1 Tuesday, 1 November 2011
2 (9.30 am)
3 (Proceedings delayed)
4 (9.59 am)
5 DR JAMES SMITH (affirmed)
6 Questions by MS DUNLOP
7 THE CHAIRMAN: Good morning, Dr Smith.
8 Dr Smith, you and I are in the same position in one
9 respect today: we don't have immediate support.
10 Professor James, who normally keeps me right on all
11 matters of science and medicine, is away in Malaysia and
12 therefore can't be present, and I gather you don't have
13 anyone present who is bound to support you either.
14 We will try to look after your interests, since
15 that's the obligation of the Inquiry when you are not
16 supported but of course, we won't necessarily know if we
17 are getting out of your comfort zone. If you feel that
18 at any time you need to pause, think about things, or
19 take such advice as we can give you, just let us know.
20 The last thing I want is for you to be uncomfortable.
21 Ms Dunlop.
22 MS DUNLOP: Thank you sir.
23 I'm obliged to you for allowing us a little bit of
24 time. I'm obliged to everybody for the delayed start
25 but I did need a little bit of last minute coaching from

1 Dr Smith.

2 Dr Smith I think it would be fair to say we have
3 heard a lot about you. I thought that I would begin,
4 now that you are here, by asking a few questions about
5 yourself and your career and we will also be talking
6 about your work at PFC and then your move to England and
7 the set-up there. And then obviously we will be looking
8 at the statement that you have provided for the B3 topic
9 also.

10 I should explain, sir, that obviously Dr Smith has
11 provided material which assists us both with our B3
12 topic and with our C3 topic, and following the sort of
13 carve-up that we have organised among ourselves, I will
14 be leading evidence from Mr Smith today on the B3 topic
15 and then Mr Mackenzie is going to carry on and pursue
16 the C3 topic tomorrow. So that is the division that we
17 have planned.

18 THE CHAIRMAN: We are only going to be able to rest Dr Smith
19 from his fastness once.

20 MS DUNLOP: Yes. since Dr Smith has travelled here from
21 France, we are very grateful to him for doing that and
22 the least we could do was to confine it to one trip
23 rather than asking you to make two.

24 So can we look, firstly, please at the curriculum
25 vitae which you have provided, which is, I fear actually

1 in twice, but the reference I have for it is WIT0030351.
2 It's also -- I'll just say this -- PEN0121780.
3 We see, Dr Smith, that you took a Bachelor of
4 Science (Honours) in pure chemistry at
5 Edinburgh University, graduating in 1962 and then you
6 did a PhD in the faculty of medicine and you looked
7 particularly at the purification and identification of
8 placental histaminase in your PhD.
9 It is interesting that Dr Foster studied chemical
10 engineering, whereas you are a pure chemist. I suppose
11 the two of you came to do more or less the same job.
12 Chemical engineering conjures up more of an image of
13 someone who is going to be intervening with the
14 chemicals he is studying and the materials with which he
15 is working, whereas you were observing the materials.
16 Was chemical engineering less developed in the late 50s
17 and early 60s?
18 A. That is true, and I think it's fair to say that chemical
19 engineering as a subject, as a career, would have
20 developed from the pharmaceutical industry, the oil
21 industry, for instance, where you are applying chemical
22 principles to moving large amounts of material around,
23 larger than we tend to do in most laboratory work.
24 Therefore, there is a greater accent in the training
25 of a chemical engineer on scale-up, on the details and

1 characteristic of different kinds of industrial
2 equipment than there would be for a scientist working on
3 the whole with millilitre or litre amounts of material.
4 Q. Right. Perhaps for your purposes we can see it as
5 a distinction between pure and applied science or is
6 that not --
7 A. There is nothing very pure about fractionation; it was
8 very applied.
9 Q. Moving on down through your CV, we can see that you list
10 for us the positions you have held, the relevant
11 positions you have held, and you went on after your PhD
12 to do post-doctoral research. At this point your career
13 seems to have had more of a directly medical flavour?
14 A. I did my PhD in the department of clinical chemistry at
15 Edinburgh, where they had an interest in enzymes to be
16 found in plasma, which might give you clues as to the
17 status of a particular organ system in the body. So
18 there was a medical application but I had, myself, no
19 connection with medicine at that time.
20 Q. Right. You then tell us that between 1968 and 1975 you
21 had a number of duties in the blood products unit and
22 later the Protein Fractionation Centre in Edinburgh, and
23 we can read for ourselves the description of some of the
24 tasks you undertook.
25 We know that you moved to work in England in 1975,

1 more particularly at the Plasma Fractionation Laboratory
2 in Oxford, and you also had duties at what you say was
3 the parent laboratory, the Bioproducts Laboratory. BPL
4 is not the only organisation which has taken advantage
5 of the process of changing its name but retaining its
6 initials. Perhaps the most obvious other one is UKHCDO,
7 which has changed the D from directors to doctors or the
8 other way round but BPL started out as the Blood
9 Products Laboratory and then became the
10 Bioproducts Laboratory, I think you have told us?
11 A. Yes.
12 Q. You, in due course, became in charge of all research and
13 development at Oxford and you say that between 1979 and
14 1982 you were seconded to additional duties as head of
15 coagulation factor production at Elstree and you
16 attended both laboratories for part of every day.
17 Dr Smith, there has been some reference in the
18 evidence of other witnesses to your move from Scotland
19 to England and in particular I think Professor Cash said
20 in terms that you had left in a huff, and I just wanted
21 to give you the opportunity to comment yourself on that.
22 A. I did note that colourful phrase from Dr Cash. What
23 I will say is it strikes me as being somewhat reductive.
24 Q. Yes. I think you yourself might prefer the term
25 multifactorial to describe your departure from

1 Edinburgh?

2 A. Indeed, excellent word.

3 Q. Is that correct?

4 If we move on to the following page, we can see

5 further description of your responsibilities in England.

6 You also mention that between 1984 and 1990, the Oxford

7 laboratory succeeded in treating all these concentrates

8 by pasteurisation or dry heating, rending them safe from

9 transmission of the most important blood-borne viruses,

10 HIV, HCV and HBV.

11 The end of the following paragraph represents

12 a comment about liaison with clinicians. You say:

13 "Save for two years at Ellen's Glen PFC, I always

14 had daily access to the advice of patient, helpful

15 clinicians and was never isolated from the painful

16 realities of life as a person with haemophilia."

17 Now, I know, Dr Smith, you are not meaning that the

18 clinicians in Edinburgh were impatient and unhelpful,

19 it's just that they weren't beside you in contrast to

20 the position in Oxford. Is that correct?

21 A. I meant nothing like that. Even when working in the PFC

22 or blood products unit in the Royal Infirmary, we were

23 exposed all the time to comments from the haematologists

24 and the haemophilia treaters and I didn't mean to --

25 it's only the period at PFC which is separate, of

1 course, from the Royal Infirmary, that that was not
2 a daily, almost daily, occurrence.
3 Q. Yes. For you the contrast will have been evident
4 because you had had the experience of being based at the
5 Royal Infirmary and then you moved to Ellen's Glen.
6 Other witnesses have said it wasn't a drawback that PFC
7 wasn't right beside a haemophilia centre or part of the
8 hospital but it may be that they hadn't had the previous
9 experience you had?
10 A. Precisely or --
11 Q. Well, you had had both?
12 A. Yes.
13 Q. Did you think it was a drawback that PFC was
14 geographically more distant from the haemophilia centre?
15 A. I could see the practicality of it. In fact I could see
16 the impracticality of having the industrial process
17 going on in the new Royal Infirmary. I can see why it
18 happened. I felt it was a loss and I felt, even more,
19 that the laboratory at Elstree, BPL, suffered from being
20 very isolated for strategic reasons from the London
21 hospitals, and it was only with the advent of Dr Lane in
22 the very late 1970s that that began to change. I think
23 he also saw it as a drawback that we were not making
24 daily contacts or frequent contact with the people who
25 were using our products.

1 Q. Yes, and of course I have couched the question in terms
2 of haemophilia clinicians but these centres are making
3 products for patients with other complaints as well?
4 A. Indeed. This Inquiry focuses on haemophilia but at no
5 time during these years were we able to neglect the
6 many, many more patients who required immunoglobulins,
7 albumin and other products, which we did not have the
8 right to interfere with too much. These patients were
9 more diffuse in their needs and the clinicians who used
10 these products were scattered. So there was no, if
11 I can call it, pressure group from patients with
12 immunodeficiencies, for instance.
13 Q. I suppose --
14 A. We all had to take account, equal account, of all the
15 users of our products.
16 Q. Yes, and I suppose the same point can be made that if
17 the laboratory is geographically distant from the
18 hospital, then you do not have access to clinicians from
19 other disciplines either?
20 A. Indeed.
21 Q. Right. You go on to narrate that PFL Oxford was closed
22 in March 1992 and you then tell us that since April 1992
23 and up to and including the present day, you have been
24 a consultant adviser on fractionation and coagulation
25 and you are -- I understand -- directly involved in the

1 world of fractionation but also you are involved in
2 giving testimony and providing reports for proceedings
3 such as the present ones.
4 A. Yes, more occasionally.
5 Q. More occasionally? Right. I have already alluded to
6 the fact that you live in France but you are a frequent
7 visitor back to Scotland. Is that correct?
8 A. Yes.
9 Q. Thank you.
10 Can we move then, please, to look at your B3
11 statement, which is [PEN0121551]?
12 You have helpfully provided us with an introduction
13 explaining your own approach to the preparation of the
14 statement. You obviously can offer us your experience
15 from the period in which we are interested because you
16 were there, and you are also able to offer a comparative
17 perspective, giving us information about developments in
18 England, which we can use to examine developments over
19 the same period in Scotland.
20 You say that you have, you think, provided
21 interpretation as well as confirmation of facts, and you
22 refer to the potential for minimising that element of
23 your statement if you are so guided, but I think
24 I should say that we have had no difficulty with that
25 and we have been very interested to read everything that

1 you have provided for us. I'm grateful for it.
2 You were sent our snapshots and landmarks document,
3 posing all the same questions as have been posed to
4 other witnesses on the B3 topic, perhaps not quite all
5 of them in fact because there were a couple that we
6 didn't include in our English schedule but almost
7 entirely the same questions.
8 You have answered the questions, insofar as you can.
9 You have also provided, towards the end of your
10 statement, some supplementary notes, notes 1 to 5 and
11 you explain on the page we can see in front of us your
12 thinking in providing these additional notes. And
13 finally you have included some comments on the specific
14 paragraphs of the preliminary report.
15 Insofar as the second section there is concerned
16 with the four bullets, I think we understand the
17 thinking which underlies all four of these bullets,
18 Dr Smith, that some questions needed a longer, more
19 informative answer, that a thematic narrative is
20 sometimes helpful in bringing together related facts.
21 Again, I think it would be fair to say that the
22 Inquiry team has been conscious of attention, almost
23 throughout, between telling the story chronologically
24 and telling the story thematically. There is no doubt
25 that some topics are best dealt with thematically. So

1 perhaps we can characterise the approach the Inquiry
2 team has ended up taking as thematic-chronological, in
3 that we have divided the material into topics but we
4 have stuck loosely to a sort of chronological order.
5 You mention also an important issue may have been
6 accorded too little or too much weight in the questions
7 or in the preliminary report, and you also felt you
8 could see some questions hovering over the text even if
9 they hadn't been directly articulated.
10 So understanding that that is your approach, can we
11 then look at the second page, which is the first full
12 question and answer? You confirm our understanding that
13 there was work aimed at removing viruses from
14 coagulation factors in the 1970s in Scotland. Our
15 understanding was that the work in the 1970s was carried
16 out on Factor IX and related to Hepatitis B, and you
17 have confirmed that that's correct.
18 We referred you to a report prepared by Mr Watt
19 in December 1973 and it would be useful if we could have
20 another look at that, please. It's SNB0016903. You
21 think you prepared this report?
22 A. I wouldn't go so far but there is evidence that I would
23 have offered suggestions, perhaps even drafted at least
24 certain paragraphs and sections of it.
25 Q. We can certainly see that the frontispiece seems to be

1 in different type from the rest of the text. So the
2 then director, Mr Watt, is shown on the front page and
3 the title of the paper is "Development of Factor VIII
4 concentrates." then if we turn into the actual text, it
5 does look slightly --
6 A. Excuse me, do we know for what purpose this report was
7 prepared? For what body or for haemophilia directors or
8 ...?
9 Q. I'm sure somewhere we have that information, Dr Smith.
10 I don't readily have it to hand. It doesn't seem to
11 have been a particularly widely disseminated report but
12 we will certainly look into what we think its purpose
13 was.
14 It seemed to us useful simply as a sort of snapshot
15 of the position in 1973.
16 THE CHAIRMAN: Do you know that Mr Watt gave a speech at
17 a symposium in 1972, covering some of these matters?
18 A. I simply can't remember.
19 THE CHAIRMAN: You do not remember that.
20 MS DUNLOP: We have looked at this document before but if we
21 can just remind ourselves of the topics dealt with in
22 it: development to date, laboratory scale, 2 to 10-litre
23 batches of plasma have been fractionated by the methods
24 of Newman and Johnson to intermediate potency and high
25 potency Factor VIII. These, Dr Smith, I understand to

1 have been preliminary steps to the achievement, ultimate
2 achievement of NY. Is that correct?
3 A. Yes. In fact Drs Newman and Johnson developed twin
4 processes. One was the process which became NY but they
5 also proposed further purification of an NY-like
6 intermediate by precipitation with polyethylene glycol
7 and glycine, I believe was involved. That never gained
8 wide use and was never continued beyond the first
9 experiments in Edinburgh. So we stopped, we were quite
10 satisfied with the performance of the NY-type material.
11 Q. I see. In terms of scale, we can see from this page
12 that initially, in 1972, people were working with
13 batches between 2 and 10 litres. The scale then
14 increases. We can see in February 1973 it's narrated
15 that the scale has gone up to 10 to 60-litre batches
16 and, and then at the foot of the page we can see that
17 there is work now going on with 100-litre batches. So
18 there seems to have been that sort of stepping up of the
19 amounts of material. Can we move on through the
20 document, please? We can see further details which are
21 really, I think, related to production methods.
22 Reference at the bottom of this page to large scale
23 crushing and thawing equipment which has been
24 commissioned in early September 1973. And also mention
25 of the strength, if you like, of the product currently

1 being prepared and a comparison with Hemofil, which we
2 know to have been a commercial preparation.
3 Can we just move on to the next page, please? Then
4 a look to the future, future high potency concentrates.
5 Next page, please. Can we go back to the statement?
6 Thank you.
7 THE CHAIRMAN: Looking at this document generally, does it
8 seem to focus on the transition from the production of
9 Fraction I AF, antihemolytic factor, into the beginning
10 of the new period of production of Johnson- and
11 Newman-inspired materials.
12 A. Precisely.
13 THE CHAIRMAN: That's what it is.
14 MS DUNLOP: Yes.
15 A. A process occurring over a period of several years.
16 THE CHAIRMAN: Yes.
17 MS DUNLOP: I should say, sir, that we may go back to
18 Cohn Fraction I, just not at the moment. Dr Smith is
19 obviously in a valuable position in that he can give us
20 a lot of historical information and we do have some
21 additional material which I may tender, and we may get
22 Dr Smith's recollections of some of the earlier
23 processes but we didn't think it would be sensible to
24 start with that. So we are going to work through the
25 statement and we may come back to that at the end.

1 THE CHAIRMAN: I keep getting corrected too, Dr Smith, by
2 showing an interest.
3 MS DUNLOP: It wasn't intended as a correction, sir, but as
4 a promise of something interesting but just not quite
5 yet.
6 THE CHAIRMAN: I look forward to it.
7 MS DUNLOP: Now, back at the statement, we can see that
8 there is also a report of research and development from
9 1975, which we had looked at, and it mentioned a paper
10 which had been presented in Vienna. We are going to
11 look at that as well.
12 A. May I say, my copy is not showing the previous
13 paragraph.
14 Q. All right.
15 A. Could we make it a bit smaller so that I can see more of
16 the page? Thank you.
17 Q. Yes. There we go. Can we also open up the other
18 document, the 1975 document, SNB0104779. This is an R&D
19 report from April 1975 and we can see that on the
20 frontispiece here Dr Foster's name is given and I think
21 you are at PFL by April 1975, are you?
22 A. No, could I just point out that by this time Dr Foster
23 had become head of R&D at PFC. So I was called "chief
24 chemist" or something like that, with main interests in
25 quality control and quality assurance of batches.

1 I left effectively in July 1975.

2 Q. Right.

3 A. Dr Foster would have been in post as head of R&D for at

4 least a year by this time.

5 Q. Thank you.

6 We notice that this document does refer to the

7 ongoing project on Factor IX concentrate with a reduced

8 Hepatitis B activity and can we look, please, at the

9 reference to this on page 5? I think it's the very

10 first item on page 5:

11 "Preparation of a Factor IX concentrate with reduced

12 Hepatitis B antigen activity."

13 We see your name. Indeed, if we just look down to

14 the bottom of this page, we can see your name featuring

15 in a number of projects although not all of them I think

16 were active at this point. For example, the second one

17 has been suspended but to go back up to the top and look

18 at the first one, a project which commenced in 1971,

19 that's a project that continued after you had gone to

20 Oxford. Is that right?

21 A. Not at Oxford, only in Edinburgh. Oxford never picked

22 it up.

23 Q. I see. I was going to ask about some collaboration

24 between Oxford and Edinburgh in the early 1970s in

25 relation to Factor IX. Did that occur?

1 A. Yes, in fact the DEFIX still being made as the basis of
2 PFC's final Factor IX concentrate and still the basis of
3 BPL's Factor IX concentrate. This DEFIX was developed
4 in very close cooperation with our colleagues at Oxford,
5 right from, I would say, about 1969/1970. We identified
6 a common interest in preparing Factor IX from normal
7 plasma and worked together very closely on it and
8 although we finally adopted some slightly different
9 techniques to accommodate our different plasma sources
10 and their different histories, these products remained
11 very, very close together for 20 years.
12 Q. Right. The essence of the project we see described in
13 paragraph 2.1, was removal of the virus, rather than
14 doing something to the complete product: heating or
15 addition of chemicals or anything to try to inactivate
16 the virus. Is that correct?
17 A. Yes, there are two forms of virus reduction: we call one
18 inactivation, that is where you hit it with heat or
19 a chemical, and the other you would call segregation or
20 separation; reduction by physical removal.
21 Q. Right. And the project described here is of the latter
22 type?
23 A. Yes.
24 Q. Right. Now, can we move back then, please, to the
25 statement and I think that brief examination of these

1 documents tells us the story of viral inactivation or
2 treatment of concentrates such as it was in Scotland in
3 the 1970s, as I understand it.
4 We then moved on, if we look at the next page, to
5 ask some questions about 1980 and thereafter. We don't
6 need to ask you question 3 because we know that the
7 answer to it is "yes".
8 Question 4 relates to Dr Cash's discovery of the
9 work of Behring in 1980, more particularly we know that
10 he learned of the developments at the first
11 international haemophilia conference in Bonn. We have
12 also at a previous session been through the various
13 different publications that we have managed to trace,
14 emanating from Behring around about this time.
15 It's not entirely straightforward to work out what
16 publication is which and what emanated from where and
17 who had what, but you, in your answer, point out that
18 the information imparted by Behring was not a repeatable
19 process description; in other words, they weren't
20 disseminating some sort of methodology which others
21 could immediately implement, and no doubt for good sound
22 intellectual property-related reasons.
23 You say that there was a very brief notice of
24 a patent application in chemical abstracts and that
25 Dr Foster would almost certainly have waited for fuller

1 publication in 1981, and that particular journal to
2 which you refer is, I think, Drug Discovery or something
3 like that, in English?
4 A. Yes.
5 Q. Is that right? Yes. You say:
6 "To be pedantic, some details have been published in
7 Behringwerke's house journal."
8 And that's the publication we understand to be
9 entitled something like "The Yellow Notebook" or "The
10 Yellow Journal," something of that sort. You say:
11 "That was an unrefereed journal. It would be
12 scarcely available in the United Kingdom and certainly
13 not on any fractionator's regular reading list."
14 A. It emerged only later as a priority document.
15 Q. At some point Behring seem to have reissued what's
16 a rather scrappy early version of the document, possibly
17 the internal version. They seem to have reissued it in
18 a more polished format with the tables which had
19 previously been completed in handwriting, typed up and
20 so on, and we have a copy of that as well.
21 A. Yes, a rather bewildering sequence of rehashes.
22 Q. It's not entirely straightforward but we think we
23 understand it slightly better -- or we think we do --
24 than we formerly did.
25 THE CHAIRMAN: I'm not sure that I can work it out to my own

1 satisfaction but I'm not sure that it matters. We know
2 that various bits of information were floated on to the
3 public stage from time to time.
4 A. A teasing process goes on. "We are not going to tell
5 you enough to invalidate our patent but wink, nod, this
6 might have some bearing on hepatitis later but we will
7 tell you about that."
8 Q. Yes. We are not going to go through it all again,
9 Dr Smith, because we looked at all the different
10 publications with Dr Foster on 6 September and we do
11 also have Dr Foster's own evidence, which is that he has
12 told us that his first awareness of the work of Behring
13 did indeed come from Dr Cash who returned from Bonn and
14 said, "You will never believe what I heard". So we do
15 at least know that and as the chairman says, it is
16 probably not necessary to probe any more deeply what the
17 order of the publication of the different materials was.
18 We then asked you our question 5 about whether the
19 research in Scotland began in response to this news from
20 Behring and you thought that that would be almost
21 certainly true. You referred too to the Cutter patent
22 application, which I think dates from 1980, and even
23 here there is a bit of a curiosity too because Hyland
24 were in on the act quite early on. You say:
25 "It was probably in 1981 that Hyland began to reveal

1 experiments on heat treatment of Factor VIII. The actual
2 treatment and process conditions were not published for
3 some years and more than one person was misled into
4 guessing that this too was pasteurisation."
5 You refer to one document, which we will come to
6 shortly but there is an even more clear explanation of
7 why people were misled. If we look at [SNB0104452],
8 please, which is Dr Foster's report of the congress in
9 Budapest in 1982. We have heard about this congress
10 before but if we look in particular at page 5, we can
11 see a heading there "Hyland Concentrate". Do you see
12 that?
13 A. Yes.
14 Q. "This topic was not listed in the programme but Dr Dolan
15 was invited to present a report of the work following
16 S-23-7 by Prince."
17 He was obviously slotted into the programme:
18 "The method was said to involve pasteurisation and
19 details of chimpanzee experiments were presented."
20 So if that was said, it's not surprising that people
21 were misled but it was not correct. At least when the
22 Hyland product emerged in 1983 it was a dry-heated
23 product.
24 A. The term "pasteurisation" was used very loosely.
25 Classically it goes back to Louis Pasteur and his

1 techniques, which would inactivate almost all organisms.
2 It would emerge as being 60 degrees centigrade for ten
3 hours. It was used in other contexts. It was used for
4 different temperatures, different periods of time and
5 might still be called "pasteurisation".
6 I think it's a simplification too far to call dry
7 heating pasteurisation but indeed, one was often heating
8 in the same baths -- heating a dry product, perhaps as
9 a stop gap, heating in the same baths that had been used
10 for pasteurisation proper.
11 Q. I see.
12 A. And in this way you get leakage of the use of the term.
13 Q. So to you, as a chemist, the defining characteristic of
14 pasteurisation as a process should be that it's wet
15 heating?
16 A. Indeed.
17 Q. However, some people were using the term
18 "pasteurisation" because of the actual protocol, say ten
19 hours at 60 degrees, and they were calling what they
20 were doing "pasteurisation", even though to a chemist it
21 wasn't. Is that accurate?
22 A. Exactly, and I don't wish to imply that Hyland were
23 going out of their way to mislead but this can arise
24 naturally.
25 Q. So there was an element of crossed wires?

1 A. Drift.
2 Q. Drift?
3 A. Drift in the meaning of words.
4 Q. Terminological inexactitude.
5 Can we go back to the statement then, please? Can
6 we turn to the next page? I should actually, Dr Smith,
7 also go to the reference which you gave in this
8 connection, which is about the puzzlement at whatever it
9 was that Hyland were doing. That's [SNB0073341]. Just
10 to show that this is Dr Foster writing to you
11 in December 1982. If we look at the foot of the page,
12 we can see Dr Foster saying that he doesn't think the
13 Hyland process is ten hours at 60 degrees centigrade.
14 So there has obviously been a degree of discussion among
15 those of you working in the field about what it was that
16 the commercial companies were actually doing?
17 A. Yes.
18 Q. And I think we can understand why that should be so.
19 Sorry, can we look at the statement again, please?
20 In question 6 we mentioned the Factor VIII study
21 group, which began its work in 1982, and you gave us
22 a little bit of a snapshot of the position around about
23 the beginning of 1982. You say that:
24 It's not sufficiently realised even in our own
25 preliminary report, how little pressure there was from

1 the haemophilia treaters and patients to take NANBH
2 seriously in this period before 1983.
3 You refer to a number of reasons for that. Firstly
4 an assumption that NHS concentrates were much safer,
5 although I think we now understand from a number of
6 different witnesses that indeed there was a very high
7 risk of infection from NHS products as well as from
8 commercial products?
9 A. That is the significance of 1983. It would have been
10 very clear only in 1983 to everyone this was the case.
11 Q. And that it's simply a function of the prevalence of the
12 virus in the donating community and the size of the
13 pool?
14 A. Exactly.
15 Q. Yes. And then also you refer to the fact that the view
16 that NANBH could have severe long-term sequelae was not
17 widely held. You say:
18 "It really took AIDS in 1983 to 1984 to get the
19 attention of the majority on to blood-borne viruses."
20 When I read that again, Dr Smith, I wondered which
21 majority, the majority of whom?
22 A. I started the paragraph with the haemophilia treaters
23 and the patients themselves.
24 Q. Right. So that's how we should understand the reference
25 to "the majority", that by 1983 to 1984, the majority of

1 haemophilia treaters and patients were taking the risk
2 of blood-borne viruses much more seriously than they
3 previously had?
4 A. And in contrast to the fractionators who could see their
5 entire industry going down the tubes unless we did
6 something about this threat.
7 Q. I wonder if you could amplify the second paragraph there
8 for us a little bit, Dr Smith. Why do you think
9 fractionators had been so much more concerned?
10 A. Elements there -- among these elements anyway, would be
11 the experience of the company Cutter in the mid 1970s,
12 when almost every batch of their Factor IX transmitted
13 Hepatitis B. Certainly it would have been ascribed to
14 Hepatitis B at that time. I couldn't be sure whether
15 some of it might not have been non-A non-B as well.
16 Q. Right.
17 A. At the time, the uses of Factor IX were expanding beyond
18 the use in Haemophilia B, to such things as protection
19 of patients during liver biopsy, reversal of
20 anticoagulants, the warfarin range of anti-coagulants
21 sometimes anti-coagulated a little too well. If
22 a patient on warfarin had to go rapidly for surgery, it
23 took several days to correct the deficiency in
24 Factor IX, et cetera, which warfarin initiates, and the
25 quick fix was to give them a shot of Factor IX

1 concentrate and restore their liver status so they could
2 undergo safe surgery.
3 Uses like this, in fact, were at one time
4 threatening to exceed our capacity to make Factor IX; it
5 was so serious. That was stalled in its tracks by
6 a report from two MRC trials which had looked at these
7 two particular applications of Factor IX, in the course
8 of which several of the trial patients had acquired
9 hepatitis and one had died from the very rare
10 fulminating version of probably non-A non-B Hepatitis.
11 That did stop us all in our tracks and make us think
12 very, very hard about what was going to happen if all
13 our products started to be infected by this virus, which
14 we could not detect, not diagnose in patients and
15 impossible to detect in donors and therefore screen out
16 affected donors, taken very seriously indeed by,
17 I think, most fractionators.
18 Q. Right. You mention some of the many difficulties. You
19 say too that you were misled:
20 "The fractionating community, I suspect, was misled
21 by persistent claims that there might be more than one
22 NANBH virus."
23 And you go on to explain that the work begun in 1981
24 at PFC would have been exploratory and it may not have
25 acquired much in the way of data or priority

1 by January 1982. So all this by way of explanation for
2 why there isn't a description at the first meeting of
3 the Factor VIII study group of work in progress on viral
4 inactivation.
5 You have supplied at this point an additional note,
6 dealing with some of the impediments to embracing
7 pasteurisation. It's convenient for us to look at it at
8 this stage. That's note 1, which we find on page
9 PEN0121551.
10 We do recognise a number of these bullets, Dr Smith,
11 because they have been mentioned by other witnesses but
12 you tell us that you were seeking to assemble in one
13 place the obstacles perceived in, say, 1980 to
14 sterilising Factor VIII, et cetera, by heating. I think
15 we can read them for ourselves and understand that some
16 of them were indeed misconceptions. So both the first
17 and second bullets, I think, would fall to be
18 characterised as misconceptions, no doubt understandable
19 at the time.
20 Number 3 is obviously true, as is number 4. You
21 refer to the difficulties of using chimpanzees for
22 research and more importantly to the fact that the model
23 wasn't a particularly good one for NANBH anyway. And
24 then the mention of the possibility of there being two
25 variants of the virus. And then you also mention the

1 stumbling block that no protein concentrate survives
2 classical heat sterilisation:
3 "A simple protectant had allowed albumin to be
4 pasteurised but this quick fix was known to be unique to
5 that protein."
6 And we will come back to your note 2:
7 "A concern that any protectants strong enough to
8 protect Factor VIII would also protect any virus."
9 And then you say that:
10 "Fractionators resisted almost viscerally
11 a conjunction of Factor VIII and high temperature. The
12 two independent discoveries that heating might be
13 feasible were made serendipitously by relatively
14 inexperienced workers in pursuit of other aims
15 entirely."
16 I think the two discoveries to which you are
17 referring at that point are the Behring discovery and
18 the Cutter one. Is that correct?
19 A. Yes.
20 Q. And then the concern which we know was articulated by
21 some of the haemophilia clinicians about the formation
22 of neoantigens. And the tension, which again I think we
23 understand to have been ever-present, between any form
24 of heat treatment really and yield, so that these twin
25 goals of trying to provide safe coagulation factor

1 concentrates and trying to provide sufficient
2 coagulation concentrates were often in opposition to one
3 another because there seemed to have been a yield
4 penalty with any additional process step, particularly
5 of heating.

6 A. Exactly.

7 Q. Right. And then lastly, if we turn over the page, you
8 say:

9 "Heating in the dry state might be less stressful to
10 Factor VIII but more difficult to apply homogeneously
11 and certainly less effective against viruses than
12 heating in solution at the same temperature for the same
13 time."

14 Dr Smith, I'm going to risk some basic science here
15 and just ask to you explain things a little further to
16 us about the different ways of heating.

17 If, for some reason, I took a pan of soup and a pan
18 of instant coffee granules, which is the lyophilised,
19 freeze-dried product, and I tried heating them both with
20 a burner, perhaps, under each, it's my understanding
21 that the heating of the soup would be much more
22 efficient than the heating of the granules. Is that
23 right?

24 A. Yes.

25 Q. Why is that so?

1 A. One simple reason is that your water, an aqueous medium,
2 is a much better conductor of heat than a dry medium,
3 which, if you can imagine, especially an evacuated dry
4 powder. It is much more difficult to get heat into the
5 core of a powder in a vial than it is, obviously, if you
6 stick a thermometer into your soup, it will be at
7 60 degrees within a minute or to. Not so with a dried
8 product.
9 Q. Yes.
10 A. But I meant -- it's more to do with the -- that is one
11 aspect of it but it also has to do with the
12 effectiveness of any chemical reaction in an ultra dry
13 powder, compared with the kinetics of heating in
14 solution.
15 Q. Yes. So the first point which you have just answered
16 for us, is really a matter of physics?
17 A. Yes.
18 Q. That in the pile of coffee granules there is air in
19 between the granules and air doesn't conduct the heat.
20 So it's not as efficient a way of heating as heating the
21 soup.
22 A. Often freeze-dried -- after freeze-drying you retain
23 a vacuum in the vial so that when you go to add your
24 needle full of diluent, it is sucked into the product
25 very fast, but the presence of a vacuum makes it even

1 more difficult to get heat into the core of the powder.
2 Q. Right. And then the second point, which you are going
3 on to explain to us, is about the kinetics of heating,
4 and does this take us into the question which I asked
5 you before -- or one of the questions I asked you before
6 we started today, which is why you don't need to apply
7 some kind of protectant or stabiliser to Factor VIII
8 before you dry heat it but you do before you pasteurise
9 it? Is that relevant to the topic of the kinetics of
10 heating?
11 A. I'll try and explain.
12 Q. Please do.
13 A. Virtually all biological, chemical reactions operate
14 with the assistance of -- through the medium of water.
15 The water which you would think is simply a background
16 material, holding the things together, is in fact
17 a player in virtually all the reactions. Turning to the
18 reactions which tend to inactivate proteins or denature
19 them, these are heavily dependent on how much water is
20 there. In a dry-heated product you are down to less
21 than 1 per cent of water. In a pasteurisation situation
22 it is all water essentially. Therefore, the damage
23 being done to -- potential damage to your protein is
24 much more severe in the aqueous pasteurisation context
25 than it is in the dry heating context. Equally, of

1 course, the damage you are doing to viruses, you hope,
2 is much more severe.
3 Q. Yes.
4 A. And in pasteurisation, in trying to protect your protein
5 from what you know will be a damaging experience, you
6 add too much of the wrong kind of stabilisers, you
7 always fear that you have also, in doing so, failed to
8 inactivate so much of the virus; you have protected the
9 virus as well as the protein.
10 Q. Yes. That kind of concept of differential protection
11 must be extremely difficult in practice, finding
12 something that will protect the protein but not also
13 protect the virus?
14 A. It's largely empirical. There are certain classes of
15 substance which have been used more than others: salts,
16 amino acids, sugars, at very high concentration,
17 (inaudible), which is a difficulty in itself. But you
18 would start with certain things, and only then, having
19 exhausted those and all the conditions under which you
20 might apply them, you would start to turn to rather more
21 exotic protectants.
22 Q. Right. So I think, from your explanation of the role of
23 water, we can understand why, with the dry heating
24 process, the Factor VIII is not damaged because the
25 material with which you are working is so dry that there

1 isn't water there to facilitate the inactivation of the
2 protein but why then is the virus inactivated?
3 A. I was -- I learned later, after all the dust had settled
4 on what we had been doing empirically that in fact, in
5 going to such high temperatures as 80 degrees in our dry
6 heating process, we were in fact approaching the melting
7 point of the nucleic acid in the virus.
8 Q. Right.
9 A. It's also true that the viruses of greatest interest,
10 the most severe pathogens, HIV, HCV and HBV, are all
11 lipid-enveloped. They all have a protective envelope of
12 fatty material. And I imagine also that we were doing
13 damage to that directly, almost without the intervention
14 of water.
15 Q. Right.
16 A. In raising the temperature high enough to approach
17 the -- say, the melting point of the lipid, or the
18 melting point of the nucleic acid, which is essential to
19 the production of the virus.
20 Q. Right. Thank you.
21 So having looked at note 1, can we then go back to
22 the statement? This is the statement [PEN0121551] and
23 we were on 1554. If we go back to that, then we can see
24 the reference to note 1 at the end of that paragraph in
25 bold.

1 Then further narrative in paragraph 7 on to
2 paragraph 8. A reference to Dr Foster's attendance at
3 the conference in Budapest and we have already looked at
4 his report.
5 We, I think, confused ourselves -- I certainly
6 confused myself by adding in yet another Behring
7 article, which you have pointed out to us was actually
8 about detailed characteristics of the products and
9 wasn't helpful in elaborating the heat treatment
10 process.
11 Then there is a further paper, which Dr Foster had
12 obtained and which he passed to Dr Cash, and this one,
13 that is referred to here, is the yellow notebook paper.
14 In fact that reference, [SNF0010929] is what I'm calling
15 the messy one, the slightly more scrappy one. We don't
16 need to go to it.
17 It's, as I have said, a less professional-looking
18 copy of the other paper, which has the reference
19 SNB0045880. It's the typewritten version of the yellow
20 notebook paper, and you say that:
21 "It too has no real process detail. It does refer
22 to what appear to have been some successful preliminary
23 studies."
24 So I think you would say that that was really as far
25 as it went. That rather tantalising discussion of -- as

1 one of my colleagues has said, "so far, so good" with
2 the Behring product. And I suppose the purpose you
3 refer to of increasing interest in the pasteurisation
4 approach, may have been exactly what the publication was
5 designed to do.
6 A. Possibly.
7 Q. Yes. Then looking at our paragraph 9. This paragraph
8 refers to another meeting of the Factor VIII study
9 group. Heat treatment was now the first option of the
10 group and we asked if it was essentially because of the
11 apparently promising results obtained by Behring.
12 I think we now understand that it was not just that; it
13 was also that other options, irradiation and the use of
14 beta propiolactone and so on, were being discredited or
15 discounted?
16 A. I would like to reaffirm just how wide-ranging SNBTS's
17 experiments were. In fact, on theoretical grounds, it
18 would seem to most people far more likely that radiation
19 would distinguish between proteins and an assembled
20 entity like a virus. This simply did not happen.
21 Nature did not cooperate in this case but it does
22 exemplify the lengths that this study group went to in
23 exploring every avenue.
24 Q. Right. We had referred in our question to the -- at
25 least superficial similarity with the pasteurisation of

1 albumin but you cautioned us against overplaying the
2 similarities between the two processes and provided an
3 additional note on that, which again we should look at.
4 Note 2 is on page PEN0121551.
5 You explain to us a little bit about albumin here.
6 We note particularly the role of protectants or
7 stabilisers, as they could also be termed, in the
8 pasteurisation of albumin. You say that if the
9 lipid-binding sites of albumin are occupied by certain
10 fatty acids, the cross linking which leads to
11 denaturation is prevented. The treatment is severe
12 enough to kill all bacteria and viruses, and you say you
13 are simplifying, and we don't doubt it, Dr Smith, but
14 I don't expect we need to go any further into that.
15 And large volumes of pasteurised albumin can be
16 given safely to boost plasma volume in patients who have
17 lost a lot of blood. Then you say:
18 "Since the protectants are harmless and do not have
19 to be removed, heating can be done in the final
20 container."
21 Then you draw the distinction with coagulation
22 factors, which we do understand are very, very much
23 harder to work with.
24 Perhaps if we can just note the description you give
25 of the effect of heating on Factor VIII, and you say

1 that:

2 "All these features of Factor VIII make it necessary
3 to work as fast and as cold as possible throughout its
4 processing. Typically in the 1980s, one would seek to
5 go from frozen plasma to vials of sterile frozen
6 concentrate within eight hours. It therefore does not
7 come naturally to a fractionator used to handling
8 Factor VIII with kid gloves, to place a dry preparation
9 into an oven at 80 degrees centigrade or to place
10 a solution in a water bath at 60 degrees centigrade.
11 Water from a domestic hot tap is usually less than
12 50 degrees centigrade and you would not want to take
13 a bath in it."

14 As well as being a vivid illustration, Dr Smith,
15 I think we can understand the common sense of that, that
16 we are talking about a protein naturally present in the
17 human body. So the idea of immersing it in
18 a temperature much higher than the human body can
19 withstand is, as they say nowadays, counter intuitive.

20 In the next paragraph you describe the preferred
21 protectants used for Factor VIII as being sugars and
22 glycine and, on a number of occasions prior to your
23 attendance, people have referred to the resultant
24 substance as being somewhat like jam?

25 A. Indeed.

1 Q. Yes. And then obviously, if you add some very high
2 concentrations of materials like that, you have to
3 remove them again, and again I think we can understand
4 that that's an extra complication. Dry heat treatment
5 offers the same advantage as the pasteurisation of
6 albumin, namely that you can do it in the final
7 container, and I suppose this is a very difficult
8 question to answer but do you think that when people
9 were very attracted by pasteurisation, they possibly
10 didn't give enough weight to the difficulty of removing
11 the protectants and this distinction of not being able
12 to heat-treat in the final container?
13 A. I think the attitude would be first things first; let's
14 see whether this very improbable preferential
15 inactivation of viruses over proteins actually holds
16 water. We will worry about the engineering later but
17 I think when confronted with the first time they saw the
18 jam, that would have been a salutary time at which to
19 reflect. Not impossible, difficult, especially if your
20 fractionation laboratory was not especially flexible in
21 allowing you to set up within the processing area an
22 entirely segregated, specially air filtered area in
23 which to remove these unusual elements of the jam
24 without incurring the possibility of recontaminating
25 your process with viruses.

1 Q. Yes. Or bacteria, presumably?
2 A. Yes.
3 Q. Yes. So it's not just that there is a technical
4 obstacle to be overcome in removing the stabilisers,
5 protectants; it's also that there is a stage then at
6 which recontamination -- or contamination of the product
7 with which you are working becomes possible and
8 precautions have to be taken against that?
9 A. At that point you are into bricks, mortar and expensive
10 air handling equipment and expensive surfaces, all of
11 which, working within the public service, would normally
12 take between two and three years to specify and
13 construct --
14 Q. Right.
15 THE CHAIRMAN: Could I just be quite clear what you mean by
16 your fractionation laboratory not being especially
17 flexible? Is it just a question of space or is it
18 a question of the interaction of space, the equipment
19 and processes and so on, what you would understand?
20 A. Space would usually be the more contentious of these,
21 again because in the public service you were never
22 allowed to build for the future. You were restricted to
23 building for the capacity which you required today,
24 which, of course, by the time you had that capacity was
25 three years ago.

1 So very few fractionation laboratories were able to
2 find within the outside walls, an area of sufficient
3 space and especially of differential air handling, in
4 which you could safely carry out aseptic operations.
5 MS DUNLOP: Right.
6 THE CHAIRMAN: It's quite difficult for us from the outside
7 to get the feel for the complexity of the exercise that
8 would have to be carried out. I think that one can
9 understand that in a service that's always catching up
10 on previous demand, you are never going to spare
11 capacity, and if that were all it involved, then it
12 becomes a fairly simple issue of financing of
13 development or finding more square footage to build on.
14 But what I was more interested in is whether it goes
15 beyond that and involves complexities of engineering the
16 solutions that would mean that the particular solution
17 had to take account of much more than square footage.
18 A. Indeed, and we exacerbated things ourselves by always
19 dreaming up new processes and new products, which all
20 had to be fitted into the building which was designed
21 five years ago and built last year.
22 MS DUNLOP: Right. What was PFL like? Was it an old
23 facility?
24 A. I have read Dr Foster's testimony on this and he
25 exaggerates somewhat. In fact the laboratory

1 originated, I think, in 1965, when it arose out of the
2 old MRC, haemophilia research unit, a Nissen hut in
3 Churchill Hospital. From that Nissen hut emerged
4 clinical treatment, assays, research and also small
5 scale production of Factor VIII so that the clinicians
6 would have something to infuse. The MRC remit is always
7 to kick-start ideas, not to continue them to an
8 industrial scale. That's somebody else's job. And in
9 the mid 60s, the MRC made it clear that they no longer
10 wished to fund this all-singing, all-dancing unit. They
11 could not -- getting beyond their expertise.
12 I believe they continued to fund the bulk of the
13 research effort under Dr Rosemary Biggs, at least for
14 a time, but the regional health authority, who were
15 great friends, went through a succession of hospital
16 governors who were much behind haemophilia and what was
17 being done by the centre. They offered to provide
18 I think probably with regional funding, a new building,
19 which would be half for clinical treatment of
20 haemophilia and half for the production of concentrates
21 to treat haemophilia.
22 They were literally in the same building. The
23 director of fractionation lab office was one brick away
24 from the director of the haemophilia treatment centre,
25 Dr Rizza.

1 Q. And that's something that was constructed in the 1960s?
2 A. That was about 1968. There was, I think in 1972,
3 additional accommodation given to the fractionation lab.
4 I think at the same time the haemophilia centre was
5 expanded as well to cope with the enormous demand which
6 gravitated towards Oxford because treatment was
7 available.
8 Q. Yes.
9 THE CHAIRMAN: What was the Lister Institute?
10 A. The Lister Institute arose -- it was a research
11 institute funded by the Guinness family, with
12 a tradition, I believe, going back to Lister himself, or
13 at least appealing to his name. It was based originally
14 at Chelsea Bridge Road and there in the post --
15 immediate probably war time and post-war years,
16 a Dr Kekwick invented a process rather like the Cohn
17 ethanol process but using ether instead.
18 I believe, just after the war, it was realised that
19 this would have to expand. It was considered unsuitable
20 strategically, especially after a long war, to site this
21 within London and it was moved out to a site, Elstree,
22 Borehamwood, in Hertfordshire, and at that time the
23 Lister Institute itself continued to carry out research
24 on vaccines and sera, that kind of thing, but the Blood
25 Products Laboratory was split off functionally from it

1 and I think funded directly from the Department of
2 Health.
3 However, since we were both on the same site, the
4 Lister administration looked after pay and rations -- it
5 was called -- for BPL people as well.
6 Q. Right.
7 A. So --
8 THE CHAIRMAN: It wasn't in the tin hut, then?
9 A. It had its share of tin huts but the fractionation was
10 slightly more salubrious than that. At the time I went
11 to Oxford, research had been confined to the tin huts
12 and we were operating in reasonable circumstances,
13 although all was tightly circumscribed by the breadth of
14 our ambitions and the space we had to work in.
15 THE CHAIRMAN: And the narrowness of your pockets.
16 A. Indeed.
17 MS DUNLOP: Yes.
18 THE CHAIRMAN: I don't know when you want to stop.
19 A. I should perhaps say that blood transfusion in Oxford at
20 that time was operating in twin Nissen huts, on
21 precisely the same site and there was an infamous Oxford
22 triangle which served later for self-sufficiency in
23 England. The plasma was collected in great amounts by
24 the very willing and helpful transfusion service. It
25 was fractionated in the fractionation lab, 50 yards away

1 in a brick building, and infused into patients 20 yards
2 away. It was a lovely model of what can be done if
3 everyone gets behind it.
4 Q. Maybe there is an article to be written about
5 Nissen huts in the NHS?
6 THE CHAIRMAN: I would go along with "Pre-fabs for the
7 people".
8 MS DUNLOP: Just since we are in England, the impression
9 that one gains about the facility at Elstree, the Blood
10 Products Laboratory, is that over much of the relevant
11 period, particularly the late 70s and early 80s, there
12 was a lot of building work in connection with BPL.
13 A. Could you help -- give me the dates again, please?
14 Q. Particularly the late 1970s and the first half of the of
15 the 1980s, there is an awful lot of material about
16 building works at BPL.
17 A. I will try to be brief and non-committal about this but
18 in 1978 or early 1979, for the first time the medicines
19 inspectors were allowed into BPL which had hitherto,
20 under the previous director, operated -- insisted on
21 operating under Crown immunity. It was plain to
22 progressive people that this was not going to last
23 forever; Crown immunity was going to be removed from
24 little pharmacies and equally from fractionation
25 laboratories eventually. Reluctantly the medicines

1 inspectors were allowed in, did not like what they saw,
2 perhaps especially in the coagulation factor side. The
3 Medicines Inspectorate were very helpful in explaining
4 to us what was required in 1979. This initiated two
5 programmes, one campaign to rebuild the entire
6 production effort at BPL sufficient to cope with the
7 then predicted demand for all products, not just
8 coagulation factors but also albumin, which ran the
9 system at that time; but realising that it would take
10 time to gain support for this, to gather the plasma
11 required for this effort, and to plan and get money for
12 it and finally build it, there was what was called
13 "Mark 1", a programme, a crash programme, of renovating,
14 improving, the existing premises and I arrived --
15 I suppose I was seconded first from Oxford to start both
16 these exercises insofar as they concerned coagulation
17 factors. We had at the same time as continuing to
18 reduce Factor VIII and Factor IX in less than perfect
19 circumstances, to rebuild step by step or at least
20 improve the facilities in each area in turn. This was
21 a very difficult programme. Unfortunately the old
22 building had to continue to process plasma much later
23 than we had hoped, because the building programme for
24 the new BPL took rather longer than planned.
25 Q. Right. Thank you.

1 I think that would be a good moment, sir.
2 THE CHAIRMAN: It sounds like the fate of most projects so
3 far, Dr Smith.
4 Thank you very much. We will have a break.
5 (11.18 am)
6 (Short break)
7 (11.38 am)
8 MS DUNLOP: Thank you, sir. Dr Smith, we are still round
9 about 1982 and if we can go back to your statement,
10 which is [PEN0121551] at 1555 and look at paragraph 10,
11 I would just like to look at an exchange of
12 correspondence from 1982. In fact the first letter is
13 a letter from Dr Foster to you, which is [SNB0073253].
14 Just before we look at it, Dr Smith, in general
15 terms we understand that there was a lot of contact
16 between PFC and PFL, particularly between you and
17 Dr Foster, and not just telephone and written contact
18 but also quite a number of visits. Is it right to
19 understand that if you were in Edinburgh, perhaps
20 visiting family or something, you would quite often make
21 a visit to PFC?
22 A. Yes, at this time and even when the virus wars weren't
23 at their height.
24 Q. Right. I suppose that's going to be something that
25 would happen in the ordinary course of things because

1 you were visiting Edinburgh anyway. I daresay if
2 Dr Foster had had relatives in Oxford, he would have
3 come and visited you when he was down there. It was
4 that kind of relationship, was it?
5 A. I think the point to note here is that I felt welcome at
6 PFC, which may cast some light on the circumstances in
7 which I left.
8 Q. Right. Fine. Looking at this letter then, Dr Foster
9 writes to you on 19 October 1982. He is asking firstly
10 about a paper that you had presented at Groningen. And
11 then secondly he is asking about -- is that
12 antithrombin 3, in the third paragraph/fourth paragraph?
13 A. AT-III. It's now just called "antithrombin".
14 Q. Okay. This is pretty technical stuff, Dr Smith, and I'm
15 not convinced that we need to understand it. So if we
16 could perhaps just note that reference to antithrombin
17 and then move to the next paragraph --
18 A. Could I just stop you a second?
19 Q. Yes.
20 A. This antithrombin is one of the proteins which, for some
21 time it had been known that pasteurisation was
22 appropriate and could be used with different kind of
23 stabilisers but already we were pasturising
24 antithrombin 3, based on work done about five years ago,
25 while we are still thinking about pasturising

1 Factor VIII.

2 Q. Right. So we, I, have been oversimplifying in thinking

3 of the precedent being only albumin; there is also been

4 pasteurisation of antithrombin. Anything else?

5 A. Factor XIII.

6 Q. Right.

7 A. At this time we were trying to prepare Factor XIII for

8 the dozen or so patients in England who relied on that.

9 Q. Are these products more obliging than Factor VIII to

10 work with? These proteins.

11 A. Antithrombin 3 was obliging in that one of the more

12 commonly used stabilisers -- that is salts -- turned out

13 to work well for that concentrate. Factor XIII, we had

14 to use syrup rather than jam but essentially sucrose and

15 things like that. It was not quite so obliging.

16 Q. I see.

17 A. You don't win them all.

18 Q. I'm sorry?

19 A. You don't win them all.

20 Q. I'm sure. And we can see, certainly amongst some fairly

21 technical details in that paragraph, the reference to

22 hepatitis. In fact it's a reference to Hepatitis B and

23 then Dr Foster goes on to say:

24 "My worry is non-A non-B ..."

25 But anyway, looking at the last paragraph on that

1 page, he says:

2 "On the Factor VIII front we are still grinding away

3 at the yield problem and have started to look again at

4 the high purity situation. We are currently pursuing

5 precipitation by metal ions, which is something we

6 stumbled on with Milan Bier a few months ago."

7 And then he says:

8 "Everyone is getting very hot about pasteurisation

9 ... "

10 Can we read on to the next page, please:

11 "... especially since Budapest. The little work

12 that we have done suggests that higher purity material

13 is needed and so far Factor VIII (using Duncan's CAG

14 assay) has always gone into the solids phase."

15 So this just, I think, orientates us in the autumn

16 of 1982 and our understanding that certainly PFC were

17 working on pasteurisation, that having started in

18 response to the information from Behring, I think the

19 year before. So we understand that this is the outgoing

20 letter, as it were, from PFC, really reporting on

21 a number of different strands, and then you write back,

22 and the response is [SNB0073267]. So that's 19 October,

23 and then this is you writing back and we suggested

24 probably -- well, I think definitely the date of this

25 letter is 3 November, notwithstanding its having been

1 dated as 3 October and you accept that, I think, because
2 it's plainly a reply to the letter of 19 October.
3 And you have provided some information about your
4 Groningen contribution. You have discussed the
5 antithrombin issue and then you say:
6 "We are doing a little on heating Factor VIII but
7 only for the moment on the gentle conditions for
8 fibrinogen removal. I cannot see us doing the
9 infinitely factorial experiments and infusions required
10 to 'solve' Factor VIII and would appreciate any small
11 signal of success from your efforts."
12 By "solve", do you think you were meaning the virus
13 inactivation aspect of it?
14 A. Indeed. By that time, 1982, that would be the case,
15 yes.
16 Q. So that's the problem you are thinking needs to be
17 solved. If we can go back to the statement, please, you
18 tell us at the very bottom that:
19 "Brief heating was being considered as a means of
20 precipitating fibrinogen as a solid while leaving most
21 Factor VIII in solution -- by no means an original idea
22 but we were ready to try almost anything short of
23 voodoo. There was no intention to inactivate NANBH."
24 So what were you trying to do then? Obviously, your
25 gentle heating, you were trying to get rid of the

1 fibrinogen. What was your actual goal?
2 A. Precisely that. In fact the way in which the
3 Behringwerke work leading to pasteurisation started was
4 through trying to apply an almost traditional method of
5 removing fibrinogen from plasma or any other solution by
6 its preferential propensity to denature a precipitate,
7 the only question being whether, in doing so, the
8 Factor VIII would also precipitate.
9 Q. So are you --
10 A. We at that time were -- had a longstanding -- all the
11 time we had been working with Factor VIII, you are
12 yearning to get rid of fibrinogen, and over ten years we
13 were working continuously on every possible avenue which
14 presented itself to us or in some publication to achieve
15 that, simply to get the potency up, to get the
16 concentration up, to make it more convenient for
17 patients to infuse, especially infuse it themselves,
18 home therapy. Of course, without losing too much
19 Factor VIII, because we were aiming at self-sufficiency.
20 Q. Yes.
21 A. So although this looks like pasteurisation in pursuit of
22 killing non-A non-B Hepatitis, the aim of the gentle
23 heating was solely to try and find a shortcut to reduce
24 the amount of fibrinogen at a cost in Factor VIII which
25 might be acceptable. It did not work.

1 Q. So you were trying to achieve a more pure product for
2 the benefit of the patient, who then requires less of
3 it?
4 A. Yes, up to a certain point purity also means greater
5 solubility at a higher concentration.
6 Q. Right. So higher purity with all the advantages that
7 that would bring?
8 A. Yes.
9 Q. Yes. And you say you were ready to try almost anything
10 short of voodoo?
11 A. We may even have tried voodoo, I don't know, I didn't
12 myself.
13 Q. We won't press you on that but this is -- I mean, does
14 this relate -- we are always coming back to questions of
15 yield. Indirectly, I suppose, if you can achieve better
16 purification processes, are you making better use of
17 your raw material or is that not a logical deduction?
18 A. I'm not sure if I have answered your questions but, say,
19 in pursuing, at least in a tentative way, heating of
20 certain solutions perhaps with certain things in them,
21 to reduce the amount of fibrinogen, if I had been able
22 to get 100 per cent removal of fibrinogen and it only
23 cost 10 per cent Factor VIII yield, I would take that
24 very, very seriously since it might eliminate other
25 steps in the process, which we were using up until then,

1 which themselves have a penalty in yield. Any time you
2 add another step to a process, you are going to --
3 almost no matter what it is, you are going to lose at
4 least 5 or 10 per cent. Just physical losses and
5 failure to segregate, separate, things cleanly.
6 Q. Yes. So I suppose I'm trying to capture what it was
7 that was concerning you so much that you were ready to
8 try almost anything and --
9 A. Non-A non-B Hepatitis.
10 Q. Right.
11 A. And also this difficulty we had had of getting rid of
12 fibrinogen from our preparations of Factor VIII.
13 Q. Yes.
14 A. All our preparations were 99 per cent fibrinogen more or
15 less, with a little bit of Factor VIII added.
16 Q. Right.
17 A. If you could lose that 99 per cent, you have purified
18 100 times.
19 Q. But in saying there was no intention to inactivate non-A
20 non-B Hepatitis, the urgency must have been related not
21 to viral inactivation itself but to what -- the related
22 issue or the unrelated issue of trying to get a higher
23 purity product?
24 A. I see what -- I see what you mean and the following
25 sentence does go on to explain that. I suppose we

1 already had the glimmer of an idea that pasteurisation
2 was going to be a whole lot easier if you could do it in
3 a small volume than if you needed to do it in a barrel
4 full.
5 Q. Right. So I suppose there then were a number of
6 potential benefits which might flow from the work that
7 you were doing, your small scale heating or the small
8 heating project that you were doing, and one of the
9 benefits might be that it would facilitate virus
10 inactivation by pasteurisation?
11 A. Later in the separate --
12 Q. Yes, downstream --
13 A. Yes.
14 Q. -- as I think some people put it.
15 A. The other night I counted six methods which we were
16 currently pursuing between BPL and PFL, different
17 attacks on better removal of the fibrinogen to get at
18 the Factor VIII in a more amenable state.
19 Q. Right.
20 THE CHAIRMAN: It's quite difficult I think for the
21 non-technical person to pick up everything that's going
22 on. In the first place it's quite a strange idea that
23 99 per cent of your mix at a certain point should be
24 fibrinogen but that you concentrate on trying to remove
25 it from the mix rather than to abstracting the

1 Factor VIII. How would one explain that?
2 A. Exactly. You have put your finger on what we were able
3 to do much later, after 1985, several magic powders were
4 developed that you could put into the mix and pull out
5 the plum of Factor VIII.
6 THE CHAIRMAN: I have no doubt we will come to that in due
7 course. It's just looking at it at this early stage,
8 where you know that the proportion of your mixture,
9 which you are interested in, for this purpose -- and no
10 doubt you will get interest in fibrinogen for other
11 purposes. But at this stage you are interested in the
12 very small proportion of Factor VIII and yet you are
13 concentrating on taking the fibrinogen out.
14 A. Fibrinogen is a nuisance but it has this important
15 characteristic that during the first stage of recovery
16 from plasma, whether it's by ethanol fractionation or
17 cryoprecipitation, under these conditions Factor VIII
18 goes along with, almost as if it was attached to the
19 major protein, fibrinogen. For reasons which I might
20 have to explain tomorrow, the amount in plasma, the
21 abundance in plasma of the proteins in the early stage
22 of coagulation, the activation of Factor VIII and
23 Factor IX, is tiny, whereas when you get to the end
24 point, which -- of clotting, which is fibrinogen going
25 to a visible clot, you got into gramme amounts, much

1 larger amounts of substance.
2 MS DUNLOP: Right.
3 A. But it's a sticky -- Factor VIII and its co-factor,
4 von Willebrand factor, are sticky proteins, as are
5 fibrinogen and fibronectin, which at this point are just
6 nuisances.
7 THE CHAIRMAN: It's really a much simpler problem. If I
8 wanted a stain off my jacket, I wouldn't think of
9 dissolving the material, if I can put it that way.
10 I would rather concentrate on the stain but you do not
11 seem to have been able to do that at this early stage.
12 A. Exactly. It was the holy grail. It didn't come around
13 until much later.
14 MS DUNLOP: Yes.
15 THE CHAIRMAN: Sorry, Ms Dunlop.
16 MS DUNLOP: No. It sounds technically extremely
17 challenging. I think we should look again at the letter
18 of 1 December, which we have already looked at, just
19 because it's part of this correspondence too,
20 [SNB0073341], if we could go back to that, please.
21 Dr Smith, you too must have been very interested by
22 this news from Germany about what Behring seemed to be
23 achieving and I suppose very pleased that even though
24 you weren't as well placed to conduct research yourself
25 in Oxford, you had friends in PFC who were taking these

1 ideas forward. It must have been quite an interesting
2 period technically.
3 A. We were very grateful indeed for that assistance and for
4 several years it was one-way traffic. It was PFL/BPL
5 receiving tips and results and details of processes from
6 the Scots.
7 Q. Right. And this is Dr Foster writing back to you on
8 1 December 1982 and this is actually work on Factor IX.
9 Then we can see that this is a, I suppose, comparative
10 exercise because you are both working on Factor IX at
11 this point, it seems?
12 A. Can I just add there that Factor IX was always more
13 robust to heating than Factor VIII. We had one
14 scientist working with Factor VIII and one on Factor IX.
15 They were both trying to make progress on
16 pasteurisation, armed with the Scottish protocols, and
17 for a time the -- I think all was in our hands. The
18 Factor IX project was going ahead more promisingly than
19 the Factor VIII, and I think the record will show that
20 our interest in pasteurisation of Factor IX ended only
21 very shortly before we took the decision to go -- in
22 fact it was something we were still considering for
23 Factor IX when we had to make a decision between
24 pasteurisation and dry heating.
25 Q. Right. We have already seen the passage at the bottom

1 of the letter about the Behring work patent and an
2 abstract from Hyland, so that point about trying to work
3 out what the commercial companies were doing.
4 On to the next page, please.
5 Information about freeze-drying, and really I think
6 the rest of the letter is pretty technical, and
7 discussion too about the role of citrate. If we go on
8 to the next page as well, please --
9 A. Could I just take you back a second --
10 Q. Yes.
11 A. -- to the previous page? You will see in one of the
12 later paragraphs on the page that PFC had a vial
13 problem.
14 Q. Yes.
15 A. They were changing to another vial and they didn't
16 have -- they couldn't get them and that our relations
17 were such that PFC could ask BPL for what might have
18 been a scarce resource at the time, and it was shared in
19 good heart.
20 Q. Yes. So this is a different vial that was in use at
21 BPL. Is that right?
22 A. Yes, we had started to use a particular vial and they
23 thought that -- PFC thought they would get a better
24 performance from it -- different dimensions.
25 Q. Right. We looked at this all in the context of trying

1 to get a feel for the cooperation between the two
2 laboratories at this stage and you have really already
3 dealt with this, Dr Smith, but we can look back at your
4 statement and see what you said there. So we are back
5 to [PEN0121551] but at 1556, where you told us that the
6 cooperation at that point was decidedly lopsided insofar
7 as virus inactivation in Factor VIII was concerned.
8 A. If you go back to that letter, you will see in the main
9 paragraph on page 2 an account of a visit by
10 John Sinclair, the freeze-drying king, at Liberton, to
11 BPL, and that would be BPL Elstree because their freeze
12 dryer was much more similar to PFC's than was Oxford's.
13 Q. Right. I'm not sure that we have heard of John Sinclair
14 before. We may have but you say he was the
15 freeze-drying king?
16 A. By that time, yes.
17 Q. Right.
18 A. In fact all -- at that time all sterile operation,
19 including freeze-drying, were under his command. A very
20 able man.
21 Q. It looks as though there was quite a lot of trial and
22 error with things like this, changing temperatures,
23 changing times and just seeing what happened?
24 A. Freeze-drying, there are theories, some helpful. But in
25 the end you come down to empiricism, I am afraid.

1 Q. Yes.
2 A. Proteins don't always behave the way they are supposed
3 to.
4 THE CHAIRMAN: I'm not sure you need to be afraid but
5 I think we do have to understand how that reflects on
6 the state of theoretical knowledge at the time. Clearly
7 there was a certain amount of theory and we have read
8 quite a lot about it, but fundamentally it wasn't
9 providing the next steps, as it were, in realising
10 a product. You had to do a fair amount of empirical
11 research, trying things out.
12 A. Yes, indeed.
13 THE CHAIRMAN: I suppose that's where looking at published
14 material will come in, both trying to replicate what was
15 published and differentiate your own processes from it.
16 A. And indeed the -- with the resources which you had.
17 THE CHAIRMAN: Yes. In some way that must have been an
18 exciting time for a chemist, I suppose.
19 A. Quite dramatic.
20 THE CHAIRMAN: Yes.
21 MS DUNLOP: In a sense, I suppose, if money is tight, as it
22 often is in public sector research and so on, a sense of
23 comfort that there is another organisation doing similar
24 research and you may each be able to benefit from work
25 done by the other.

1 A. I have no doubt in my mind that if PFC discovered
2 something as important as a promising lead on
3 inactivation of a blood-borne virus, I would have full
4 access to it, and I'm sure they would have the same
5 confidence. Anything material that we were doing would
6 be shared.
7 MS DUNLOP: Yes.
8 Back to the statement, page 1556, please. You have
9 covered these topics about cooperation and we have
10 certainly seen ample evidence of regular communications
11 between yourself and Dr Foster, and you say that there
12 was a degree of tension in the upper layers but that
13 didn't affect the two of you.
14 A. Exactly.
15 Q. Yes.
16 THE CHAIRMAN: I think you should appreciate there, looking
17 at the preliminary report, we were very heavily
18 dependent on what was recorded, and what was recorded
19 tended to be in correspondence between, or minutes
20 passing between people at the upper echelons. So
21 getting a feel for what is happening on the ground is
22 actually very important, Dr Smith.
23 A. I do understand.
24 MS DUNLOP: And you have also mentioned in this answer the
25 point about actual visits, so not just telephone and

1 written communication but going and seeing people too.
2 A. Can I just add that there were very few telephone
3 conversations. Most of the things we wanted to share
4 with each other involved detailed evidence, as you see,
5 and we would not present each other with rumours or
6 rumours of rumours, which we knew would simply tend to
7 confuse the other. We would wait until we had something
8 which we could stand by and provide in sufficient detail
9 to be useful to the other. We were not in each other's
10 pockets or on the phone every other day. Most of it was
11 done by detailed letters and topping up the background
12 with the occasional visits.
13 Q. We went on to ask about the relative importance of viral
14 inactivation in research and development at BPL. And
15 you told us that Dr Lane was among the earliest to
16 realise that NANBH was becoming a very serious problem.
17 Was Dr Lane in effect your line manager?
18 A. In effect. I had various line managers in various
19 incarnations at BPL but for the time we are talking
20 about he is the person to whom I would go for
21 a decision, which I felt had to be made at a higher
22 level. Also in that would be Dr Snape, who was in
23 charge of quality control/quality assurance, who would
24 also come from the Oxford stable. So these are the
25 people I would naturally report to, if you like. At one

1 time, I think Dr Snape was actually my line manager,
2 whether he remembers it or not, I'm not sure.
3 Q. Right. You go on to tell us that a measure of your
4 frustration and desperation is that in designing the
5 coagulation section of the new BPL, you planned -- and
6 this is in April 1981:
7 "... an area in which uneconomically small pools of
8 10 to 20 donations could be fractionated to Factor VIII
9 and Factor IX, either aseptically or under tight
10 environmental control. This idea, which thankfully
11 never had to be played out, envisaged only sufficient
12 product to protect infants and other previously
13 untreated patients from NANBH until a solution was
14 arrived at by someone, buying time until the cavalry
15 appeared."
16 This is an interesting comment, Dr Smith, firstly
17 because in April 1981 it was really quite soon to be
18 planning a sort of emergency response to take account of
19 NANBH. But does this link back to what you were telling
20 us earlier about fractionators always being concerned
21 about blood-borne viruses?
22 A. Exactly, and also by that time I was the person in the
23 dock -- or the driving seat, depending how you care to
24 put it -- who was responsible for having contingency
25 planning and it would seem to me in 1981 that we might

1 not be arriving at a solution to non-A non-B Hepatitis
2 by the time we wished to move into the new building. So
3 we had to build-in contingency plans.
4 Q. Right, and was that contingency plan actually
5 incorporated in what was built?
6 A. Very interesting question. It never functioned as
7 originally intended but purely serendipitously that was
8 the area of a suitable scale and air handling surface
9 quality, which allowed BPL retrospectively to put in
10 a virus-safe area to avoid recontamination of the
11 product after it had been through -- already been put
12 through a virus inactivation process.
13 Q. Right.
14 A. It was the right place at the right time and of the
15 right size and quality. But that was not my brilliant
16 foresight --
17 Q. All right. So you had an area which was then available
18 for what would have been the post-pasteurisation
19 handling of products. Is that right?
20 A. Yes.
21 Q. So products which had been treated not in their final
22 containers and which required further aseptic processing
23 could be treated in this area, which you had originally
24 envisaged as being for the reason you set out in this
25 answer?

1 A. Exactly. BPL staff went into the new building with 8Y,
2 which did not require a mid stream protection --
3 Q. Right.
4 A. -- facility but within a few years, with certain
5 products, we had introduced the solvent-detergent
6 process, which was a mid stream inactivation process,
7 and at that point, very shortly after -- in fact it may
8 be while some parts of the building were still being
9 constructed or finished -- this extra mid stream
10 facility was inserted.
11 Q. Right.
12 Now, the other thing that's interesting about that
13 answer is to probe a little bit what your thinking was
14 when you were at the drawing board in April 1981 about
15 the circumstances in which this area might need to be
16 used. You are speaking of it as "contingency planning",
17 and we can understand that and you have explained to us
18 what the planning consisted of -- that is an area in
19 which uneconomically small pools of 10 to 20 donations
20 could be fractionated, really to produce product for
21 infants and other previously untreated patients. So
22 when you were at the drawing board in 1981, what
23 circumstances did you envisage as being those in which
24 you would need to resort to this planned area?
25 A. It was the only solution I could envisage in 1981 to

1 protect the most vulnerable patients. There was no
2 possibility at all of an approach like this coping with
3 300,000 litres a year. It would be cottage industry,
4 requiring a large number of operatives, and even if you
5 wished to reduce the pool size to, say, 50, which would
6 be commensurate with what was called "small pool
7 material" in the past, there was no possibility of
8 installing sufficient capacity for all treatment of
9 haemophilia in England and Wales.
10 And I must confess that I have always thought that
11 if there is a limited resource which will most obviously
12 benefit a particular group of patients, then that to me
13 would trump the objection that the same treatment should
14 be available to absolutely everyone.
15 Of course, any fractionator would want to be able to
16 produce the best possible, safest possible concentrate,
17 for everyone, but the dogma at that time was once you
18 had non-A non-B Hepatitis, you had had it and you would
19 not be vulnerable to a repeat dose. So the coldly
20 rational conclusion you come to is that if at least you
21 can do something for the people who are not yet
22 infected, you would hope that somewhere in the world,
23 perhaps Scotland or perhaps our own resources, we would
24 find a more comprehensive solution.
25 Q. Right.

1 THE CHAIRMAN: Could I ask this? At that stage did you have
2 in mind a method that would produce a virally
3 inactivated product in this small scale?
4 A. No, the small scale would be obviating viral -- virus
5 inactivation. It was simply a way of providing for
6 someone not yet infected the minimum possible exposure
7 to blood donors.
8 THE CHAIRMAN: I see. So it's a function of the number of
9 donors rather than any other aspects of the process?
10 A. It might have been possible to plug in later, if we were
11 smart enough, some kind of virus inactivation process or
12 virus limitation process which would have helped
13 slightly but that was not envisaged. The worst case was
14 no virus inactivation available; what do we do?
15 MS DUNLOP: Yes.
16 THE CHAIRMAN: Did you envisage screening the donors in some
17 way?
18 A. There was no ability -- until 1989, there was no means
19 of screening out non-A non-B Hepatitis.
20 THE CHAIRMAN: So it became purely a reduction of the
21 statistical risk.
22 A. As simple as that.
23 MS DUNLOP: Yes. So just to be sure that I'm following,
24 Dr Smith, your first choice obviously -- and what you no
25 doubt hoped would happen -- would be that the whole

1 problem would be solved. So some R&D, either you or
2 somewhere else, would come up with the solution to the
3 hepatitis problem.
4 A. Yes.
5 Q. But failing that, you thought that some sort of
6 contingency planning had to be achieved so that if
7 matters remained as they were, there was at least some
8 small way of trying to protect infants and other
9 previously untreated patients, and that was really the
10 best you could think of. And I intend no disrespect but
11 you were thinking, what we could do is we could at least
12 prepare product from very, very small numbers of
13 donations, which would offer some protection in the
14 absence of anything better. Is that a reasonable
15 summary?
16 A. Exactly, and I should also point out that the not yet
17 infected patients fell into two categories: infants, you
18 know, coming, as they do, relentlessly, and patients who
19 had previously -- mildly affected patients who
20 previously had received little or no treatment, who
21 might still be vulnerable to non-A non-B Hepatitis.
22 Both these categories are small users. They do not use
23 much. Children are small. They don't need so much
24 concentrate to get their plasma level up and the mildly
25 affected patients are less frequently needing infusions.

1 So the amount we required was a fraction of what you
2 would have needed for the same number of severely
3 affected patients.
4 Q. Right. Now, moving to paragraph 11, I think -- sorry,
5 excuse me a moment, doctor. (Pause)
6 I mean, yes, just so that we are not
7 misunderstanding, Dr Smith, that plan didn't proceed
8 because the new area wasn't built at that point. Is
9 that right or am I wrong about that?
10 A. By the time the new area was built, we were
11 manufacturing 8Y.
12 Q. Yes.
13 A. By the time the staff moved into BPL to make coagulation
14 Factor VIII and IX, et cetera, we were already making
15 virus-safe concentrates which were heated in the final
16 container, and we had a big hall in the middle of the
17 plant waiting to be exploited. It was never fitted out,
18 put it that way. The air handling, the surfaces were of
19 appropriate standard but it was never completely fitted
20 out or manned.
21 Q. I see. Thank you.
22 Paragraph 11 refers to that letter of 1 December and
23 we have already looked at that. You remark that you had
24 forgotten that work on Factor IX at Oxford had advanced
25 even so far. And then there is a misconception on my

1 part about the reference to freeze-drying which you have
2 corrected.
3 Then paragraph 12. I don't think we need to ask you
4 about because others have commented on the meeting and
5 the correspondence.
6 One explanation for Dr Foster's serenity maybe is
7 that he has told us, Dr Smith, that he didn't know about
8 these letters but I don't think we need to have any
9 further comment on that.
10 A. Nor did I.
11 Q. No. Can we move on to the next page, please, and
12 I don't think we need to ask you about anything until we
13 come to 15 and you say you would have continued to
14 inform PFC without constraint of anything notable that
15 you had discovered, and that is the answer you gave
16 earlier in the same terms about cooperation between the
17 two centres.
18 16 refers to a meeting on 22 March 1983, Scottish
19 meeting of the haemophilia and blood transfusion working
20 group, and we asked about an apparent lack of
21 cross-reference between heat treatment and AIDS. Your
22 response is that:
23 "There was some resistance among haemophilia
24 clinicians to the idea that AIDS was caused by
25 a blood-borne virus. I don't think that this affected

1 the urgency felt by SNBTS."

2 Then on the following page you develop this answer

3 a little further by telling us that you think most

4 fractionators thought it likely that AIDS was caused by

5 a blood-borne virus. In fact, the publication to which

6 you are referring, Dr Smith, is 20 May 1983. That's the

7 date of the article, the Barre-Sinoussi article in the

8 periodical "Science".

9 This is a topic that we have considered on a number

10 of occasions and in different contexts but I was

11 interested in your memories of your thinking around this

12 time. When you first heard about AIDS and more

13 particularly heard about people with haemophilia having

14 AIDS, can you remember what your reaction was?

15 A. I first heard about it from my American colleague, who

16 brought back a cutting from the Boston Globe. I did not

17 hear about AIDS through the scientific literature first.

18 Q. Right. Can you remember when that was, even roughly?

19 A. Perhaps even 1982.

20 Q. Okay.

21 A. My first reaction was, "Baloney, they are conflating

22 several different things. It's a scare, it is a

23 newspaper report, I'll wait for some facts." I suppose,

24 also allied with this hope which everyone had, that it

25 was somehow going to be an American phenomenon. But

1 very shortly, as more and more haemophilia sufferers
2 came down, and also it was being transmitted pretty
3 obviously through blood-borne routes, or secretion
4 routes, I remembered insight I was given, I think during
5 my time in Edinburgh, probably by Robert Cumming, that
6 they had a huge overlap between the sexually transmitted
7 diseases and the blood-borne diseases. So anyone with
8 that mindset would tend to be making a connection
9 perhaps before the evidence really justified it.
10 Q. Right. And you recollect that the publication in 1983
11 was taken by transfusionists as strong support for
12 a working hypothesis, that is a working hypothesis for
13 a blood-borne virus being involved?
14 A. Exactly.
15 Q. We are referring in this part of our questions document
16 to some thinking emanating from Dr Foster at the
17 beginning of May 1983 and I would like to ask you one or
18 two questions about that. In particular we are actually
19 looking at a memo which we should have before us,
20 I think, [SNB0073635]. We have looked at this before,
21 Dr Smith. I think we know our way around it a bit.
22 Dr Foster begins by rehearsing the existing plan,
23 which appears to have been to concentrate on those who
24 have not been heavily exposed to untreated products so
25 far. So he is saying that the plan has been to try to

1 develop enough heat-treated concentrate for those who
2 would benefit from it, mild and moderate haemophiliacs.
3 We can see the three-part plan outlined there. Four to
4 six pilot scale lots in 1983 and then a full-scale plant
5 to handle 30 per cent production for 1984 to 1985 at the
6 earliest, and then mild and moderate haemophiliacs
7 continuing to receive single donor cryo meanwhile.
8 We do understand that this would have been a plan
9 which would have gradually increased, so it would only
10 be in the early stages that you would be saying, "We
11 don't need to worry about people who are affected with
12 severe haemophilia," because in due course you would
13 hope to move on to offering a better product to
14 100 per cent of patients but the logic of it, I think we
15 follow that, in the early days you could aim to
16 inactivate maybe 30 per cent of the product.
17 A. I wouldn't say that we were happy with this.
18 Q. No.
19 A. It was a very inadequate response. We would never like
20 to discriminate between one and the other. The history
21 of fractionation is of clinical ideas which seem only to
22 require a small amount of material to begin with but
23 anti-D, I would quote, is another example that where the
24 clinical need expands, it expands and sometimes we lag
25 behind in providing it -- the best, in our view,

1 concentrate for everyone and the rational thing seems to
2 be to be more selective, if you have to.
3 Q. I think we understand that this plan, which is sketched
4 out here, was a way of rolling something out as soon as
5 possible, albeit not reaching everybody in the early
6 stages. But then Dr Foster goes on to say that the
7 possibility that another more serious infectious agent,
8 AIDS, is now involved, means that the strategy may need
9 to be reviewed. And he points out that the patients
10 with haemophilia most at risk in the new landscape are
11 the severe patients, rather than the mild and moderates.
12 And he says:
13 "There is already evidence of a panic recourse to
14 cryoprecipitate."
15 He goes on to point out that:
16 "Heat treatment of everything looks to be the most
17 likely possibility that we have to face up to, and if
18 this is so, we will have to plan to pasteurise all of
19 the Factor VIII rather than 30 per cent and we may also
20 want to review the timescales noted above."
21 And he points out why timing may become crucial,
22 firstly the long lead-in time and secondly the
23 possibility of a return to cryo, removing huge
24 quantities of the raw material from which the
25 concentrates are being prepared.

1 And then he goes on to the second page, to develop
2 what I have previously called a worked example of what
3 might be achievable with existing equipment.
4 We understand from Dr Foster that that worked
5 example, the 1,000 kilogramme pool of fresh-frozen
6 plasma, was the size of pool which was at that point
7 being started off in PFC. I think he told us it was
8 approximately twice a week, a pool of that size would be
9 started with the end product being concentrates. So he
10 is talking about this idea of trying to heat-treat
11 everything and he gives a five-day programme for how
12 that might be achieved.
13 You have described this as a very resourceful memo?
14 A. Yes, we are driven at times to make use of equipment and
15 premises and staff not designed for the job.
16 Q. Right. So a degree of improvisation?
17 A. "Improvisation" is the watchword.
18 Q. Yes. And you have confirmed our suspicion that it is
19 essentially what occurred at the end of 1984 as far as
20 the heating step was concerned, so the equipment which
21 was in place was used for heating, albeit dry
22 heat-treating, when there was the introduction of
23 heat-treated product at the end of 1984. But we tried
24 to find out what actually happened to this memo, more
25 correctly, I suppose, what happened to the suggestions

1 contained in it.

2 Perhaps we can summarise the memo as saying firstly

3 we need a different strategy in terms of the amount of

4 product we are going to have to plan to heat-treat and

5 then secondly, we need to do things on a swifter

6 timescale. So we need to do things more promptly than

7 we perhaps have previously been intending.

8 Now, if we go back to your answer, that's

9 [PEN0121551] at 1560. You have said that there was no

10 undue delay between these energetic moves in 1983 and

11 the costing and schedule developed in February 1984 for

12 a national rollout in February 1985.

13 But it does seem that the suggestion made in

14 Dr Foster's memorandum of a somehow quicker move to

15 pasteurisation of a larger volume of material wasn't

16 implemented, not as it stands, and one explanation that

17 Dr Foster has given for that is that -- well, it

18 couldn't have been implemented without successful

19 clinical trials. So that was one thing that had to

20 happen. Whether the original plan of going ahead with

21 the pasteurisation of 30 per cent or moving to try to

22 heat-treat everything had been chosen on either view, it

23 was necessary to do clinical trials, and indeed

24 Dr Foster has pointed out that that bit of the plan did

25 proceed. So they did initiate some clinical trials of

1 pasteurised product.

2 I think the other answer to the question of why this

3 wasn't implemented as it stands, I think you give us.

4 You say that:

5 "Work on purification in conjunction with

6 Alan Johnson was going so well it was thought likely the

7 next generation of pasteurised Factor VIII would be

8 based on chromatographic purification, rather than on

9 the less pure product of the zinc heparin

10 precipitation."

11 So I don't want to misstate the position, Dr Smith,

12 but I think given that this is an important memo and we

13 have tried to understand what happened to the

14 suggestions contained in it, perhaps the best answer is

15 to say, well, in part it was progressed because of the

16 move to clinical trials, but also it was superseded by

17 the promise of a better method, which was held out by

18 the cooperation with Alan Johnson, and we know that

19 Alan Johnson and Dr Foster met up again in Stockholm

20 in June 1983. Does that seem to you to be a reasonable

21 explanation of the status of this memo? Or am I missing

22 something?

23 A. Yes, I would add that if you are trying to explain the

24 gap between this memo and the February 1984 date, for

25 instance, by February 1984 there was at least a question

1 mark over these rather nebulous clinical trials of the
2 pasteurised product. The promise of the Johnson method
3 for its impact on getting the volume down and making the
4 pasteurisation process easier, to that you could now add
5 the promise that by using a chromatographic process,
6 there might be fewer potentially interfering materials
7 in the product, after -- before and after
8 pasteurisation, and that anything of that nature which
9 might have been contributing to the adverse reaction in
10 one patient might be solved at one blow. So this
11 additional incentive, if you like, to try a bit harder
12 on pasteurisation.
13 Q. Yes.
14 A. And it was still on the main line to the contingency for
15 AIDS, should it strike; should it strike Scotland, we
16 are still on course to be ready for it.
17 Q. Yes. I'm going to borrow your expression, if I may,
18 about still on the main line. So the core parts of the
19 project were still proceeding, as I understand it, but
20 with some changes to certain parts of the process, one
21 of which is this work with Dr Johnson, which offered
22 a different methodology.
23 A. Another connection here is that if the chromatographic
24 process had been successful in getting the volume down,
25 prior to pasteurisation, all the problems which arise

1 from pasteurisation are ten times more manageable and
2 although it's not explicit, I'm sure that in Dr Foster's
3 mind at the time was this is also a way of preparing us
4 to handle all our plasma this way.
5 Q. Yes.
6 A. Because the patients who now need protection are all
7 patients because they are all potentially susceptible to
8 AIDS if we are right, whereas with non-A non-B Hepatitis
9 only a few remain susceptible.
10 Q. Yes. And I think we can understand that, that if you
11 have only got one tenth as much material to work with,
12 then things are perhaps not ten times easier but
13 considerably easier than that would be with greater
14 volumes?
15 A. For instance, ultra-filtration process, which only
16 arises with pasteurisation, at least at that time, was
17 cutting edge at the time to exploit on an industrial
18 scale. In fact I believe PFC did exploit it and it was
19 put to use when they adopted Z8 but it was a major
20 achievement to get that far. Such a bold idea as
21 ultra-filtration to remove the sucrose and glycine.
22 All that becomes much easier if you have a much
23 smaller volume to work with and for instance, you might
24 be able to do it in a much smaller room whose
25 environment you can control more readily, and the

1 problem of value, that is can be put through the entire
2 volume of plasma collected from Scotland, all of
3 a sudden becomes feasible.
4 Q. Yes, and you go on to develop this a little bit further
5 in your answer to paragraph 19, where you talk about
6 what seemed possible but in fact was not finally adopted
7 and in fact, the anticipated progress didn't bear fruit
8 within the period up to 1985. You guessed that PFC was
9 not convinced of the necessity of high purification for
10 physiological reasons. I'm not sure, Dr Smith, if
11 that's right, given that Dr Foster has told us that as
12 early as 1981 he took from a meeting with haemophilia
13 clinicians, particularly Dr Ludlam, that there was this
14 yearning for a higher purity product. So that was
15 something that he was trying to achieve in its own
16 right; something which clinicians were keen to see?
17 A. As I have explained, it was in all our minds for the
18 last ten years prior to this but this is in pursuit
19 primarily of high potency, higher concentration, and the
20 terms HP and -- it was sometimes taken to mean by one
21 person "high purity", others "high potency". I'm fairly
22 sure that in Dr Ludlam's mind in 1981 it wasn't anything
23 about rubbish proteins or some other noxious substance
24 in these impure Factor VIII concentrates. He would be
25 thinking in terms of the convenience of home therapy.

1 Q. So these are really discrete problems with low purity
2 products, one, that you need very large amounts of them
3 to get the therapeutic benefit and, two, that there may
4 be all sorts of other stuff in there that the patient
5 doesn't want or need.
6 A. Exactly.
7 Q. Yes.
8 A. On top of all this, this wish to get higher potency,
9 higher purity, overriding all that is a need to get
10 a sensible kind of yield, not -- obviously you will
11 accept a small penalty to get a very large benefit but
12 you can't afford to lose 50 per cent.
13 Q. Yes. Excuse me a moment. (Pause)
14 All other things being equal, do you think that the
15 Johnson process, if we can call it that, would have
16 offered an increased yield as compared with the ZHT
17 process that PFC at that point were pursuing?
18 A. I was not in the loop with the Johnson process, although
19 Dr Johnson did propose his methods to BPL, somewhat
20 later than this, not earlier than 1985 I don't think,
21 when we had already moved on. If the chromatographic
22 process had been sufficiently discriminating, and
23 sufficiently gentle, there may have been, say, in excess
24 of 90 per cent recovery from that part of the process,
25 and given the reduction in volume, it could have meant

1 fewer losses in the necessary pasteurisation steps.
2 Q. Right.
3 A. So it might very well have either been neutral or
4 conceivably beneficial, but life is seldom so simple.
5 Q. Yes. You go on to refer in your answers to the problems
6 of intellectual property and at this point it was PFC
7 who had these problems because they had signed
8 a confidentiality agreement with Dr Johnson, and we had
9 some evidence from Dr Foster about possible reservations
10 on the part of some in New York concerning the
11 collaboration. You say:
12 "Proprietary information released under
13 a confidentiality agreement never featured in our
14 exchanges. In fact during the early 1980s, we
15 communicated almost exclusively on technical aspects of
16 virus inactivation and did not seek to stay abreast of
17 our respective national policies."
18 I wanted to put to you, Dr Smith, an answer Dr Perry
19 gave on this topic. Can we look, please, at the
20 transcript for 13 September? I think it's at page 71.
21 If you see the chairman's question:
22 "In the first place, was there any arrangement that
23 you knew of as between the English and the Scottish
24 scientists that would have given either of them a right
25 of access to the results of the other's research?"

1 And then Dr Perry says:
2 "I'm certainly aware that, certainly from the
3 perspective of the PFC -- and this was the policy of my
4 predecessor as well -- any development, any invention,
5 any patent or any intellectual property that we
6 established would be made freely available to the rest
7 of the service.
8 "I think to an extent, although I cannot judge to
9 what extent that took place at BPL, my understanding was
10 that was a fairly reciprocal arrangement. I think that
11 was also underpinned -- and I remember discussions,
12 although I can't place this in time -- that legally the
13 whole position of one part the Crown preventing access
14 by another part of the Crown to intellectual property
15 through patent was just simply a non-starter."
16 Obviously the Dr Johnson episode is different
17 because it involves a third party and PFC was not in
18 control of what information it could or couldn't release
19 because it had contracted with a third party on the
20 matter, but in connection with other advances or
21 developments in research between the two laboratories in
22 Scotland and England, does Dr Perry's answer capture
23 your understanding of the position?
24 A. His answer is -- covers a lot of ground, which I think
25 we have to unbundle.

1 Q. Right.
2 A. There is talk about development. Well, taking
3 pasteurisation as an example, here was a case where we
4 were freely exchanging information, although much of it
5 one way, while it was still a development.
6 As we come on to Dr Johnson's proposals, we are
7 going into development which will inevitably involve
8 third parties. So there there is no question of sharing
9 that with BPL. When it comes to patent, then the end of
10 Dr Perry's answer is quite correct. There was no way in
11 which the Crown was going to pay patents to the Crown.
12 It was always, throughout this period, a facility called
13 a "Crown record", which was thought innocently to offer
14 protection to the originator.
15 During this tricky period, where something is
16 a development that looks as if it may be patentable,
17 when we were strenuously warned by our patent agents
18 that as soon as it begins to look patentable, you will
19 have to stop talking details to all other parties or it
20 constitutes prior disclosure. So in the case of the
21 Johnson patented material on PFC's side, and for a very
22 brief period BPL's patent intentions for 8Y, there was
23 an embargo on providing sufficient detail to be able
24 to -- for some opponent of the patent to call it
25 disclosure.

1 But the degrees of sharing of information within in
2 a -- that is the tricky period, when you think something
3 is going to be a goer and -- but you do want to keep
4 your pals informed. It is very tricky.
5 Q. Yes.
6 A. The Crown record system was thought, when the patent
7 agents told us, "Oh, you have to keep it quiet." "From
8 whom, even our friends in Scotland?" We were told,
9 "Yes, even them and their grandmothers". We said, "Does
10 the Crown record system not protect us during that
11 time?" and we were told, "No, it would be challenged and
12 would not stand". I'm quoting the Ladybird Book of
13 patents. That was my understanding at the time.
14 THE CHAIRMAN: It's probably as good as any at this stage.
15 You will appreciate it was that period that was of
16 particular interest because if the unity of the Crown,
17 which of course meant that there would be no patent fees
18 payable, were indeed comprehensive, then the parties
19 would be the same. What fascinated me, although it will
20 never form part of the final report -- it's just an
21 interest -- was how disclosure worked. There is no
22 doubt at all about the generality that prior disclosure
23 can undermine the validity of any patent that's then
24 sought, that's easy, but prior disclosure usually means
25 in that context disclosure to some third party, not to

1 oneself, even if one's granny happens to be in the same
2 research department. That's why I was interested.
3 A. You enlighten me, as you speak, I was always rather
4 vague about it.
5 MS DUNLOP: Is there a degree of empiricism here to? Is it
6 just that if you tell your friends in Edinburgh, they
7 might tell somebody else? You lose control of the
8 information. It is not that you want to prevent them
9 knowing because you want to keep them out, it is just
10 that the more people you tell, the more danger there is
11 of leaks.
12 A. Between ourselves, we were always very careful not to
13 gossip, not to buy information from some other party
14 with information we had between ourselves. I would have
15 trusted PFC, any of my interlocutors at PFC. If I said,
16 "we are thinking of patenting this, keep it under your
17 hat," I would have trusted them.
18 Q. Right.
19 A. But a clever patent agent for a party opposing our
20 patent would doubtless have found holes in that.
21 Q. Yes, and also you trust your colleagues at PFC but the
22 people giving you the advice, they don't know that and
23 they have no way of judging if your colleagues at PFC
24 are leaky or not?
25 A. Of course.

1 Q. So they are erring on the side of caution and saying to
2 you, "Keep mum"?
3 A. I think the patent agency we had at that time was
4 Ministry of Defence. They were not quite minded of the
5 civic responsibilities --
6 Q. No?
7 A. -- at that time.
8 Q. "Loose lips sink ships" and all that?
9 A. Yes.
10 Q. Okay. Can we go back to the statement then, please? We
11 are now at 1561. We have said:
12 "The second half of 1983 saw progress in Scotland
13 with trials of heat-treated product and discussion of
14 related issues."
15 Actually at this point I wanted to look at your note
16 3, which is relevant here. Note 3 is to be found on
17 page 1569. You say that:
18 "The purpose of note 3 is to offer an independent
19 interpretation of PFC's pasteurisation programme from
20 its 1983 clinical trial up to its undated demise."
21 I think we can just read this for ourselves. You
22 make reference to the incident with Dr Ludlam's patient
23 and then you go on to summarise the situation in late
24 1983.
25 A. That paragraph is to try and give a complete outsider's

1 view of what seems to be the state of play.

2 Q. Yes. And we understand from Professor Ludlam and others

3 that just because a reaction may be capable of being

4 described in a meeting as "minor", doesn't make it

5 acceptable. So on any view it was something that had to

6 be taken seriously.

7 A. I'm not trying here to say that Dr Ludlam put a spanner

8 in the works with his interpretation of "minor

9 reaction". I'm trying to paint a picture of just how

10 ready PFC was, having responsibly delayed things until

11 an unambiguous clinical result had come out -- that they

12 were ready with an improved product, well within the

13 time schedule they had set themselves.

14 Q. Yes. And you go on in the third paragraph to refer to

15 this as a "setback". I take it you are meaning the

16 problem with the clinical trial?

17 A. Yes --

18 Q. That's the setback?

19 A. -- the fractionator has to accept at face value.

20 Q. Yes, and that PFC set to vigorously in pursuit of

21 significant improvements.

22 In the final paragraph on that page you say at the

23 end of November 1983 -- I think that should perhaps be

24 1984?

25 A. Sorry, yes.

1 Q. Yes:

2 "Dr Perry acknowledged that, in the wake of CDC's
3 advance results reports at Groningen, dry heating was
4 being proposed as a short-term measure to deal with HIV
5 but it is clear that an improved pasteurised
6 Factor VIII, only some months away, was still intended
7 to be PFC's sole Factor VIII concentrate thereafter."

8 Then I think we just need to read for ourselves the
9 final paragraph of your note 3, which is on the next
10 page. (Pause)

11 We do understand that there was, as it were,
12 a formal departure from the pasteurisation project at
13 a meeting in December 1985, and I'm sure that
14 Mr Mackenzie is going to come on and discuss that period
15 with you, but note 3 is your view of the progress of the
16 pasteurisation project at PFC, really from its inception
17 into 1983 and even 1984. Is that correct?

18 A. Yes.

19 Q. Yes.

20 A. This, of course, was before I knew that Dr Foster would
21 be appearing to give you it in a much more authoritative
22 fashion. I'm simply going by the evidence presented in
23 the report.

24 Q. Yes, thank you.

25 Can we go back then, to page 1561. We observe that:

1 "In England more attention appears to have been paid
2 to dry heat treatment."
3 Actually, sir, it's five to one. This is quite
4 a long chunk.
5 THE CHAIRMAN: Yes.
6 MS DUNLOP: It is probably quite sensible to stop.
7 THE CHAIRMAN: We will stop at that.
8 (12.57 pm)
9 (The short adjournment)
10 (2.12 pm)
11 THE CHAIRMAN: Yes, Ms Dunlop.
12 MS DUNLOP: Right, thank you, sir.
13 Dr Smith, we had stopped at paragraph 22 of your
14 statement and there it is on the screen in front of us.
15 Paragraph 22 reads:
16 "Meanwhile in England, more attention appears to
17 have been paid to dry heat treatment."
18 You felt that that paragraph, whilst correct,
19 required some exposition and you have given us some
20 notes on this. Can we go then to that set of notes,
21 actually 4.1 to 4.3, which begin on page 1570.
22 Actually it's worth looking at the introduction,
23 which is in italics, as well. I think we shall just
24 read it for ourselves, at least the first part. (Pause)
25 It is, however, I think, worth highlighting,

1 Dr Smith, what you say at the end of that paragraph in
2 italics:
3 "Out of admiration for my own diligent and
4 resourceful colleagues at PFL and BPL, I always contest
5 claims that we were just lucky. That's not how it
6 works. However, I do have to admit that we had
7 a smoother ride than usual to 8Y, while PFC kept having
8 the success they deserved dashed from their grasp by
9 external events beyond their control."
10 Developing that, you have posed in 4.1 the question:
11 "Why did PFC start to take an active interest in
12 pasturising Factor VIII?"
13 I think we have largely covered that, save for your
14 specific comment about Behring. We did look at that,
15 Dr Smith, in the earlier evidence about B3. You have
16 referred really to the reputation of Behring and said
17 that if they said something was feasible, that meant it
18 was worth pursuing. So they were a respected company
19 and that's what you say there:
20 "Fractionators usually believe that they can improve
21 on the original and possibly avoid patent problems."
22 Then, 4.2:
23 "Why did BPL appear not to take such an active
24 interest in pasturising Factor VIII?"
25 You say:

1 "We may initially have been more sceptical than PFC
2 about the chances of inactivating NANBH."
3 You refer back to your note 1:
4 "But promising noises did start to emerge from
5 Germany and formal trials were being set up."
6 You go on to make the point, which I think we
7 understand, about the gap between the demand for
8 coagulation factor concentrates and the supply being
9 much greater in England than it was in Scotland. In
10 other words, Scotland was much closer to
11 self-sufficiency so trying to close that gap in England
12 was perhaps more of a focus for you than the
13 inactivation work, or is that not quite --
14 A. That's going too far.
15 Q. It's too far? Right.
16 A. They were equal preoccupations. There is no point in
17 having a wonderful method and no plasma to apply it
18 to --
19 Q. Yes. You say yourself -- I should just use your words:
20 "A Factor VIII product with reduced yield certainly
21 could not be envisaged except for selected patients."
22 And that was the position in England. And you also
23 say:
24 "BPL was in the throes of a stop gap building
25 improvement programme, while a modern plant was being

1 designed, authorised and constructed."
2 And you didn't have either premises or staff to
3 undertake a difficult long haul.
4 So I think in this 4.2-paragraph you are really
5 explaining partly why PFC pressed ahead with the
6 pasteurisation research and you didn't.
7 A. Precisely.
8 Q. Yes. Then to look at the other side of the coin, 4.3:
9 "Why did BPL appear to take more interest in dry
10 heating than did PFC?"
11 You say:
12 "PFC was alerted to the feasibility of dry heating
13 of Factor VIII by the curious Rubenstein abstract at a
14 conference in Budapest in 1982."
15 And Dr Foster kindly shared with you what little he
16 had gleaned from the meeting, and that's a reference
17 back to that report we have looked at:
18 "Most people interpreted the undisclosed heating of
19 Hyland product as pasteurisation of some kind."
20 This is back to the terminological inexactitude
21 problem, isn't it? Yes.
22 So one answer to why PFC were perhaps not pursuing
23 dry heating at this point is that they were already
24 pursuing their own pasteurisation project and that seems
25 to be what you are covering in your first paragraph?

1 A. Exactly.

2 Q. Then you say that:

3 "Dry heating was something you could do in England."

4 In circumstances in which you very much wanted to do

5 something.

6 A. Yes.

7 Q. And you describe for us what dry heating research was

8 begun in England. Again, I think if we read that

9 paragraph beginning "on the other hand" for ourselves.

10 (Pause)

11 You describe for us, Dr Smith, the particular

12 conditions of routine freeze-drying at PFL and BPL and

13 you call this a happy accident. In other words, there

14 was a connection between the particular freezing process

15 at PFL and BPL and the success of your early dry heating

16 experiments.

17 A. That is what I wish to point out.

18 Q. Did you know at the time that it was connected to your

19 particular freezing condition?

20 A. No, we did not have many options with the rather

21 inflexible dryer we had, which had been a bottle dryer

22 and they had been fitted out to take vials but it was

23 not ideal for this purpose. It had the deficiency that

24 the vials at one end of the dryer dried faster than the

25 vials at the other and if you then tried to dry heat

1 that, all you get is a sticky mess, even worse than the
2 jam. To combat this, we had to continue drying to
3 accommodate the worst case vials, if you like, and in
4 the course of the -- developing these very long cycles,
5 by accident almost we found ourselves with very dry
6 products.
7 Q. Was it as basic as needing to turn the vials around?
8 I mean, if you are saying it wasn't homogeneous, were
9 you needing to turn your vials around within the freezer
10 to make sure that all vials were equally frozen, equally
11 dried?
12 A. In a freeze-dryer there is already quite a lot
13 happening. You are drawing a very, very intense vacuum.
14 You are applying very, very intense cooling and then
15 heating. We had not got to the point where we could
16 have a turn table as well, not a bad idea. It did not
17 occur to me, I must say --
18 Q. I was even just thinking of manual turning, opening the
19 door and turning them round.
20 A. No, you daren't open the door because the vacuum goes
21 off.
22 Q. I see.
23 A. The cooling in the vials, therefore. The cooling by
24 evaporation stops and you start to get the sticky mess.
25 Q. Right.

1 You go on to tell us about your investigation of the
2 PFC zinc heparin precipitation and we know that
3 a technician made an error in calculating the weight of
4 heparin to be used and counted an unusually heavy
5 precipitate of fibrinogen. So this really was
6 accidental --
7 A. Yes.
8 Q. -- I gather. Yes. Perhaps we should just look at the
9 letter that refers to this. Can we have [SNB0074402],
10 please? If we go a little bit further down the letter,
11 please, I think that's that paragraph beginning:
12 "As I mentioned ..."
13 Isn't it? You say we have stumbled literally on an
14 intriguing alternative to zinc. So the intriguing
15 alternative was use a much greater quantity of heparin.
16 Is that right?
17 A. Yes, as we found, the zinc was unnecessary.
18 Q. Yes. And you say you were trying to get a Crown record
19 entered. Yes, if we could go back then to the
20 statement, please, at 1571 and just complete that note:
21 "The technician and the principal investigator went
22 ahead with the planned assay of the Factor VIII
23 remaining in solution and were astonished to find a very
24 high recovery."
25 You outline for us, therefore, this serendipitous

1 discovery of a successful method of achieving a higher
2 purity product.
3 A. Yes.
4 Q. Yes.
5 THE CHAIRMAN: Could you help with the role of your
6 two-stage assay as compared with the Canadian and
7 Scottish single stage assay, which seem to have made it
8 impossible to handle high concentrations of heparin?
9 MS DUNLOP: I wonder, sir --
10 THE CHAIRMAN: Are you coming to this?
11 MS DUNLOP: I was going to let Dr Smith read what Dr Foster
12 said about this as a sort of introduction.
13 THE CHAIRMAN: You haven't read what Dr -- let's do it
14 Ms Dunlop's way.
15 MS DUNLOP: The transcript for 26 October, if we could look
16 at that, please. 26 October at page 17. It's exactly
17 the same point, sir. It's just to look at this as
18 a sort of prompt really.
19 THE CHAIRMAN: It's a better way to get the right answer,
20 Ms Dunlop.
21 MS DUNLOP: If you see the question at the top, Dr Smith:
22 "Can you just explain what you mean by the
23 Factor VIII assay."
24 Perhaps we should go a little further back to get
25 the context properly. There we are:

1 "The mistake being made in Oxford which Dr Smith
2 described as having stumbled literally ..."
3 And so on. (Pause)
4 If we read on to 17, please (Pause)
5 Perhaps down a bit, please. About the one-stage and
6 the two-stage assays. (Pause)
7 And perhaps on to the next page as well, thank you.
8 (Pause)
9 I think what we had understood by Dr Foster's
10 evidence, Dr Smith, was that, because of the type of
11 assay that you used at PFL, the effect of this greatly
12 increased use of heparin was more evident and more
13 accurately measurable than it would have been had the
14 one-stage assay been used?
15 A. Yes.
16 Q. Does that make sense?
17 A. Yes.
18 Q. I think it might help if you explained that in a little
19 more detail to us. I can see the chairman nodding. I'm
20 not sure that we are on top of the concepts of the
21 assays and their role in the episode?
22 THE CHAIRMAN: I think we do understand the starting in
23 Canada. When they tried with a single stage assay, they
24 just weren't getting any measurable success in
25 identifying the amount of F8 that they had.

1 A. It was more that the Canadian group got an exaggerated
2 impression of how much Factor VIII they were getting.
3 THE CHAIRMAN: An exaggerated --
4 A. Yes.
5 THE CHAIRMAN: And that was the same with the Scottish
6 approach, was it?
7 A. The Scots were aware of this difficulty of assaying by
8 the one-stage method, a preparation which contained
9 contamination with heparin.
10 MS DUNLOP: Right.
11 THE CHAIRMAN: So just what was it that was happening? How
12 was it happening?
13 A. Can I try and give you a quick explanation and see if
14 you want a deeper one?
15 MS DUNLOP: Try the short one first.
16 A. You are familiar with the concept of coagulation as
17 a cascade of sequential reactions in which a proenzyme
18 or potential enzyme is activated to an active form by
19 the removal of a small piece of the protein.
20 The enzyme produced from the proenzyme in that
21 reaction goes on to catalyse the activation of another
22 proenzyme to another enzyme. And this goes on in
23 a cascade of four or five sequential reactions. At each
24 stage the amount of proenzyme and therefore the amount
25 of enzyme formed increases greatly. It's a multiplier

1 system, an amplification system. If you start with
2 a tiny amount of Factor VIII activated by, say, tissue
3 damage, totally invisible to the naked eye, and you end
4 up, after -- in normal plasma, after less than a minute
5 with a very, very evident solid clot, a mass of protein
6 having been converted.
7 In the one-stage assay you use -- you take
8 Factor VIII deficiency plasma, typically from a zero
9 Factor VIII haemophiliac. When you give that
10 a kick-start by the addition of calcium, that plasma
11 takes a long time to clot, at least several minutes.
12 However, if you add back into the haemophilic plasma
13 a known volume of, say, a concentrate which you have
14 just made, if the clotting time is greatly shortened,
15 then you know you have some Factor VIII in there. And
16 by a process of standardisation, doing the same reaction
17 with a known standard containing Factor VIII, you can
18 quantitate how much Factor VIII you had in that sample.
19 The more Factor VIII you have, you have added to the
20 haemophilic plasma, the shorter will be the clotting
21 time. That's a very quick look at it.
22 Q. Right.
23 A. In this process, at each stage only a relatively small
24 amount of enzyme has to be manufactured in order to
25 start the next stage, and in the one-stage assay

1 everything goes to completion very rapidly, from the
2 addition of the Factor VIII or the calcium to the clot.
3 In the two-stage assay the clotting cascade is
4 interrupted at the stage immediately following
5 Factor VIII. Factor VIII is responsible for catalysing
6 the activation of Factor X to Factor XA. In the
7 one-stage assay, that Factor XA would go on to activate
8 the next stage. In the two-stage assay you do not
9 present the assay with the components necessary to use
10 up the Factor XA. You provide it with just the
11 components required to go to 10A. The 10A accumulates
12 in the first incubate and you move to a completely
13 separate second stage, where you, in another separate
14 reaction, again involving clotting, estimate how much
15 10A there was in the original incubate.
16 You still have this direct relationship between the
17 amount of Factor VIII present in the first incubate,
18 producing only a certain amount of 10A, proportionality
19 and then the amount of 10A you put into the second mix
20 is proportional to the rate of clotting you finally get
21 at the end of the day.
22 Q. Right.
23 A. With me so far?
24 Q. Possibly.
25 THE CHAIRMAN: I'm not absolutely sure about that last

1 stage. I can see the interruption and in that way you
2 get a relationship that you can apply forward to the
3 final result, but what you say is that there is a direct
4 relationship between the amount of Factor VIII present
5 in the first incubate producing only a certain amount of
6 10A and then the transcript doesn't actually help me at
7 the moment particularly. I'm trying to read it so
8 that I can go back to it, Dr Smith, and I'm not
9 following this section.
10 A. I meant that --
11 THE CHAIRMAN: You don't, of course, have the transcript.
12 Can I read this to you and you will see. What it says
13 is:
14 "You still have this direct relationship between the
15 amount of Factor VIII present in the first incubate,
16 producing only a certain amount of 10A, proportionality
17 and then the amount of 10A you put into the second mix
18 is proportional to the rate of clotting you finally get
19 at the end of the day."
20 I find that rather difficult because it anticipates,
21 in a sense, the end product at the point you are
22 introducing it and I find that a bit difficult. Would
23 you like to go over that again?
24 A. I'll try to reword. You start from --
25 THE CHAIRMAN: Starting from interruption.

1 A. Yes, interruption, and at that point your Factor XA has
2 accumulated and is going nowhere as it would in the
3 one-stage assay until you put it into a second mix, and
4 now what you are doing is measuring the amount of 10A.
5 THE CHAIRMAN: Right.
6 A. I meant to underline that the proportionality remains
7 unchanged throughout this, that the Factor VIII is still
8 the rate limiting factor in the production of 10A. And
9 when you move to the second incubate, the 10A is the
10 limiting factor in the production of a clot. And the
11 rate at which the clot forms.
12 Therefore, despite the interruption, you have
13 maintained -- if the conditions are right, you have
14 maintained the proportionality between the amount of
15 Factor VIII you started with and the rate of formation
16 of a clot in the second incubate. That does not
17 answer -- I'll come on to -- if you accept that for the
18 moment, I'll try and explain why that deals with the
19 problem of interference by heparin --
20 THE CHAIRMAN: Yes.
21 MS DUNLOP: Yes.
22 A. -- which is not obvious.
23 In the two-stage assay, because -- in the one-stage
24 assay it is very vulnerable to interference by another
25 anticoagulant or coagulant. The two-stage assay,

1 because it accumulates 10A at the middle stage, it can
2 therefore be said to be more sensitive. That is that
3 you end up with more 10A in your first incubate than was
4 necessary to make the one-stage reaction go. You have
5 accumulated a large signal, a large amount of 10A, which
6 can then be quantitated very precisely.
7 The end result of this is greater sensitivity. You
8 need less Factor VIII in the original incubate to make
9 a final impression on the clotting time. This means in
10 turn that the sample that you put in may be more dilute
11 and in diluting the sample, you also dilute out the
12 effect of any interfering substance, in this case
13 heparin.
14 So in essence, the two-stage assay escapes the
15 limitation of the one-stage assay by virtue of being
16 more sensitive, requiring less Factor VIII to go in and
17 therefore also less of the interfering substance enters
18 the incubate.
19 MS DUNLOP: I think that summary you give at the end may be
20 enough for our purposes.
21 THE CHAIRMAN: I think it may be it will enable us to
22 express a view without disclosing our ignorance, which
23 is often as much as a judge can do.
24 A. I'm obviously not the best person to explain this but
25 Dr Foster, I believe, volunteered me.

1 THE CHAIRMAN: When you talk about the 10A accumulating at
2 the end of phase 1, that's clearly the result of
3 a process of development of the amount of 10A in that
4 first stage, but does accumulating imply an end to the
5 process of development of 10A there?
6 A. It can go no further because it has not been provided
7 with the rest of the system to start eating that part of
8 the system.
9 THE CHAIRMAN: Fine. So that gives you a fixed
10 proportionate relationship between Factor VIII and 10A
11 at that point?
12 A. Exactly, and there is more of it. There is more of the
13 10A at that point than there would have been if you had
14 allowed the whole cascade to rip by having the whole
15 plasma in there, using up the 10A that has been produced
16 by the Factor VIII.
17 THE CHAIRMAN: Right. So the mechanism by which the
18 proportions alter in the stage -- in one assay is that
19 the clotting process absorbs the 10A --
20 A. Exactly.
21 THE CHAIRMAN: -- and disturbs the proportions.
22 A. Yes. This is my picture of what is happening.
23 THE CHAIRMAN: That's the best we can get, Dr Smith. I was
24 just looking for some physical hook, as it were, to hang
25 the difference on. Is that the essence of it, do you

1 think?
2 A. That is the essence of the reason for interference by
3 heparin in the one-stage assay. There are other
4 differences between the one-stage assay and two-stage,
5 which Dr Foster, I'm sure alludes to, other reasons for
6 preferring the one-stage assay, but that is perhaps the
7 one reason for preferring the two-stage assay in that
8 particular context.
9 THE CHAIRMAN: I think I can see that if the heparin stays
10 in the mix and the 10A is reducing, then you get
11 a completely skewed reading by the end of the process,
12 in the one phase.
13 A. It is more that there is less heparin there to start
14 with. You are starting with a more dilute solution of
15 the Factor VIII concentrate.
16 THE CHAIRMAN: Sorry, yes. You don't dilute your solution
17 down and therefore there is less to influence the final
18 result?
19 Ms Dunlop, I have no doubt I'll forget it all. So
20 long as we have got the words.
21 MS DUNLOP: To be sure we haven't missed anything from
22 Dr Foster's evidence that you need to comment on,
23 Dr Smith, can we just scroll on a little bit further
24 down, please? Then on to the next page, please.
25 This is hard for us, Dr Smith, as lay people. It's

1 very hard. And I think what we had understood from
2 Dr Foster was that this news from England wouldn't be as
3 attractive to him because he would know that, as a user
4 of the one-stage assay, a new methodology involving
5 large quantities of heparin possibly wouldn't work.
6 A. It was an impediment to knowing how much Factor VIII you
7 would have if you only have the one-stage assay to
8 apply.
9 Q. Yes.
10 A. He would know that because he was au fait with the --
11 our Canadian skirmish.
12 Q. Yes. Right.
13 A. But he also had good reasons, other good reasons
14 positively for choosing the one-stage assay and counting
15 his blessings.
16 Q. Yes. Could it have been a situation in which this news
17 could make him think, "It's time that we changed to the
18 two-stage assay so that we can perhaps seek to adopt
19 this technology that they have discovered in England"?
20 Is it not like that?
21 A. No, (a), it was only an impediment; there was no reason
22 why other techniques could not have been used, and in
23 fact there always was another technique used to apply
24 the one-stage assay to a concentrate containing heparin
25 and that was to first neutralise the effect of the

1 heparin by adding a substance called protamine sulfate
2 but this involved very tedious titration, by trial and
3 error, of the precise amount of heparin by a precise
4 amount of protamine sulfate. If you got that wrong, you
5 got interference by the protamine sulfate. So it was
6 not a popular task. You can assay concentrates with
7 heparin in them in the one-stage assay but you have to
8 go through a fiddly process beforehand.
9 There are also, as I am sure Dr Foster enumerates,
10 at least two other difficulties or impediments to
11 adopting the two-stage assay, one of which is the
12 expertise required. I can certainly vouch for that.
13 The two-stage assay takes a good technician at least
14 a year to do. It takes two years to make a good
15 technician. In the course of a day, a trained
16 technician can produce typically four results, in the
17 course of a long day's assays. Most of these assays
18 inevitably go to the quality control of your routine
19 production and I can say that although at the seat of
20 the invention of Factor VIII and with probably most
21 adept technicians, that I -- at the height of 8Y
22 development, I had a ration of eight assays per week
23 with which to develop a new Factor VIII concentrate.
24 Q. Right. So I think these are reasons why it wouldn't be
25 attractive to contemplate a change to the two-stage

1 assay if you were accustomed to using the one-stage
2 assay?
3 A. Exactly.
4 Q. But you did allude to another possibility, which would
5 have been continuing to use the one-stage assay but
6 building in different steps?
7 A. Yes, and the clotters there would know very well what
8 a palaver that was going to be and it would have cut
9 down the number of assays which could have been handled.
10 Q. Right. So can we just read a little bit further down,
11 please? Yes. I think that's the killer question there
12 at the bottom of the page:
13 "Question: Is there anyone you know who can give us
14 an easy and understandable explanation as to why the
15 one-stage and two-stage process assays were different
16 and why one was effective and the other not?
17 "Answer: Dr Smith might be able to help you with
18 that.
19 "Question: We will store that one for Dr Smith."
20 So you knew this was coming, Dr Smith?
21 A. That's my friend, so called.
22 THE CHAIRMAN: We are accustomed to reality being in inverse
23 proportion to the declaration of degrees of friendship.
24 MS DUNLOP: Right. Can we go back to Dr Smith's statement,
25 please, at 1571? I think we do understand that for

1 several reasons, at least some of them being connected
2 to the different assay systems involved, Dr Foster
3 wasn't immediately attracted when he heard this news
4 about your happy accident with the heparin. He didn't
5 immediately think, "I need to have details of this so
6 I can do it myself."
7 I think you are telling us that the role of the
8 assays is a significant factor in that consideration.
9 A. I think we will come to further impediments tomorrow.
10 Q. Right. We are actually on the following page, please,
11 and this is the discussion of the use of the increased
12 quantities of heparin. You said that:
13 "The very dry concentrate we were producing could
14 then be heated at quite high temperatures without loss
15 of solubility and with an acceptable loss of Factor
16 VIII. This dry-heat concentrate was coded 8Y in the
17 research and development lab and the name stuck."
18 But you say:
19 "Satisfying as this successful development might be,
20 there was no eureka moment. I was still firmly
21 convinced that dry heating would be much less effective
22 than pasteurisation against tough viruses like NANBH."
23 And that that was your conviction is illustrated by
24 the fact that you persisted with catch-up on
25 pasteurisation of both Factor VIII and Factor IX well

1 into 1984 on the basis of PFC's updates.
2 So I think what you are saying, Dr Smith, is that
3 albeit that you were achieving more severe heating,
4 80 degrees at 72 hours, with the particular product that
5 you had, you continued to believe that the actual
6 heating method was not as good as the wet heating step,
7 which PFC were pursuing in that research?
8 A. Exactly. In fact our dry heating of what we would call
9 the front end 8Y was tongue in cheek almost. The
10 primary reason for developing the higher purification
11 and potency would still have been to make it easier to
12 do pasteurisation once we could do it. But it was an
13 intriguing perhaps -- we pushed it as far as it could go
14 and we were astonished how far it would go, but there
15 was no decision at that point that's what we must do,
16 because I had no confidence whatever that it would touch
17 a tough virus.
18 Q. So you are thinking, "It is good that we have achieved
19 this much more pure product, that is what we have been
20 seeking to do and it so happens that we are also able to
21 heat this product much more severely than we had been
22 expecting".
23 A. Yes, and as I said, there the formulation we found --
24 that is the recipe for the addition of stabilisers and
25 other things necessary to put the 8Y precipitate into

1 people's veins, that fell into our hands very readily,
2 unexpectedly. So within a matter of weeks from applying
3 our new precipitation techniques, all of a sudden we had
4 something we could dry-heat at 80.
5 Q. Yes. I meant to take you to a report to Dr Foster of
6 your research at the end of 1983. So we are going
7 slightly back in time if we look at it now. But can we
8 just look at your memo of 5 January 1984, which is
9 [SNB0074052]? I think you had better read this out to
10 us, Dr Smith, just so we are not misreading any of it?
11 A. If I can:
12 "I attach a copy of our VIII dry heating results to
13 date, having removed sections which are of internal
14 interest only, ie how to go about application, resources
15 needed. Please let me know if I can add anything of
16 practical value:
17 "The SDS/PAG patterns of wet heated VIII (and
18 presumably dry-heated Armour VIII) are astonishingly
19 similar to dry-heated VIII."
20 Q. Right. What are the SDS/PAG patterns?
21 A. It was a technique for looking at the molecular
22 breakdown, the structure of the proteins in the sample.
23 If you run it down, sieving gel by electrophoresis, it
24 sorts out the proteins by size. The wet heated VIII
25 I would be talking about there would probably be our

1 limited pasteurisation of VIII, and the dry-heated might
2 well have been by that time either -- I don't know,
3 heated intermediate material or 8Y. I would need to see
4 the context.
5 Q. If we just have a quick look through the documents
6 annexed, we can see how you were reporting your results.
7 A. Yes, this is entirely on the intermediate -- the current
8 intermediate purity concentrates, not on 8Y.
9 Q. Yes. I'm sorry, we are going back in time. We are now
10 back before the happy accident, the stumbling across the
11 increased precipitation with heparin.
12 A. These were on Oxford's version of routine Factor VIII,
13 which was simply a slightly improved cryoprecipitate,
14 very analogous to NY.
15 Q. Yes.
16 A. It represents not just one day's work but a kind of
17 promising interim report on a number of experiments.
18 Q. Right.
19 A. That would be fairly typical. I would not phone up
20 Peter Foster and say, "Oh, we will get one batch of ACRB
21 through at 70 degrees," I would wait until we had a few
22 batches and had something to tell him.
23 Q. Right. Can we just scroll down through this, please?
24 Yes, we can see you are talking about experiments
25 in July 1983 and we can see what I guess are really

1 quite respectable percentage recoveries of Factor VIII
2 after heating at 75 and 80 degrees for even 24 hours.
3 So you would be pleased to get that sort of percentage
4 recovery, would you?
5 A. Surprised and pleased. We would immediately start
6 looking for what has gone wrong here or what is the
7 penalty. There must be something going wrong here.
8 Q. Right. Can we just quickly move through the other
9 pages, please?
10 I think this is basically very technical, Dr Smith.
11 So perhaps all we need to know is that it is a summary
12 of work sent at the beginning of January 1984; work that
13 you had carried out for about the previous six months or
14 so?
15 A. Yes.
16 Q. On different methods of heating different products
17 indeed.
18 A. We would be in no rush to give results prematurely to
19 PFC because we knew they were totally preoccupied with
20 pasteurisation, depending on us to tell them anything
21 that was really promising about dry heating.
22 Q. Right. Then the next page, I think. We can see there
23 the reference to the SDS/PAG measurements?
24 A. We are referring to it there because we knew that there
25 was ongoing interest in precisely the same techniques in

1 the SNBTS, I think it was Joan Dawes, to the central
2 lab, who was -- had a particular interest in molecular
3 structure, the results of -- the damage which might
4 result from heating.
5 Q. Right. Perhaps if we just look at the next page as
6 well, please. That's it? Thank you.
7 Right. Can we go back now to the statement at 1561?
8 So it's true that Scotland was sticking with
9 pasteurisation, you were interested in some of your dry
10 heat experiments, some of them had shown quite promising
11 results, but we were suggesting that this progress with
12 dry heat treatment in England was still taking place
13 against the backdrop of a preference, at least in
14 theory, for pasteurisation, as offering a more efficient
15 form of heat treatment.
16 A. Very definitely. We were quite near achieving what
17 looked like success in recovering Factor IX from
18 pasteurisation and on Factor VIII we were still working
19 well into the early summer of 1984 on pasteurisation.
20 I think that's the point at which Lowell Winkelman and
21 I went up to BPL to see their scaled-up pasteurisation
22 process, and I think even to take photographs.
23 Q. At PFC?
24 A. At PFC, yes.
25 Q. Yes, I think we have that in the timeline, that you took

1 away some photographs.

2 A. Yes, that was very late into 1984.

3 Q. Yes. The reference to the CBLA paper, perhaps we should

4 look at, because you point out that the paper contains

5 several misconceptions. It's [DHF0024489].

6 This is a snapshot of the position insofar as

7 research on both types of treatment is concerned. If we

8 scroll through it, we can see that it narrates that

9 plasma fractionation organisations have been reexamining

10 means whereby hepatitis virus can be inactivated in

11 large-pool concentrates. Then on to the next page,

12 please. Then AIDS:

13 "The means of heat treatment of blood products."

14 And that contrast between wet process heating or

15 heating a finished freeze-dried product.

16 I just wondered if you could highlight for us any --

17 what you would describe as important misconceptions in

18 this paper?

19 A. I think the major one follows this page in which someone

20 makes a claim -- a point -- sorry, a date by which

21 a dry-heated concentrate might be ready for clinical

22 use.

23 Q. Yes. I should have said, of course, we can see the date

24 there. It's 26 July 1983. So there was --

25 A. Second paragraph on the last page.

1 Q. Yes.

2 A. I neither composed nor assembled any paragraph in this
3 document.

4 Q. Yes.

5 A. So I do not know who wrote it and I don't know where
6 they got their information leading to the second
7 paragraph on the last page.

8 Q. Right.

9 A. Late summer 1983 we had only our very first results on
10 dry heating, the ones I reported to Dr Foster
11 in January 1984.

12 Q. Yes, we noted from your report that you do refer
13 to July 1983 and then I suppose somebody has got hold of
14 that information, because they are referring in line 2
15 to the preliminary studies, and I think that must be the
16 studies we saw in that table, which was included in
17 the January 1984 memo?

18 A. Yes.

19 Q. But you take issue with the author in predicting when
20 routine manufacture might be achieved, it would really
21 have been quite extraordinarily optimistic to suggest
22 late summer 1983?

23 A. Extraordinarily optimistic, yes. The date of the CBLA
24 meeting was when?

25 Q. The date of this memo is July 1983. I'm not sure that

1 we are very clear to which meeting this relates. But
2 I think the other thing we took from it -- and you do
3 agree with this bit -- is the suggestion that
4 pasteurisation is perhaps to be preferred, at least in
5 theory.
6 A. I agree with that, yes.
7 Q. Yes, that pasteurisation is more homogeneous and
8 efficient and to satisfy reliability in manufacture is
9 to be preferred. I think that may be on the second
10 page. Can we just go back, please, to the previous
11 page.
12 Yes, there it is. Under the heading "Means of Heat
13 Treatment of Blood Products," we can see that comment
14 about the homogeneity of wet heat treatment.
15 I suppose the rider is correct, isn't it, that wet
16 heat treatment is associated with more molecular damage
17 of heat unstable proteins than occurs by the dry heat
18 route? Is that arguable?
19 A. You cannot really wet heat and dry heat in the same
20 medium. You are not going to have the same other things
21 present -- stabilisers present, therefore --
22 Q. It's apples and pears?
23 A. Therefore it's a rather loose statement.
24 Q. One would never really be able to perform an experiment
25 which would have only that as the different variable?

1 A. You would expect more damage in -- I prefer to call it
2 heating in solution rather than wet treatment -- unless
3 you had introduced other elements to protect it.
4 Q. Okay. Right.
5 Can we go back to the statement then, please?
6 I think the only remaining point on this page is that
7 when we asked about an apparent contrast, you thought
8 that there wasn't a contrast between the minutes of
9 a meeting of the CBLA working group on AIDS and this
10 document. You said that you didn't think there was
11 a contrast because there is no inference in that memo
12 that we have just looked at that NANBH would be
13 inactivated by dry heating.
14 I think perhaps the only point we were trying to
15 make was that the memo seems to be cautiously optimistic
16 about dry heat treatment, whereas the CBLA working group
17 on AIDS is aware that dry heat treatment hasn't worked
18 from the results of work with the Hyland product. So
19 it's perhaps more negative about dry heat treatment.
20 That was really all that we were asking about.
21 It is being pointed out to me, Dr Smith that
22 actually in November 1983 the CBLA, Central Committee On
23 Research and Development in Blood Transfusion, does
24 appear to have been told by Dr Lane that a dry
25 heat-treated product was now available at BPL.

1 I suppose that's not the same as the statement that it
2 might be available for routine manufacture. It might
3 have proceeded to routine manufacture by the summer of
4 1983, but it does look as though there is perhaps not
5 quite such a gap between what was being said and
6 reality, if there was a dry heat-treated product
7 available at BPL in November 1983?
8 A. Well, as my letter to Dr Foster in January 1984,
9 recounting fuller experience with dry heating over the
10 autumn of 1983, would suggest, and as you yourself
11 pointed out, the table, which I offered Dr Foster, did
12 include at least two quite attractive-looking options.
13 Q. Yes.
14 A. And without being able to produce an exact sequence of
15 events, I can only imagine that we did some further work
16 on dry heating to perhaps go through the entire range of
17 assays which you would apply to a routine product going
18 forward into quality control and found no significant
19 points on which to condemn it.
20 Q. Yes.
21 A. About this time we -- I'm sure it was made plain to the
22 haemophilia community that if they asked -- if they took
23 responsibility for asking for a heated product from NHS
24 plasma -- put it that way -- we were open to
25 suggestions. In fact two clinicians did just that in

1 the spring of 1984. I don't think at any point, once we
2 had promising results on dry heating -- I don't think at
3 any point we said, "Well, we are not satisfied with it,
4 although we are not holding it up unduly. If you give
5 us a case for this and you are prepared to take the
6 responsibilities attaching to named patient use, ask us
7 and -- or talk to us and we will do what we can."
8 Q. Right, and that happened in relation to two clinicians?
9 A. Yes, Dr Colvin and I believe Dr Machin in the spring of
10 1984.
11 Q. Right, but obviously that's on a very much smaller scale
12 than anything connoted by the suggestion of routine
13 manufacture?
14 A. Well, the batches produced at PFL at that time were
15 300 litres, quite a large-scale. Therefore, incurring
16 a fair number of donations, over 1,000 donations. So if
17 you are talking about number of donations, yes, but
18 there is a confounding factor here, which I think
19 I expand on much more in C3, that through 1983, again as
20 part of contingency planning, to produce perhaps a small
21 amount of safer concentrate because of lesser exposure
22 to infected donors, we had a wheeze going called the
23 northern centres trial, in which PFL was fractionating
24 at a 100-litre scale plasma, which would effectively
25 only be from about 10 or 20 donors, each of whom had

1 given at least four blood donations without the
2 recipients showing any signs of hepatitis. These are
3 our green four patients.
4 Q. This is the green plasma?
5 A. Green four means that the green light after at least
6 four blood transfusions. They were in fact all highly
7 experienced blood donors and were recruited from a pool
8 of well thought of, experienced blood donors. They were
9 phoresed repeatedly and their plasma was stored until we
10 built up perhaps 5 or 10 litres from the same donor.
11 Therefore, really only the one donor exposure in all
12 that 5 or 10 litres and we would put together 20 such
13 bowl assays from different donors, so that we had 100
14 litres of plasma with only about 20 donors' exposure.
15 The product which Drs Colvin and Dr Machin got in
16 the spring was heated -- a heated version of that
17 limited donor Factor VIII.
18 Q. Yes.
19 A. The remit was -- Dr Lane asked me, "What can we do for
20 these people? What is the best we can do?" And
21 I suggested that we add to our safety margin from small
22 pool aspect of the green four product that if they
23 wished, this could be supplied in dry-heated form, and
24 that was in fact what was adopted.
25 Q. Yes. You do cover this in a supplementary statement

1 that you recently provided for us, Dr Smith, and as
2 I understand it, there is a slight confounding here
3 because it was difficult to be sure about how effective
4 the heat treatment had been in inactivating viruses
5 because the source material was itself particularly
6 safe.
7 A. It had an extra margin of safety.
8 Q. Yes.
9 A. Without any guarantees.
10 Q. Yes. I think we need to come back and look at your
11 supplementary statement just to cover the points you
12 make there.
13 Can we move on to the next page, please?
14 Paragraph 23. We have covered this memo already. Then
15 you mention your note 4.5, which we are going to go to
16 in a moment, and then 24 is Dr Ludlam's letter of
17 11 January about the adverse reaction in his patient.
18 Note 3 we have looked at. The information from England
19 being referred to at the Factor VIII study group meeting
20 at 12 January, we note. And then this question:
21 "Was there any suggestion at all of the possibility
22 of changing tack?"
23 Can we go, please, to notes 4.4 and 4.5? That's
24 page --
25 THE CHAIRMAN: Should we do that immediately?

1 MS DUNLOP: I'm happy to have a break just now.
2 THE CHAIRMAN: I think before we get into 4.5, it might be
3 a suitable time to break.
4 MS DUNLOP: Yes.
5 (3.15 pm)
6 (Short break)
7 (3.34 pm)
8 THE CHAIRMAN: Yes, Ms Dunlop?
9 MS DUNLOP: Thank you. Dr Smith, we were going to look at
10 your notes 4.4 and 4.5, which are your statement
11 [PEN0121551] at 1572.
12 You have posed and answered the question:
13 "Why did BPL decide to run with dry heating in late
14 1984."
15 You say:
16 "Briefly, as a stop-gap measure in the hope of
17 making Factor VIII safe from transmitting AIDS."
18 Of course, at that point there had been known
19 transmission in England from NHS product as well,
20 I think, in the autumn of 1984?
21 A. I wouldn't like to say.
22 Q. Right. You say:
23 "Many UK haemophilia centre directors were
24 clamouring for these products. BPL continued to be
25 unconvinced that inactivation was sufficiently proven to

1 justify heating of the national product. Sufficient
2 proof was forthcoming at the Groningen meeting in
3 early November which I had managed to attend."
4 Then you explain the steps that were taken when you
5 returned from Groningen. You say you have:
6 "... limited ability to document actions in
7 England." Because you thought we were struggling
8 slightly and I think we were. To understand the
9 sequence of events in England you have provided
10 a supplementary statement and it would be helpful if we
11 could just look at that now. [PEN0172198]. This is
12 entitled "Introduction of dry-heated concentrates of
13 Factor VIII and Factor IX in England". Prepared within
14 the last couple of weeks, I think, Dr Smith. Is that
15 right?
16 A. Yes.
17 Q. And firstly, on page 1 you give us a little bit of
18 description of three products: 8CRV/HL, 8Y and 9A.
19 Looking perhaps particularly at 8CRV/HL, because that's
20 the stage we have reached in your evidence, you say
21 that:
22 "This product was not designed for dry heating but
23 a survey of recent batches in the second half 1983
24 showed that all batches survived fairly well after
25 heating at 60 degrees for 24 hours, and most batches

1 withstood 70 degrees for 24 hours, and these are
2 respectively HT1 and HT2."
3 This, of course, links back into your memo of
4 5 January 1984 to Dr Foster, when you are telling him
5 what has been going on with heating at PFL.
6 Perhaps we should note, without going to it, that at
7 the reference centre directors' meeting -- in fact we
8 will just look at it quickly -- in December 1984. Can
9 we look at [SNF0013850]? There it is again,
10 10 December 1984. You were there and it's in that
11 document that you explain this same information about
12 what has been achieved so far with dry heat treatment in
13 England. I don't know if you perhaps want to look at
14 the minutes as far as you are concerned. I think it's
15 quite a bit further on. Could we go to page 3, please?
16 Sorry, further on yet; where this section on heat
17 treatment begins, "Factor VIII concentrates," starting
18 there, and then on to the next page, please, and
19 further -- we are not at Dr Smith yet. I can't
20 remember, I think you may be in the afternoon actually.
21 Can we go on to the next page, please? Yes, there we
22 are, afternoon session.
23 You are reviewing the current work programme.
24 (Pause)
25 About that sentence:

1 "This material had been available since March 1984
2 on a limited basis in solution."
3 A. I am afraid the minute is badly garbled.
4 Q. It's garbled?
5 A. Yes.
6 Q. Right. Well, that's a concept we can understand.
7 A. Dr Lane, two options, I can't really distinguish between
8 these two.
9 Q. On to the next page then, please. I don't think we need
10 to spend a lot of time on this, Dr Smith, it was really
11 one of these exercises for completeness, to show that
12 you were reporting on progress so far at that important
13 meeting in December 1984.
14 THE CHAIRMAN: Just go back to the bottom of the page
15 before.
16 A. It's the last two words on that page I simply don't
17 understand.
18 THE CHAIRMAN: Yes. They don't sit easily between the
19 previous sentence and what follows at the top of the
20 next. Shall we just treat this really as an inadequate
21 minute altogether?
22 MS DUNLOP: Yes.
23 Q. Sorry, that's all I wanted --
24 A. The first sentence there says it all:
25 "The current product had been dry-heated at

1 60 degrees in conditions suitable for recovery of Factor
2 VIII activity ... "
3 Nothing at all about promise of non-A non-B, and the
4 reference, in the second sentence, to there had been
5 difficulties with the effectiveness, that would be
6 referring to the Hyland product.
7 Q. So a lot of things are being rolled up together which
8 should have been --
9 A. I am afraid so.
10 Q. -- or probably were narrated separately?
11 A. I don't understand 1 and 2.
12 Q. No. Right. Okay, let's move away from that minute then
13 and go back to your supplementary statement,
14 [PEN0172198].
15 THE CHAIRMAN: I was using the break to revise a university
16 court minute and it won't be a consolation to know that
17 the risk of total confusion persists to this day.
18 MS DUNLOP: So on the second page, having given us that
19 little bit of narrative on the first page about these
20 three different products, on the second page you have
21 talked about the introduction of heated 8CRV/HL. And
22 you have said:
23 "Clinical trial for safety and efficacy: early 1984
24 ...
25 "Clinical trial for virus safety: early 1984 ... "

1 We do not need to go to it but that reference,
2 [PEN0171782], is to Dr Colvin's paper, which we looked
3 at when he gave evidence.
4 A. Yes.
5 Q. And that's really about the use of the product that you
6 were telling us about before the break?
7 A. Yes.
8 Q. The use in three patients of a product which actually
9 was heated with what looked to us to be quite a low heat
10 treatment regime, 60 degrees, I think it was, but, of
11 course, the extra margin of safety was there, in that it
12 had been made from this specially selected plasma.
13 A. The threshold for acceptance of loss of Factor VIII was
14 rather mobile throughout the latter part of 1983 and
15 1984 and I think, based on our autumn 1983 results, our
16 option at that time would have been to tolerate less
17 Factor VIII yield. (Inaudible) loss of Factor VIII and
18 therefore go for the milder conditions, and 60 degrees
19 for 72 hours was on the whole found to be easier on the
20 Factor VIII --
21 Q. I see.
22 A. -- than 70 degrees for 24 hours.
23 Q. And you mention Dr Colvin and Dr Machin.
24 A. The paper also mentions a further use by Dr Preston,
25 which frankly I could not remember but there was

1 a fourth patient with the same result.
2 Q. Okay. And then details relating solely to this
3 particular product in the next paragraph down, and
4 I think there are one or two corrections here, Dr Smith.
5 Is that right?
6 A. Yes. Do you wish me to make them?
7 Q. Which would you prefer?
8 A. I will make them. I will put my hand up. I can only
9 plead insanity and pressure of work but in the third
10 paragraph:
11 "Samples of all batches were trial heated
12 from November 1983."
13 That was November 1984. In the fourth line:
14 "For general use in January 1984."
15 That should read "in January 1985". In the last
16 line of the paragraph:
17 "No unheated HL was issued from BPL after
18 2 May 1984."
19 Again, it should read "1985".
20 Q. Right. Thank you.
21 A. I apologise to everyone who has been misled by that.
22 Q. Yes. No, thank you very much, Dr Smith; it's just to
23 clarify those dates because it all fits better with the
24 narrative that you give in your main statement of coming
25 back from Groningen with the information and obviously

1 moving very quickly to try to introduce heat-treated
2 product.
3 A. In both countries, the Groningen meeting was the
4 trigger. It was the first time we had solid evidence
5 that heating was going to do anything against HIV.
6 Q. Yes. And then you go on to describe the introduction of
7 8Y, and then also the introduction of 9A. And I think
8 perhaps we can take this narrative as read because
9 I don't think any of it is controversial.
10 We note that you were unofficial trial gofer in
11 relation to 8Y. You liaised frequently with Dr Rizza?
12 A. Yes.
13 Q. We know Dr Rizza was another expat?
14 A. Yes.
15 Q. Yes?
16 A. As was his first consultant, James Matthews. It was
17 quite a colony.
18 Q. Right. Can we go back to the statement then, please,
19 and we are on to 4.5, which is page 23 of [PEN0121551].
20 And again you have posed and answered a question:
21 "Why did PFC not take shortcuts to a hepatitis-safe
22 Factor VIII by buying in successful processes?"
23 I think in the first paragraph you are saying that
24 insofar as any suggestion is made that PFC could have
25 bought in Behring work's process, really they had no

1 need to because they achieved a process themselves. And
2 indeed a process which had a better yield than the
3 Behring process?
4 A. Yes, can I also point out, which I have not said here,
5 that the first publication of Behringwerke's clinical
6 success in defeating non-A non-B was in 1987.
7 Q. Right. You say it was Cutter which adopted Behring's
8 improved process. It's a little difficult to work out
9 exactly what happened actually but perhaps the only
10 thing is that the Humate does look to have been an
11 Armour product. But we do have an article from Kasper
12 about the different products that were made, and I think
13 she lists Humate as a product that was manufactured by
14 Armour but I'm sure nothing turns on it?
15 A. Profilate was Armour's.
16 Q. I'm sorry?
17 A. I thought Armour's product was called "Profilate".
18 Q. I think they did that too?
19 A. I think Dr Kasper's perhaps nodded(?) there. Humate was
20 the Cutter name for -- in Germany, the name was, as
21 I recall, "Hemate".
22 Q. Then you move on to consider 8Y. And you say:
23 "It's hard to find a point in our development when
24 it would have been rational for PFC to change horses."
25 You continued to have reservations about the

1 effectiveness of dry heating against NANBH. And you say
2 if you had been in a position to adopt a good
3 pasteurisation process, you would have pressed for it,
4 at least as an option in 1985. You go on to talk about
5 various features of 8Y. And I think we would be
6 straying into some of tomorrow's territory if we spent
7 too long on this.
8 A. Can I just add that in the middle there, at least as an
9 option in 1985, the significance of 1985 is that that
10 was the initially projected date for BPL to move into
11 its new palace.
12 Q. Right. And you didn't achieve that?
13 A. We did not achieve that, no.
14 Q. When did you move in? Is it 1987?
15 A. It is not just doors open and you started again; there
16 is a process of commissioning successively completed
17 sections of the plant, and I believe that would not be
18 until late 1987, effectively.
19 Q. Right.
20 A. Meanwhile, the old building was processing as much as
21 they could of the plasma coming in.
22 Q. Yes. And you say that by the middle of 1986, PFC had
23 caught up on the dry heating front. And we referred
24 earlier to the decision that was taken in the meeting
25 in December 1985 to go with dry heating in Scotland as

1 well.

2 A. Yes.

3 Q. Yes.

4 A. Could I also say that from about the spring of 1985

5 I was no longer really au fait with -- I wasn't paying

6 much attention to how Scotland was progressing, and

7 obviously I wouldn't be invited to comment, so much of

8 what the Inquiry has uncovered I'm really seeing for the

9 first time.

10 Q. Right. In a way I think that's gratifying, at least for

11 us, you know, that we have managed to uncover things

12 that are not generally known.

13 Can we go back to the statement at 1563, please? We

14 did ask about funding and I'm not going to ask you about

15 that because you are not in a position to comment on the

16 position regarding funding in Scotland, and then 29,

17 "Significant developments towards the end of 1984".

18 We do know that there was a meeting in Cardiff

19 in October 1984, at which Dr Mannucci indicated that in

20 a group of patients given heat-treated Factor VIII --

21 and that was the Hyland or Travenol product, Hemofil --

22 there had been no seroconversion. That is no one had

23 developed AIDS. Although, as you say, there was little

24 or no protection from NANBH with that product.

25 Then the same information appears to have been

1 imparted at a plasma fractionation conference in
2 Groningen. I think all that we were saying there,
3 Dr Smith, was that that same remark about Dr Mannucci's
4 findings is contained in Dr Foster's report of the
5 Groningen conference, and perhaps we can just look at
6 that. That's [SNB0086528]. These are Dr Foster's notes
7 from the conference in Groningen at the beginning
8 of November 1984. If we look into the text, please, the
9 story, as it then stood, as far as American haemophilia
10 patients with aids were concerned. Then a little bit
11 further down, please, and on to the next page:
12 "The heat inactivation studies, probably by Cutter."
13 On to the next page. Dr Foster has corrected that,
14 the first reference should be 60 degrees wet heating and
15 then you see the reference under the heading "Removal of
16 Virus Infectivity" to the Mannucci finding:
17 "No sign of HTLV-III after one year."
18 It suggests that the Hyland method will inactivate
19 HTLV-III, says Dr Foster. And you say that this was
20 crucial information and I think we understand why that
21 was.
22 Can we go back to the statement then, please?
23 You say that:
24 "This information did appear to swing the balance,
25 possibly for the first time, towards doing something

1 quickly about AIDS and coming back to NANBH and
2 pasteurisation when resources permitted. That something
3 was done with remarkable speed."
4 I assume you don't take issue with the table in
5 Dr Foster's large paper on this topic, which shows
6 Scotland being the first country in the world really to
7 heat-treat its entire supply or to provide to all
8 haemophilia patients, product heat-treated sufficiently
9 to inactivate AIDS.
10 A. I think the latter.
11 Q. Yes. That supply being in December 1984.
12 Then we went on to ask one or two additional
13 questions, which really relate to a group of patients
14 who became known as the "Edinburgh cohort". I don't
15 think it's necessary to ask you any questions about the
16 meeting of the heads of department on 26 October 1984
17 because we have been over that with Drs Perry,
18 Cuthbertson and Foster.
19 Then on to the next page, you have confirmed our
20 understanding about how practically this heating was
21 achieved in December 1984. And then finally we put to
22 you this question that all witnesses on this topic have
23 addressed and that question is really, given that the
24 equipment necessary to carry out this dry heat treatment
25 was already installed at PFC or easily obtained at the

1 beginning of 1984, why was dry heat treatment not
2 initiated at that time? And in your answer you are
3 speculating because you weren't party to the
4 decision-making process, but you were swimming in the
5 same soup. I think if we just perhaps read for
6 ourselves the particular points that you make in
7 response.
8 (Pause)
9 You will know, Dr Smith, that your points are
10 similar to points made by other witnesses and that's
11 hardly surprising.
12 The second bullet point refers to a lack of
13 appreciation at the start of 1984 that AIDS had entered
14 the UK donor population. This is not a factor that has
15 been mentioned by everybody but certainly, reading it as
16 you have expressed it, it does seem common sense that
17 that must have led to a different assessment of risk.
18 If it had been known at the start of 1984 that AIDS was
19 in the donor population, the assessment of the risk and
20 the timescale within which some sort of viral
21 inactivation process would be required would have
22 necessarily have been different. Would you agree with
23 that?
24 A. Yes, and I could be wrong. This is my recollection from
25 the time but it is a long time ago and, generally

1 perceived, is rather loose. But I have said it here,
2 this would be a factor, how you perceived the balance of
3 risk/benefit in going to heat treatment, which was still
4 being perceived by some people as very dangerous.
5 Q. Yes.
6 A. So if you thought your plasma supply, for instance, was
7 already infected, but you would probably err on the side
8 of doing something about it, heat treatment, whereas, if
9 you thought that heat treatment was going to cause each
10 recipient to develop Factor VIII inhibitors, you would
11 have to weigh the risk much more carefully, and some
12 would come down in favour of not heating and unheated
13 Factor VIII was used by choice by some clinicians
14 through much of 1985.
15 Q. Yes. But what about the majority? I mean, after the
16 end of 1984, when there had been infection of patients
17 with haemophilia in the United Kingdom by NHS product,
18 the majority of haemophilia clinicians were seeking
19 a heat-treated product, were they not?
20 A. Yes, and in particular a heat-treated NHS product
21 because they thought there would still be an additional
22 margin of safety from the quality and motivation of our
23 donors.
24 Q. Yes. And perhaps if we can go on to the final page,
25 please.

1 THE CHAIRMAN: Could I ask one question, before we leave
2 that?
3 MS DUNLOP: Yes, certainly.
4 THE CHAIRMAN: In retrospect, was there not a degree of
5 naivety in treating the donor population as in some way
6 hermetically sealed within the boundaries of the
7 United Kingdom? Didn't people travel in those days?
8 A. Yes, they did, and already by 1983 the Fletcher and
9 Rizza paper had shown that there was no safety from
10 non-A non-B but there were inhibitions against -- AIDS
11 was being seen as, like TB and leprosy and syphilis in
12 previous times, as a kind of dirty disease, and you do
13 not want readily to think that your patients or your
14 donors are in that category. This is just
15 psychopathology. It's not good reasons for it. But
16 when I say "perceptions", I don't know how many
17 percentage of which groups -- treaters, patients,
18 transfusionists -- would have subscribed to that view.
19 THE CHAIRMAN: Yes.
20 A. We only knew it had entered the donor population.
21 I doubt very much whether in early 1984 anyone had
22 contracted AIDS from an NHS product. Pretty sure
23 certainly not a BPL one, and it was during 1984 that
24 kits became available in a very limited supply and
25 patients began to be monitored. But, as you know, it

1 took a long time for donors to be screened for HIV.
2 There is rather a lot bundled into that two and
3 a half lines, I am afraid.
4 MS DUNLOP: It's perhaps easier, Dr Smith, to assert that
5 that extra piece of information would have made
6 a difference than it is to quantify what the difference
7 would have been.
8 A. Yes.
9 Q. Then on to the last page, please. I think we can read
10 for ourselves what you say. (Pause)
11 Sir, given that it's just after 4 o'clock, there are
12 some bits and pieces which I do need to finish with
13 Dr Smith. I wonder if it would be in order for us to
14 rise now and if I could do that briefly tomorrow
15 morning, intruding into Mr Mackenzie's time obviously.
16 THE CHAIRMAN: If Mr Mackenzie agrees. There is no doubt on
17 a rational assessment of the time that's required, if
18 it's not going to prevent us finishing and releasing
19 Dr Smith, I'm sure that we could all do with a break.
20 MS DUNLOP: Yes. Thank you.
21 THE CHAIRMAN: Tomorrow morning.
22 (4.06 pm)
23 (The Inquiry adjourned until 9.30 am the following day)
24
25

I N D E X

DR JAMES SMITH (affirmed) 1

Questions by MS DUNLOP 1