taken my memorandum into account.
16 Q. Right. So he is summarising recent research. Noting,
17 before we turn over, what the viral reduction is for
18 heating at a higher temperature for a short period --
19 and I think that's now known to be less than one hour --
20 that that's much more effective than previous
21 experiments. Then can we look on to the second page,
22 please? He is saying in the first big paragraph on the
23 second page that there is a pilot lot. I think matching
24 lots in fact because one of the lots, 760, will have
25 been a control lot. Is that correct?

1 A. That's correct.
2 Q. So a control lot and a heat-treated lot, 761, but
3 unfortunately the control lot, 760, failed its
4 laboratory release because it failed on grounds of
5 pyrogenicity and shouldn't be issued for clinical use,
6 but Mr Watt is saying that he wants to get some clinical
7 experience of 761. Then can we go down.
8 Talking about some further lots and then on to the
9 final page. He doesn't seem, Dr Foster, to be saying in
10 terms the same as what you were saying in your
11 memorandum; in other words, he is not spelling out
12 a plan that seems to accord with what you had suggested,
13 but the general theme seems to be also one of
14 acceleration?
15 A. Yes, I mean, he is dealing with the first pilot
16 preparation that we had prepared of the pasteurised
17 process and addressing how that is going to be
18 progressed in terms of -- from Dr Cash's point of view,
19 how it will be evaluated clinically, rather than jumping
20 straight in to say, "How we are going to accelerate this
21 programme?" Although he does say in the final paragraph
22 about how it could be speeded up substantially. So he
23 is perhaps alluding to my later memorandum.
24 Q. What's rather strange actually just to my eyes -- and
25 this is no doubt my fault, but the last sentence in

1 which he records that colleagues are costing an
2 expedited programme, and everything in the letter up
3 until now has seemed very logical and seemed to be
4 something Mr Watt is supporting, but in the last
5 sentence he says:
6 "Public opinion rather than science may dictate the
7 best course of action."
8 Were you trying to respond to public opinion when
9 you wrote your memorandum or was it more objective than
10 that?
11 A. My memorandum was a kind of scenario planning because
12 there was so much uncertainty and lack of knowledge, and
13 I think that's what Mr Watt is alluding to when he says
14 "rather than science". We didn't have all of the
15 scientific answers and I was just laying out scenarios
16 and really leaving it for Professor Cash and Mr Watt to
17 judge what was the best way forward.
18 Q. Right. So you don't think that Mr Watt is actually
19 trying to say that what's in the letter might be
20 unscientific or bad science; it's just that the science
21 is, at the moment, missing?
22 A. I think that's a better way to put it, yes.
23 Q. Right, okay.
24 Can we just go to your answer, in which you deal
25 with this memo? That's page 24 of [PEN0121438]. We asked

1 you about the circumstances in which you came to write the
2 memorandum, and at first I think you thought it was in
3 response to the report of Gallo's research, but Gallo's
4 material wasn't published until May 1984. So you
5 thought on reflection that it may have been the reports
6 in the Lancet in April 1983 about AIDS and 11 people
7 with haemophilia in the USA and three in Spain.
8 Dr Smith suggests that it might actually have been in
9 response to the Barre-Sinoussi work, which would have
10 been around about this time. I suppose it's just very
11 difficult to remember?
12 A. I wouldn't have been aware of that at the time. I think
13 it was such a low-key publication, it's not one that
14 I would have been aware of at the time.
15 Q. I think it's actually slightly later in May. So you
16 would have had to have heard about it on the grapevine
17 rather than read about it, I think. But doing the best
18 you can, you think it was possibly reading these reports
19 in the Lancet?
20 A. It seems the most likely. We did take the Lancet and
21 I did try to look at it. That was the most likely
22 trigger for my thinking at that time.
23 Q. You give us a little bit more information about what
24 happened after you had sent the memo.
25 I'm conscious, sir, that it's quarter past four and

1 we are unfortunately in the middle of a long answer in
2 this statement. I wonder, rather than trying to rush
3 through it, although it's not a natural break, it might
4 be better to stop here?
5 THE CHAIRMAN: Can you remind me when the Stirling
6 conference was?
7 MS DUNLOP: June 1982.
8 THE CHAIRMAN: Did you ever hear anything about a conference
9 in Stirling, of interest, primarily, to leukaemia
10 specialists and others, at which AIDS was discussed as
11 an emerging problem?
12 A. No, I knew nothing about it until it came up in these
13 proceedings.
14 THE CHAIRMAN: I see, yes. I just wondered if that's
15 another factor that might have led to some discussion in
16 Scotland, although the evidence we have heard from the
17 one person who did know about it suggested it wasn't
18 disseminated very widely by him. But you can tell us it
19 had nothing to do with inspiring your thoughts.
20 A. It certainly didn't. I didn't know anything about that.
21 THE CHAIRMAN: The other question you might like to consider
22 is what was necessary for you to write to Mr Watt to lay
23 a basis for future planning and what Mr Watt might write
24 to Dr Cash. It might be different because of the
25 context in which they would see each other and you would

1 see them, but you don't think it could be that Mr Watt
2 would be persuaded by your analysis but recognised he
3 had to approach Dr Cash in a different way?
4 A. I'm not sure really how to answer that.
5 THE CHAIRMAN: Well, that may be an answer in itself.
6 Thank you.
7 (4.19 pm)
8 (The Inquiry adjourned until 9.30 am the following day)
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DR PETER FOSTER (continued) 7
Questions by MS DUNLOP 7