THE TRIBUNAL RESUMED ON FRIDAY, 13TH OF JULY, 2001, AT 10:30 A.M. AS FOLLOWS:

MR. DURCAN: Good morning, Madam Chairperson. The next witness is Dr. Colvin.

DR. BRIAN TREVOR COLVIN, HAVING BEEN SWORN, WAS EXAMINED AS FOLLOWS BY MR. DURCAN:
A. I'm Brian Trevor Colvin.

THE CHAIRPERSON: Good morning, Dr. Colvin.
A. Good morning Madam Chairperson.

Q. MR. DURCAN: I think what might be helpful for you, if you have a copy of your statement in front of you when you're giving your evidence. Doctor, could you tell us where you're employed and in what capacity?
A. I'm Assistant Warden of Student Affairs in the Royal London School of Medicine and Dentistry at Queen Mary & Westfield College University of London, but my clinical appointment is as consultant haematologist at Bart's in the London NHS Trust in East London.

Q. And how long have you been there, how long have you held that appointment?
A. I've been assistant warden for the medical school for the last three years and I've been consultant haematologist and haemophilia centre director since 1977.

Q. I see. Could you tell us a little bit about the haemophilia centre or how many patients would be under your care?
A. The haemophilia centre at the Royal London Hospital has about 600 patients on its books and we have about 100 regularly treated patients, so we have about -- we see about 100 patients a year; not always the same patients, but about 100 patients a year. And in 1985, I had about 40 antiHIV-positive patients. And there are about 80 antiHCV-positive patients under my care.

Q. I see. What, again -- perhaps if we look at -- perhaps the best time is the early /mid-1980s. What sort of staffing would there have been in the unit at that time?
A. Well, there was myself, as the consultant and director, and there were junior medical staff who would be attached to the department of haematology. We didn't have a specific geographic haemophilia centre. And there would have been really one nurse, whole-time equivalent, available to me; and laboratory staff to undertake laboratory work.

Q. I see. I think from 1993 to 1996 you were Chairman of the United Kingdom Haemophilia Centre Directors organisation?
A. Yes, I was.

Q. And I think from 1994 to 1999 you were Chairman of the Panel of Examiners for Haematology at the Royal College of Pathologists?
A. That's correct.

Q. And I think you were Chairman of the Clinical Ethics Committee at Bart's and the London NHS Trust?
A. Yes. That's an appointment I still hold.

Q. And have you published material in regard to haematology and blood products over the years?
A. I have; about I think 50 invited or peer-reviewed publications in the field of haematology.

Q. Okay. Now, I think in your statement at page three you set out the basic background in regard to haemophilia and the various products which were available in regard to the treatment of persons with haemophilia. And rather than going through them separately, as the Tribunal will be quite familiar with this territory, perhaps I could just ask you a couple of questions.At paragraph two, subparagraph three, you deal with concentrates and their introduction in the early '70s. Looking back at that time, what was, as a treating doctor, what was the reaction to concentrates when they became available?
A. Well, I think the feeling about freeze-dried concentrates was that they were extremely convenient to use and they opened up the possibility of home treatment for patients with haemophilia and, therefore, the opportunity to lead a normal life and to go to normal schools and to have the prospects of employment for the future. So that in those early days, it was an atmosphere of optimism and enthusiasm.

Q. Was there an awareness that these concentrates were made from multidonor pools at that time?
A. There certainly was such an awareness. And really, everybody has always understood that blood products have their potential disadvantages, and it wasn't very long before it became evident that there were disadvantages to the large pool nature of these products.

Q. And what were those disadvantages?
A. Well, the disadvantages really were those of non-A non-B Hepatitis. There was a little bit of Hepatitis B, but that wasn't a huge problem numerically, but it was clear that some patients who were treated with large pooled concentrates developed overt clinical liver infection. And then later it became apparent that, when you looked at the liver function tests of people with haemophilia who had been treated particularly with large pooled products, that these were often abnormal, and the implication was that this might be due to some kind of a virus infection. It should be added that although it was perceived correctly that the risk of non-A non-B Hepatitis from cryoprecipitate was very much less, that nevertheless, the single donor product, cryoprecipitate, still had -- still derived from human blood donors, and therefore, had its own risk of non-A non-B Hepatitis, which, through later study, seems to have been around 0.3 percent in the United Kingdom. So cryoprecipitate wasn't completely safe. But it was quite early on that the freeze-dried concentrates were more likely to cause clinical or subclinical hepatitis.

Q. When you would you say that became obvious, Doctor?
A. I think the first publication that I recall that made it very obvious to treaters with haemophilia was the first publication referred to, in my opinion, in 1975, but I'm not for a moment implying that that was the first publication that demonstrated the risk.

It's just that the Craske, Dilling and Stern was something of a watershed for us. We sort of knew after Craske, Dilling and Stern this was really quite a significant problem for the future, at least in terms of numbers.

Q. I see. Now, perhaps looking back, just take the period perhaps from 1975 to 1980, look being back at that, again, as a treating doctor, how was Hepatitis -- non-A non-B Hepatitis, how was it viewed at the time; how was it viewed in terms of seriousness?
A. It was viewed as being unfortunate, obviously, for people who became ill, but the majority didn't become ill. And the perception, I think, was that there was a risk of long-term sequelae but that nobody had seen long-term sequelae. And I suppose there was a perception, maybe based more on hope than evidence, that this would be quite a mild problem which didn't need to -- didn't need to trouble us or our patients too much.

Q. Did that view of non-A non-B Hepatitis change over time?
A. Well, it did change, particularly when the Sheffield group in the United Kingdom started doing some more detailed work, including liver biopsy. And there was some American work, which demonstrated that it was possible for people with haemophilia to suffer long-term sequelae, by which I mean the development of chronic active hepatitis and cirrhosis. But even now there's quite a lot of doubt about what the real outcome of infection is, and those of us who have been in the haemophilia community for many years have seen relatively little long-term chronic illness as a result of the non-A non-B Hepatitis, except for those who were also antiHIV-positive, who often have developed serious liver disease; and for those who have abused alcohol, who also sometimes develop severe liver disease. But it's important that you appreciate that I'm not saying that non-A non-B Hepatitis doesn't cause severe liver disease, because I know it does. But the number of people that I've seen at London over the last 30 years with serious liver disease who had not abused alcohol and who were not HIV-positive and yet have had serious liver disease, has been very small. I think that's still true in other people's experience.

Q. When would you say, though, that the knowledge that non-A non-B Hepatitis could cause serious liver disease, at least in some people, when would that have been fairly -- or when would it have been obvious?
A. Well, I think it was really obvious by the early '80s at the latest.

Q. I see. Well, perhaps having dealt with that in a general way, we might move on now to the next part of your statement. You just -- sorry. Just to deal with one final thing there, and it's at page four. How would you -- again, look at, let's say, the late '70s. How would you have quantified the risk of infection with Hepatitis -- non-A non-B Hepatitis from concentrates as opposed to from cryoprecipitate?
A. Yes. I think that, if I can put myself to the late '70s, I would say that my perception of the risk of cryoprecipitate causing hepatitis was that it was low; and that my perception in the late '70s of freeze-dried large pooled concentrates causing hepatitis would be that the -- that the risk was substantial.

Q. Would it have been the case that treating doctors, would they have a view as to whether concentrates would cause hepatitis as a matter of almost certainty?

A. I think the papers that relate to that were really published in '83 and '85. And I'd refer to Fletcher, Trowell and Craske for the fourth of my references, in which it was really rather clear that the majority of people who were treated with large pool concentrates for the first time would develop non-A non-B Hepatitis. And then Peter Kernoff's paper from 1985, reference five, I think demonstrated to all of us that if you were treated with a large pool concentrate for the first time, then you would inevitably develop non-A non-B Hepatitis. And since I used the word "substantial" when I was describing my perception towards the end of the '70s, that is a slightly different word from the "inevitable" that I would use for my understanding once we got to '83 or '85.

Q. So it moved on in terms of knowledge?
A. Exactly.

Q. From a -- a probability, perhaps, to -- almost to a certainty?
A. That's correct.

Q. I see. Now, if I could move on to the question of AIDS, and I think this is dealt with at page five in your statement. What I want to try to identify, Doctor, is, again, as a treating doctor who is very experienced in these matters, when would you have first come to the conclusion that there was a real threat in regard to the spread of the HTLV-III virus by way of blood products?
A. Well, of course, we knew about the risk of AIDS before HTLV-III was identified. And the development of the first cases of AIDS in the United States is well-described in a paper that's just been published in The New England Journal of Medicine, where, on the 5th of June, 1981, five cases of pneumocystis carinii were described. And it wasn't very long, I think, before people began to be concerned that this might be a virus infection and, therefore, that there might be a risk to the population. But really, it was only, I suppose, when the first cases were described in the blood transfusion community that we began to realise that there was a substantial problem. And the initial case in three persons with haemophilia were described on July the 16th, 1982. So there was a gap between the first description of AIDS and the first description of something occurring in the haemophilia population. I mean, I think during that period there - it's difficult to remember 20 years ago, but I think we all had a feeling of anxiety because, of course, we didn't know what AIDS was in those days and many different proposals were made as to what it might be to do with, and not all of them were to do with viral infections. So there was a feeling of anxiety. But it wasn't really until we got cases in the haemophilia community that we realised that there was a serious problem.

Q. I see. Would it be fair to say that there was a feeling of anxiety from, perhaps, the summer of 1982 onwards?
A. Yes. In my report I highlight by 1983, because I think by that time, we all, if you like, got the message. The initial report in July of '82 I think didn't immediately become apparent to all haemophilia treaters. So I think we have to look at the period between July '82 and beginning of '83 to say, by that time, in that period of time, really all haemophilia carers must have known that there was something very badly afoot.

Q. By the beginning of 1983, in your opinion, would it have become clear that there was a real threat of the transmission of the virus by reason of blood products?

A. Yes.

Q. I see. Did that have implications for the choice of products that were being used in terms of treating persons with haemophilia?
A. I have some difficulty recalling what my treatment policy at that time was to do with. What I recall is that in the early '80s, I was trying to treat my young children with cryoprecipitate. Now, we were also trying to develop the home treatment programmes and we were trying to improve the care of our families. And I think it's fair to say that for the moment severely affected children with haemophilia, we had to give them, in our perception, Factor VIII large pool concentrates, and I certainly had about half a dozen children who did develop HIV infection. But it was certainly my policy to try to give children cryoprecipitate, because children are small and they can be treated with perhaps one or two or three donor units of cryoprecipitate. And I think there was a feeling amongst some haemophilia treaters that the cryoprecipitate approach was rather old-fashioned, and indeed in many ways perhaps it was. But I think I was trying to use cryoprecipitate, not to prevent HIV infection, but to try to limit the amount of non-A non-B infection in my children's community. But I fully acknowledge many of my children did develop non-A non-B and some developed HIV infection, because the imperative was to try to stop the bleeding and improve the schooling and treat in what was perceived as a modern way. As far as the adults were concerned, we did our best, I think, when the HIV, or at least when the AIDS problem started; we did our best to make the use of the resources available to us. And that meant using NHS in the United Kingdom, heat -- NHS material, which was not sufficient for all our needs. So the NHS material in my centre was largely allocated to the home treatment programme, because I knew how much I'd need for a particular group of patients over the year, and I had a rough idea of how much I'd be allocated by the NHS, and then I'd use commercial concentrates, which I perceived to be more risky. I'd use those for serious illnesses or serious injuries or for unavoidable surgery. And again, I think that those rules were put in place before, really, the HIV epidemic began. At that time, we believed that NHS concentrates perhaps would be less likely to transmit hepatitis than American concentrates. In fact, that was false, because as we now know from 1985 data, that whether you were using NHS material or commercial material, it would all transmit hepatitis. But there was this feeling that the British products were safer than American products, maybe partly for emotional reasons and maybe partly for good reasons. And so that was our policy: To use cryoprecipitate for the young children; to use NHS concentrate when it was available for the home treatment programme; and to use commercial concentrate to deal with disasters and surgery.

Q. Two questions arising out of that: When you say "young children," would you give us some idea of what we're talking about?
A. Really we were dealing I think particularly with a sort of group of, sort of, nought to ten. In those days, the children's ward would quite often have children with haemophilia as inpatients, and because of the -- because of the way the childcare is orientated, it's relatively easy to say to the children's department, 'you'll give cryoprecipitate', and not to give them access to the concentrates. So I think nought to ten particularly, but perhaps nought to fourteen in terms of treating people on the paediatric wards on a regular basis. And as I say, most of the treatment would be given as inpatient. We didn't have a very effective home treatment programme at that time, although we did have some home treatment cryoprecipitate, but it's quite

difficult to organise. So I think that it was particularly for the younger children whose mothers would bring them up to the hospital; we'd treat them with the cryoprecipitate on the children's ward knowing that the children's ward didn't have access to the concentrate unless I said so. But as the children got older, as we tried to introduce home treatment programmes and as the ease and sort of convenience of large pooled concentrates became obvious, so the older children tended to eventually be treated with large pool concentrates in the sort of ten to sort of 15 age groups. It was really the children perhaps under ten that I was doing my best to use cryoprecipitate for, but it's important to emphasise for the Tribunal that I don't claim any sort of special precedence over this. I was just trying to avoid hepatitis where I could. And sometimes we were successful, but by no means all the time.

Q. Which brings me to my next question: That policy was driven by a wish to try to avoid hepatitis, hepatitis infection?
A. That's correct. And also, I think I've indicated it was driven a little bit by knowing that it was something that I could logistically do. Because if I had children in the ward and I'd got paediatricians there and I told them to use cryoprecipitate and nothing else, then I could actually do that easily without a large risk of being given the wrong product.

Q. When the knowledge became available, perhaps going into 1983, about the risk of HIV infection through blood products, did the policy which you've told us about, did it change in any way, or what happened?
A. Well, if we look at 1983, I continued to give cryoprecipitate to the children. In fact, I didn't change the children's cryoprecipitate policy until we changed over to NHS 8Y in the -- April of '85. Again, I have to emphasise that some of my children did receive large pool concentrates and did get infected with HIV as well as Hepatitis C. So it wasn't by any means a perfect policy. As far as the use of concentrates was concerned, I don't think we really did change our policy, because we continued to give NHS material to the home treatment programme where we could. And I can remember two patients who did develop HIV infection, one of whom who came in to have their wisdom teeth out, I think, in the middle of '82; and another who needed a rather urgent operation in the spring of '84. And both those patients were given commercial Factor VIII concentrate according to the policy I've just outlined and did develop HIV infection. So I know, really, the date on which they were infected. So no, I think that policy was retained.

Q. I see. Now, was there any factor that caused you to move children from the cryoprecipitate on to concentrate or to use concentrates?
A. It was mostly the difficulty with bleeding that didn't seem to be controlled with cryoprecipitate. And certainly you do sometimes find that venous access is a problem, maybe that cryoprecipitate doesn't seem to work. And particularly for introducing a home treatment policy, it's quite difficult to manage a home treatment programme with cryoprecipitate. Also, sometimes I'd be sent a patient from another hospital where they'd been receiving concentrates, and I certainly wouldn't -- I wouldn't reintroduce a cryoprecipitate policy if I was referred a patient who had been given concentrates elsewhere. So again, I have to emphasise for the Tribunal this was not a perfect policy.

Q. Did you have any specific policy in regard to previously untreated patients?

A. No, we didn't. But in the period around the sort of early to mid-'80s, we began to get involved with specific studies of previously untreated patients. And so I was, I think, the main contributor to study six, which was published in '88, but, of course, dealt with patients who were treated from '85 onwards, which was the study group dealing with the use of 8Y; the concentrate referred to in 1988 publication is actually the 8Y material. We had one or two studies that we did for BPL before then. So I think in the middle of '84 I published a -- two or three case reports of patients who had been given a BPL product that was an early heat-treated product, in an attempt to avoid Hepatitis C infection. And published successful results in those patients. But it's possible that the lack of non-A non-B Hepatitis arising from the treatment of those patients during '84 was more to do with the small number of donors within the donor pool of that particular product that was being prepared at Oxford. It might have been that and the fact that they came from what was sort of known as 'trusty donors' - those people who had been giving for years, rather than the -- necessarily the effect of the viral inactivation process to which the -- to which the products had been subjected. So I guess I was doing some scientific work, particularly early scientific work in '84, certainly; I'm not sure about '83, but certainly in '84 we were looking at previously untreated patients, particularly -- perhaps mildly affected patients who had not ever been treated before and then suddenly did a treatment, partly for scientific reasons. But I think one or two of those did avoid both Hepatitis C and HIV infection as a result.

Q. But do I take it from that answer you didn't have any general policy at the time, '83 /'84, in regard to previously untreated patients?
A. No. There wasn't a general policy but I did my best I think to try to limit the risk of HCV infection for those patients. But for the very young children I would still have given them cryoprecipitate because their -- that group of age is difficult to study. And maybe I thought that it would be better to study those who were adults and easier to take serial samples from those who had never been treated before. So I think for the very small children it would still have been an attempt to use cryoprecipitate.

Q. When did you become aware that heat-treated products were becoming a possibility and would be coming on the market?
A. Well, I think we were aware of the existence of viral activation by heat treatment by -- I mean, I was aware by the beginning of -- middle of '84. But of course, at that time we were trying to avoid Hepatitis C infection rather than HIV infection, because HIV was not known about. And we were trying to avoid non-A non-B because, of course, Hepatitis C wasn't known about either. So we were, during '84, looking at some early heat-treated products in an attempt to avoid non-A non-B Hepatitis. Then in -- I think it was October'84, the first reports of viral inactivation of HTLV-III, as it was then known, started to appear. And I think I probably refer to that in my reference eleven, that's the Levy paper. My concern then was that our early experience with the viral activation of concentrates by heat treatment with reference to non-A non-B Hepatitis as being disappointing. And the Colombo reference, which is reference three, particularly relates to the lack of effectiveness of heat treatment as it stood then in eliminating non-A non-B Hepatitis when studied in the clinic. So I felt that it was going to be very important to have clinical confirmation of the efficacy of heat treatment by the study of individual patients. And the reference that I've used for that is reference 12, which is the Mosseler reference, because that study in The Lancet in 1985, I think, gave some clarity to the fact that not only could HTLV-III be

neutralised in vitro - that is in the laboratory - but that it -- a heat-treated product could prevent the transmission of HTLV-III in vivo. Now of course I fully appreciate that there were recommendations before that time to use heat-treated concentrates because of the perception that it might be successful, but it's important to appreciate that I and many colleagues were concerned that if we used commercial heated products immediately, and that the heating process was not fully effective as viral inactivation, then we might finish up transmitting HTLV-III to patients previously uninfected because the heat treatment didn't work, which is what had happened with non-A non-B Hepatitis.

Q. So what happened, what was your product choice between, let's say, October '84 and June '85; firstly in regard to Factor VIII?
A. So my product choice was either to use NHS unheated material or to use heated commercial American material, because the NHS wasn't producing any heated Factor VIII at that time, or at least in extremely small amounts. And we, therefore, either went entirely for commercial heat-treated material or we used a mixture of NHS unheated material and commercial heated material. And in my centre we used a mixture of NHS unheated material and commercial heated material, and of course, the cryoprecipitate that I've referred to earlier, until about April '85 when the NHS 8Y product became available.

Q. I see. Well, if we just deal for a moment just prior to that April '85. You've told us you were using both commercial and unheated -- heated commercial but unheated --
A. Yes.

Q. -- NHS product. Had you any preference between the two or did you use them for specific groups?
A. I think we continued really to -- with the sort of policy that I've already outlined to you. Still using the NHS material for the home treatment programme and still using the American commercial material for everything else.

Q. But at this stage the American material would have been heated?
A. Yes.

Q. And when would the use of unheated American material have ceased?
A. That would have ceased around October '84, I think. I mean, as soon as -- as soon as we knew about the potential importance of using heat treatment and as soon as we had availability of American heat-treated concentrates, then we changed over to them.

Q. And your recollection would be that was sometime around the end of --
A. End of '84; maybe it was December rather than October. I might need to be corrected on that, but that's my perception: That by the end of '84, I think we were using American heat-treated concentrates rather than unheated concentrates. I think it was about October '84 that we really became aware of the potential. So I think probably the end of '84 before we changed over.

Q. I see. Now, the -- I think you've just told us, the NHS heated concentrate became available in April 1985. What effect did that have on product choice?

A. Well, I don't think it had a huge effect, except that we stopped using cryoprecipitate. So that as soon as the NHS 8Y came in, we stopped using cryoprecipitate for the children. That was a big moment of decision to go over to that material. As far as the adults were concerned, the NHS 8Y really replaced the NHS unheated material and we went on using commercial American material as we had been.

Q. So would it be fair to put it in this way: The policy which you've outlined continued, except the children now got heated NHS product?
A. Correct.

Q. The adults got, insofar as possible for home treatment, heated NHS product?
A. Correct.

Q. And then for more serious bleeds and perhaps operations, commercial heated product was used?
A. Correct.

Q. That would have been the policy from April 1985 onwards?
A. Yes, correct.

Q. And did that policy then continue -- I suppose the question really is this: Did the balance between NHS product and commercial product change during 1985; did more NHS product become available?
A. Yes. I think from '85 onwards the NHS supply situation did improve, but I can't recall exactly how much. But we certainly needed -- we needed to use commercial material for a long while after the NHS 8Y came in. But I think that really from 1985 onwards, the Blood Transfusion Fractionation Laboratory really began to increase production quite a bit. There are some graphs, which I think are being photocopied at the moment, of a report that appeared just this month in Haemophilia, of haemophilia care between 1981 and 1986, I think the paper is. And that shows very clearly what happened to the use of NHS and commercial concentrate in the United Kingdom over that period.

Q. Perhaps if we could just deal with in general for the moment, and we'll see how we do in regard to that. If, perhaps, we look at Haemophilia B patients for a moment?
A. Mm-mm.

Q. And again, I'm interested in regard to, again, 1985?
A. Mm-mm.

Q. Perhaps the end of 1984 /beginning of 1985?
A. Yep.

Q. What was the policy then or what was your policy in regard to treating persons with Haemophilia B?
A. My policy had, of course, been to use NHS Factor IX concentrate for people with haemophilia. We really stopped using fresh frozen plasma many years earlier because it's extremely inconvenient material to use and it doesn't have any real concentration other than removal of the red cells. So that fresh frozen plasma, which was being

used to treat Haemophilia B, Christmas Disease when I qualified, was quite quickly replaced by the NHS Factor IX concentrate, which was known to be potentially thrombogenic; that is, that it sometimes seemed to cause thrombosis, particularly after orthopaedic surgery. Of course, Haemophilia B is much less common than Haemophilia A, and in the United Kingdom there are -- have been for many years, about 1,000 people with Christmas Disease, Haemophilia B. And so the NHS had always been self-sufficient in the production of Factor IX concentrate and I had never used any commercial Factor IX concentrate. So the policy that we adopted between the end of '84 and the middle to later period of '85 was that we went on using NHS Factor IX unheated concentrate. The NHS wasn't producing any heated concentrate. And the perception was for some of us, including myself, that there was a greater risk of HIV infection from a heated Factor IX concentrate that might be very thrombogenic than from the continued use of an NHS Factor IX product which wasn't heat-treated. And this was based on two factors really: One of them was the perception, which I think was wrong, that the donor pool in the NHS was not infected with HIV. We discovered later that, sadly, it was. And the perception which I think was true, but not absolutely true: That the fractionation process for plasma resulted in the HTLV-III passing mostly into the Factor VIII fraction rather than into the Factor IX fraction. And there's good scientific evidence that that was indeed the case. The result was, of course, that very few patients in the United Kingdom with Haemophilia B developed HIV infection, but sadly, a number did, including one of my own patients who was seronegative at the end of '84 but was seropositive by the end of '85 as a result of using NHS unheated Factor IX concentrate. Now, obviously an alternative strategy would have been to use the heat-treated commercial Factor IX concentrate that was available to us. And the reason we didn't use that, in my centre, was the reasons I've explained; which was that the perception of the risk of HIV in the British donor pool was low, and the feeling was that the HIV might well have gone to the VIII rather than to the IX fraction. If you look at the graphs that I've made available to you, and I think which perhaps you saw yesterday, you can see that some UK Haemophilia Centre Directors went over to heated commercial Factor IX, and some continued with, as we did, with unheated NHS Factor IX.

Q. I was just about to ask you that: You've told us the choices you made?
A. Yeah.

Q. Did other people make other choices?
A. Some people made the same choice and some people made a different choice, and I think that's brought out clearly by the graph of overall use of product.

MR. DURCAN: I understand, Madam Chairperson, that Dr. Snape actually referred to this graph in his evidence, and we will have it, in a moment, photocopied. But it is the same graph that Dr. Snape referred to.

Q. Now, when did heat-treated Factor IX become available to the NHS?
A. The first -- the first trials I think were in July of '85. And really by sort of -- I think it's about September '85; I've actually given the personal communication from Terry Snape to you to photocopy. But it was towards the end of '85 - I think August /September, probably September - that supplies of NHS Factor IX became available. And I've said in -- it's certainly my view that, by the end of 1985, really was the last time that anybody should have been using unheated material of any kind.

Q. Yes. Can you recall, I think Dr. Snape indicated that when the heat-treated Factor IX became available, I think he may have written out to doctors saying that any heat-treated Factor IX -- sorry, unheat-treated Factor IX which was in the hospitals should be returned. Can you remember, was there a general withdrawal of?
A. I thought about this and I'm afraid I cannot recall what the withdrawal process was, if one existed. I'm certainly aware that from time to time I would discover that patients of mine still had unheated material when they should have stopped using it, because getting material back from patients is not always terribly easy. And I think it was probably into '86 that we were still getting dribs and drabs of unheated material being returned to us. And I think the process of withdrawal of Factor VIII and Factor IX, whatever it was, and I can't recall it very well, was almost certainly imperfect.

Q. It seems to, from what you're saying, it seems to be the case that whatever happened, it doesn't seem to have been absolutely effective in bringing about a stopping of use of unheated product and a complete changeover to heated product?
A. I think that that did take place over a period of time. There wasn't a single day when you could be absolutely confident that nobody would ever use an unheated product again.

Q. Doctor, would it be fair to characterise that in 1985, over time, from perhaps April/May of that year, there was a buildup of knowledge that the heated Factor IX was safer than the unheated Factor IX; and that the later you got in the year, the stronger the evidence to that effect?
A. Yes, I think that is fair. Two reasons really: I think one of them was that the Mosseler paper had come out in the middle of '85, and although that I think was - I'd need to just check the paper - it was only to do with Factor VIII, but nevertheless, there was a growing realisation that, really, everybody was going to have to use viral inactivated products as soon as possible. And whatever happened to HCV, or non-A non-B as it was known then, as '85 wore on, I think for myself, I became increasingly convinced that the heat-treating process was going to address the issue of viral inactivation for HTLV-III. The other thing, of course, was that, during '85, there would have been a marked reduction in the amount of viral contamination because of the process of selecting out donors who were antiHTLV-III positive. And therefore, I think there would have been an increasing confidence that even if there might be one or two HTLV-III positive donors getting through, that heat treatment had a better chance of getting rid of the infection. It's important to notice that these processes were not absolute. It wasn't a question of whether any heat-treating process would inevitably render a concentrate sterile; you had to consider the donor pool, the level of infection, the method of heating - both its temperature and duration. And during '85, all those things were moving in a favourable way. So that we were, I think, getting better donors, we were getting much better removal of contaminated units and the process of viral inactivation by heat treatment was improving. It's like all those things led to an understanding that, whatever we had done during '85, by the end of '85 it was mandatory to have virally inactivated products.

Q. I see. Now, I should have asked you just to go back to your own choices about in -- let's say, once the heated NHS Factor VIII became available from April 1985 onwards. You were still using commercial product, you told us that, because there simply wasn't enough NHS product available?

A. Correct.

Q. What was your product of choice at that stage? Was there a particular one you used?
A. I think that we mostly used Alpha Profilate. I can't remember exactly the date of being aware that some commercial concentrates were transmitting HIV; but I can, nevertheless, place it exactly, because I was in the Milan conference of World Federation of Haemophilia. It would be very easy to work out when that took place because I became aware at the World Federation of Haemophilia meeting in Milan of news that one of the commercial concentrates that had been heat-treated was suspected of transmitting HIV, because I can remember phoning back to the London Hospital to my colleagues to say, 'Have you got any of that product in the hospital? Don't use it'.

Q. Clearly we know about this, so this would be the Armour product that we're talking about?
A. Correct.

Q. I think we'll attempt to identify the Milan meeting as we're going along, and perhaps you could put a specific date on this and I'll come back to it?
A. As you can see, the actual event is still quite fresh in my mind, even though I can't tell you the exact date.

Q. Can I take it it's fresh in your mind because it was a considerable shock to you?
A. Precisely so.

Q. That that was the case. We'll look for a date for that, Doctor. And perhaps we can move on. I want to ask you about one thing in your statement: If you look at page six, top of the page, heading "Conclusion of Infections." Just the last sentence there: "Virtually all transmission of HIV and HCV infection by clotting factor concentrates had ceased by the end of 1986." Could you just explain to us why you came to that view or why you have that view?
A. I mean, that was really to include in my statement the recognition that the Armour product, to the best of my knowledge and belief, had been transmitting HIV infection in 1986. So I think that I don't have absolute knowledge of exactly when all that material had been withdrawn, and when no further infection took place. It's also important to appreciate that there were little sporadic reports of hepatitis infection taking place in haemophilia sufferers after that date; either Hepatitis A, or occasionally people would talk about Hepatitis B infection, and maybe even sometimes there was a suspicion that Hepatitis C had been infected by a particular -- had been transmitted by a particular concentrate, although I think actually these reports didn't eventually come to anything. So it's quite difficult to give you an absolute date about when. But we know that all infection had ceased.

Q. I think the evidence which has been available to the Tribunal suggests that dry heat treatment of commercial products - and I'm not talking about the superheat-treatment that the NHS used - but the dry heat treatment of commercial products did not destroy or -- HCV virus?
A. Yep.

Q. Would there -- I think -- would you yourself have been using such dry heat-treated products after, perhaps, 1986?
A. I can't recall exactly, and we certainly didn't have a rule that I'd produced saying 'you mustn't use a dry heated product'. We certainly tried to use the superheated product that you referred to, and we'd been involved with Peter Kernoff in the -- in one of the studies, which I think wasn't eventually published, of the Alpha Profilate material. There is a paper which I think is in the grey folder which I was invited to look at this morning, from a United Kingdom group, including Peter Kernoff at the Royal Free, which demonstrated that with the use of the Alpha Profilate, not everybody got non-A non-B Hepatitis. And so there was a sort of perception that maybe the n-heptane Profilate might be better for Hepatitis C than some of the other products. And so I think we were using the Profilate in preference and using it partly for scientific study. But although the Kernoff paper implies that maybe the Profilate didn't transmit Hepatitis C to everybody, it looks, on rereading the paper, as though it's fairly clear that it did transmit non-A non-B Hepatitis to some people. So I think even the wet heated or the n-heptane material certainly wasn't free of risk of Hepatitis C.

Q. Is it possible for you to give us some idea of a date when you would have had knowledge that the superheat-treated product wouldn't or didn't transmit HCV?
A. Well, I was part of the -- of the study under reference six, the study group of 8Y. And so I was looking at effectively untreated patients for the period leading up to the publication in 1988. But I would have got a personal view of the safety of that product probably by 1986 or early '87, because I started my experience of 8Y in mid-'85. We then started entering all the patients we could into the study that was looking at the use of 8Y, and therefore, it would have been well before '88 when the publication of paper six took place. Though I would have had an opinion of my own that 8Y didn't transmit Hepatitis C, but I couldn't give you a date on that.

Q. And you had -- because you were involved in the study, perhaps your knowledge in regard to that or your perception might have been slightly earlier than others?
A. Absolutely, because, of course, for instance, when we look at, say, the Mosseler paper demonstrating the effectiveness of heat treatment in preventing HTLV-III infection, first I knew of it was when I read it in the journal; whereas with the study of 8Y, I was part of the process.

Q. Now -- well, given what you've told us about your knowledge and your perception of the safety of the superheat-treated product in terms of Hepatitis C infection, did you have any policy in regard to previously untreated patients in regard to what product they should get, perhaps after -- let's take in 1986 going into 1987?
A. Yes. I mean, I can certainly recall that we treated all the babies with 8Y, so we had a clear policy for the babies who -- the majority of the previously untreated patients, they would have been given 8Y. I was involved with Peter Kernoff in a study of previously untreated or virtually previously untreated patients being treated with Profilate - that is the Alpha Profilate; and I can't recall exactly what year that study was wound up. I think it was actually never published, partly because I think Peter became ill and partly because we moved on. But I think that I was certainly involved in studying previously untreated patients, who were adults, with Profilate, and that must have been before '88 when we published the 8Y study, because clearly, once I knew that the 8Y wouldn't transmit non-A non-B, I wouldn't then have been

ethically able to put people into a study that was actually looking to see whether commercial products would transmit the products. So I think that somewhere between'86 and '87 I would have been giving previously untreated patients exclusively 8Y, but before that period there was certainly probably about a year between sort of '86 /'87 when I know I contributed to a study for Profilate for previously untreated patients, because at that point I wouldn't have known the 8Y didn't or couldn't transmit HCV.

Q. And would it be fair to say, therefore, that certainly from, let's say, 1987 onwards, you would have felt that it would be inappropriate to give previously untreated patients anything other than the superheat-treated product?
A. Well, I don't know about that, because we only had a limited amount of superheat-treated product available to us, and I think the perception -- the perception was that the risk of bleeding was the greatest of all risks. And therefore, if we didn't have the superheat-treated product, we would use the -- what we regarded as being the safest product. And I think it's important to appreciate that a lot of our knowledge is now sort of retrospective. So what we were doing at the time was based on our knowledge then. And it's quite difficult to remember exactly what one's knowledge was on a particular day.

Q. I understand that. What -- I suppose what I'm trying to get at is this: Is it possible to identify a moment in time or at least a general idea of when it would be that previously untreated patients would have moved on or would have only been treated with superheat-treated products?
A. Well, I think it's probably around '86, '87, between -- somewhere between '86, '87, I think. But of course, at about that time - and I can't recall the exact date of introduction - about that time -- I can certainly find out by referring to the notes I brought with me, which I don't have at the moment. But at about that time, the third generation products like the monoclonal antibody products were becoming available. But they were -- they were being marketed in a way which implied that they were particularly good for people who were HIV-positive. There was an implication that these very high purity products were good at preventing damage to the immune system by the HIV. Some people used them; I must confess that we didn't, and the reason we didn't was that I was unconvinced by the argument, and the products were certainly much more expensive than the intermediate purity products. So there was this issue, as the '80s wore on, about whether we should be using high purity, third generation products, because they were better for patients; or whether the intermediate purity products that had been proved, through the studies we had conducted in the United Kingdom, were adequate for the purpose.

Q. I think I'd like to move on to another matter. In or around the end of 1984, I think testing -- a test kit became or a testing or procedure became available for HIV. And did you make arrangements for your patients with haemophilia to be tested in or around the end of 1984?
A. I looked at my records recently because I was coming to the Tribunal today, and it's clear that I began to test for HTLV-III infection in November of '84. And the professor of virology, Professor Leslie Collier, at the London Hospital, as it was then, had an interest in this area, and was doing his own immunofluorescence testing, but I think he was also sending material off to Colindale for confirmation. But the results of the test as they came through were difficult to analyse because we still didn't know

much about HTLV-III, we didn't know much about false positive and false negative results. And I think we were also conscious that it was our responsibility to talk to our patients about what we were finding. I think there was one patient that I saw who I initially thought was antiHTLV-III positive - and I think I discussed it with him - who later turned out to be antiHTLV-III negative, and so he wasn't, in the end, infected. So there was quite a sort of period of doubt at the end of '84 /early '85 as to what these results really indicated, and how that information should be communicated to our patient group.

Q. And if we take it in stages: One set of tests were done first, is that correct?
A. Mm-mm.

Q. And then were confirmatory tests done?
A. I mean, I think that's the case, but I -- it's difficult for me to swear that, really, because it's such a long time ago. All I've got in my records are positive and negative results for antiHTLV-III. But I -- my recollection is that Professor Collier wasn't, at that time, willing to take a view finally on whether these samples were antiHTLV-III positive or negative without some kind of confirmatory test, but I really can't remember, or maybe I never knew the exact status of any individual test. And I suspect that even Professor Collier may not have really known.

Q. Perhaps as far as we can take it is this: Is it your belief, without being absolutely certain, that some form of confirmatory testing was done?
A. I believe so.

Q. And once that was done, did you then proceed to tell your patients of the outcome of their test?
A. Yes.

Q. Firstly, of the persons who -- of your patients with severe haemophilia, approximately what proportion were found to be HIV-positive?
A. It's about two-thirds.

Q. I see. How many people would that have been?
A. 40, 42. I mean, the exact number is uncertain because people come and go from one centre, but my recollection is that around 40, 41, 42, of my patients were antiHTLV-III positive.

Q. Who told them of their test results?
A. Well, that duty fell to me. I think I often tried to involve my nursing staff in the process to have more than one person perhaps in the room at the time. But to the best of my knowledge and belief, it was my responsibility and I told them all personally.

Q. Obviously that was a very traumatic episode for everybody involved?
A. Indeed so.

Q. I see. Was -- can you recall, were counselling facilities available at the time?
A. I -- I think that in those days, counselling really hadn't developed in my mind as a sort of event which was as clearly stated as it is now. My recollection of counselling was that, as the epidemic developed, we began to talk with our HIV

infection immunity doctors as they were appointed, and it wasn't very long before we had a social worker who was particularly interested in HTLV-III/HIV. So I can't tell you the exact date that this happened, but we arranged for the HTLV-III social worker from the infectious diseases unit to be part of my team for a while; we used to see patients together. And then when I explained what was happening, then he would often talk to the patients separately without my being present. What I can't recall very well is how long it was before we started telling patients, and when this sort of social work service developed. But it wasn't -- it certainly wasn't very long before -- it wasn't very long before we worked quite closely with the HIV specialists who provide a -- what I think really was -- you can almost call it a social rather than a counselling service, although I think it was really quite effective. The introduction of Zidovudine took place in March 1987, and certainly by the time we got AZT available, then we were using the infection and immunity service, at least at the social work level, quite a lot. And the social worker would come out of his unit and I would see the patients in medical Outpatients, and at that time I was running the HIV haemophilia service myself with his help. Later we moved into the HIV unit itself. But my recollection of all that, first of all, was the immense courage of my patients, who I felt managed the whole thing with immense courage and dignity. And then really I remember the very considerable help I had from my nursing staff and also from the HIV social worker who worked very closely with me and helped me to deal with the very many problems that we had. We also had a support group for healthcare workers. Dr. Colin Murray Parks was at that time a consultant psychiatrist at the London Hospital and he had a particular interest in bereavement and distress, and for a long time ran a support group for healthcare workers which included nurses, doctors and social workers working in the field of HIV. And certainly my team sort of bolted into that service, which I think we found very helpful to deal with our own difficulties as well as I think, perhaps, giving a better service to our patients.

Q. I think you've already indicated you may have difficulty in remembering this, but is it possible for you to say from the time that the -- what you believed to be confirmatory tests became available to you, the results of those tests, how long would be it have taken to tell the -- all the positive people and, indeed, the negative people of their test results?
A. Well, you're right; that I'm not sure I really remember the answer to that question. I would be surprised if we hadn't completed the transmission of the information on HTLV-III positivity by the end of '85. But there may be one or two patients actually who we didn't know were antiHIV-positive until the very early part of '86. I think we can be quite confident they must have seroconverted before that period, but it's quite difficult to get hold of patients under all circumstances, and certainly some of my patients have been unwilling to attend the hospital and some were attending more than one hospital at once. So I would hope that by the end of '85 or beginning of '86, that we dealt with the vast majority of the problem, but again, I think it's quite difficult to be absolutely certain of the last day that we'd stopped breaking that kind of bad news.

Q. I understand that. I suppose what I'm getting at is this, whether you can recall it: Was there a process -- you were talking -- I think you've told us that there was 42 positive people. Was there a process of, over a period of months, a month or two months, bringing those people in as a deliberate exercise for the purpose of telling them the news that had come to hand?

A. I think a "deliberate" policy would perhaps be an overstatement, and I think that the reality was that I got a pretty good idea who the people were at risk, and I think I tried to contact them. But I mean, even as late as, probably, 1990, I was still occasionally seeing a patient who I realised -- maybe even as late as 1995, I was still occasionally seeing a patient who would -- who had perhaps been to my centre and I'd lost touch with them and then they'd sort of come back and go away again, and I'd find that somebody would come back to me who hadn't been seen perhaps anywhere for some years and who I realised actually was at risk of HIV infection. So I don't think that there has -- it is yet the case that I can absolutely say that we couldn't, even now, find somebody who had disappeared off the map who could still conceivably be diagnosed. I had a patient some -- I suppose about five -- probably about five years ago who was a rarely treated patient who had been to my centre some years before and had disappeared off the map. And I can remember now sort of coming into my clinic and going through his story with him and thinking, this chap's at risk of HIV infection. Fortunately he wasn't infected. But oddly enough, the more mildly affected a patient, the greater the risk of their getting lost, because if you've got somebody who's quite severely affected, you're going to see them regularly and they're going to have a bleed from time to time anyway. So even if your process has failed you'll still probably pick this up fairly quickly. But if you've got somebody quite mild who's had treatment for a nasty bleed, I'm not sure that our record-keeping system was necessarily good enough to pick absolutely everybody out with absolute certainty.

Q. I think there's two separate things here, Doctor, if I deal with it this way: Are you suggesting or saying that the record system was such that it wouldn't have been the case that necessarily everybody who was at risk was tested, and that even to this day one couldn't say absolutely clearly?
A. I think that's fair comment.

Q. But then there's the separate question, which is that the people who were tested and the issue of them being told one way or the other about their test results, would there have been a system that the 42 people were written to or in some way communicated with and told to come in because they had to be told their results?
A. Yes. I mean, I think that it's important to understand how we did this work, because I think that ethically it's quite questionable. Because what actually happened was that we had a lot of stored samples in the hospital from people with haemophilia, because over a period of years I had kept samples, and the virology department doesn't throw stuff away. So my recollection is that what we did was to look at the serum samples of people with haemophilia and, therefore, we didn't, in the early days, do what we now regard as being ethically mandatory, which is to seek their consent. We tested these samples and we knew, therefore, from the tests that we did, who was positive. And so, in a sense, once we got the results on the samples we tested, we then called the patients in. Now, it was ideally much better to have identified who we believed to be at risk, contact them to ask their permission to perform an antiHTLV-III test, perform the test and then tell them the result. But you know, the reality is that, in 1985, that wasn't what we were doing.

Q. So in that sense, it would have been an even greater shock in that if they were called in, they mightn't even have known they were being -- had been tested?
A. Yes, that's entirely possible. And even likely.

Q. Yes. But I think, from what you've told me, you've indicated that it would have been the case that anybody who was positive or had been found to be positive, arrangements would have been made to call them in in some way to tell them the result?
A. Yes. I mean, that was the advantage of the stored sample testing without consent, was that one would pick up the people who were truly infected and be in a position to call them in. The disadvantage is that, according to modern standards of consent, it wasn't a perfect system.

Q. I can see the difficulty. But the one thing, so we're clear, the one thing that would come out of all that is that all the 42 who were found to be positive would have been told -- would have been brought in and told they were positive?
A. Yes, that's correct. But the actual sort of database of who was really at risk was really in my brain and, therefore, if I hadn't -- because I'm obviously in the centre for a long time, I know the patients well; I think in those days of the early '80s, information technology wasn't doing what it now does, which is to sort of create databases where you know exactly what's happening, you can recall the people with particular characteristics. Those days, really what I was doing is saying to myself, I know these patients I think reasonably well, and I picked up the patients fairly readily. But particularly for an occasionally-seen patient that I didn't recall, I might not have tested their serum and I might not have picked up that they were at risk until they came back to see me sometime later and I looked at their records and think 'help, this patient's at risk'.

Q. So that goes back to the issue of whether a test was done at all?
A. Yes.

Q. If I can just move on briefly to deal with another matter: When did tests for Hepatitis C become available?
A. Well, the test for Hepatitis C became available locally about the middle of 1990. I looked at my records to -- I looked at my own personal records yesterday, and I was beginning to test for antiHCV antibodies about the middle of 1990.

Q. I see. And when would it have been the case that all of your patients with haemophilia would have been tested for Hepatitis C?
A. Why, that's an extremely difficult question, and more difficult to answer than the -- than the HIV question. And I think the straight answer to that is that we probably haven't completed that process, necessarily. I mean, I have 80 odd patients who I have clearly recorded as being antiHCV-positive, but, in my view, it is entirely possible that somebody could attend in the near future and -- for me to appreciate that they had been at risk. This is still happening. I don't know when the last one was, probably about a year or two ago, but I last saw somebody who turned up at my clinic and I knew that they were at risk of antiHCV antibodies, and indeed they were positive. So in very small dribs and drabs, that's still happening.

Q. And would that simply be because they just hadn't attended or hadn't come to your attention in the intervening years?
A. Yes, that's correct.

Q. But in regard -- perhaps if I put the question a slightly different way, then: In regard to the generality of your patients with haemophilia, when would they have been tested?
A. Well, I think we would have probably managed to get most of the information by, probably, 1992, but that's a little bit of sort of speculation on my part. I didn't have a specific record that tells me when I got most of the patients tested. I'd need to go through all my records and find out when the last person in bulk was found to be antiHCV-positive.

Q. I'm just trying to get a general picture here?
A. It could easily have taken a couple of years to get them all together.

Q. I see. But you think 1992?
A. I would have thought something like that. But there were still odd people, I mean, occasional people, turning up and being diagnosed later than that, even up to the present day.

Q. Now, I think there's just two things left over from the evidence you've given: You've mentioned about your knowledge about the Armour product, and I think you've been able to relate it to a very specific event, although you haven't been able to recall the event. We know there was a meeting of the World Haemophilia Federation, from our records, in Milan, on June the 8th to June the 13th, 1986?
A. That, I think, clinches it. That's the date.

Q. Would that tie in with your recollection?
A. Absolutely, yes.

Q. This is the first time you became aware about the Armour -- a possible difficulty with the Armour product?
A. Yes.

Q. And what did you do?
A. Well, I phoned London and told them to get rid of any Armour product we had in the department.

Q. I see. But I think you've already told us that was a shock to you, and prior to that you had no knowledge of this, good, bad or indifferent?
A. Yes, that's correct.

Q. Excuse me for a second. Do you have any recollection, Doctor, of -- at the conference in Milan, as to whether there was a preliminary report in regard to the study about the effectiveness of the superheat-treated product in regard to eliminating infection by HCV?
A. Would that be related to the 8Y?

Q. Yes, I think it was?
A. Yes, I can't recall, but it would be easy enough to confirm.

Q. I think we have an article here which indicates that that -- a preliminary report was given at that conference?

A. It's what you'd expect.

Q. I see. And your knowledge, again, you would have had knowledge of that along the lines you've been telling us; that the 8Y product was effective in eliminating the HCV virus?
A. Well, yes, because I was a main contributor to the study. I had more patients in the study than I think anybody else did, so I must have known -- the report came from the UK Haemophilia Centre Directors but I was intimately involved in that study.

Q. But I suppose the point would be this: If the preliminary results of the study or the preliminary results were given at that conference, that knowledge would have been becoming somewhat more widely available?
A. Yes. I mean, not all the Haemophilia Centre Directors in the United Kingdom would go to Milan, but it would be surprising if most of the Haemophilia Centre Directors of the larger centres weren't present and, therefore, understanding what was happening.

Q. The only other thing I want to deal with is just the book of documents which I think you've just been given. I think the last indent is a very, very recent article by Rizza and others?
A. Mm-mm.

Q. And I think it may have appeared in a journal within the last week or two?
A. Correct.

Q. I think the only real significance is at page six, or the main significance is at page six. I think there's a series of graphs that show Factor VIII usage in the UK haemophilia centres between 1969 and 1996. And the -- that's the top, figure two; and figure three deals with Factor IX usage in the centres between 1969 and 1996. Is that correct?
A. Correct.

Q. And I think what we see there is, on figure two, is mapped out the various different products, including -- that's it there. I think what we see is the use of the various products such as cryo, NHS Factor VIII --
A. Yep.

Q. -- commercial Factor VIII. And the graph indicates the ebb and flow of the different products?
A. Correct.

Q. I see. And perhaps if we look at the one next down from that. What we see here, I think these have already been referred to by Dr. Snape, but we see this characteristic drop I think in -- could you just perhaps explain it there, in 1985?
A. What's happening is that a significant number of Haemophilia Centre Directors are deciding to abandon the use of NHS unheated Factor IX, and to use, instead, commercial heated Factor IX. So the dip you see is the reduced use of NHS Factor IX. And the little spike you see is the increased usage of commercial heated Factor IX.

Q. Which I think reflects a particular choice?
A. Exactly.

Q. Which I think was slightly different or different to the choice you yourself perhaps made?
A. That's true. I did use a very small amount of commercial heated Factor IX at the very end of 1985, but it was a very small amount. So that I was more in the category of those who used NHS unheated Factor IX. That's quite right.

Q. Your contribution to the blip, if I put it that way --
A. Was very small.

Q. Very small indeed?
A. I think the other point that perhaps does come out of the studies that I presented to you was the sentence or two on page nine. If we can -- if I may refer to that, Madam Chairperson --

THE CHAIRPERSON: Certainly, yes.
A. -- where it says on the top of the second paragraph: "This obviously created a dilemma for clinicians and patients at the beginning of 1985 who were forced to choose between imported heat-treated and American concentrates and the equivalent British products that had not been heat-treated. While it's accepted that some people with haemophilia could have been exposed to HIV through the use of British product in preference to heat-treated products during this critical period, it must be remembered that HIV seroconversions with a heat-treated commercial Factor VIII were reported in 1986, leading to withdrawal of this product in the UK."And I think that sentence very succinctly summarises some of the things that I have been explaining to the Tribunal. I think it applies also to Factor IX as well as to Factor VIII.

Q. And you would agree with the sentiments there as to that dilemma?
A. I think it's a very fair statement, in my view.

MR. DURCAN: I have no further questions. Thank you.

THE CHAIRPERSON: Thank you, Mr. Durcan. Mr. McCullough, please.

MR. McCULLOUGH: Thank you, Madam Chairperson. Madam Chairperson, in relation to this last article, I would like to reserve my position on that. I have just been handed it in the last few minutes, so if anything arises on it I may wish to --

THE CHAIRPERSON: Would you like me to give you a few minutes to read it?

MR. McCULLOUGH: I would, Madam Chairperson.

MR. DURCAN: Perhaps, Madam Chairperson, I'll make this suggestion: I don't know whether My Friend is likely to go over the lunch break. If he was, the sensible thing, I would suggest, is that he might start his cross-examination, have a look at the article over lunch and he could then deal with the article, as he thinks appropriate, after lunch.

MR. McCULLOUGH: That suits me, Madam Chairperson.

THE CHAIRPERSON: Very well.

MR. McCULLOUGH: Thank you.
A. Perhaps I should apologise, Madam Chairperson, for bringing this article up at this late stage, but it really was published last week and it seemed to me the work done by UK CDO was particularly well-summarised by this article.

THE CHAIRPERSON: Thank you. Mr. McCullough, please.

THE WITNESS WAS EXAMINED BY MR. McCULLOUGH AS FOLLOWS:

Q. Dr. Colvin, my name is Jim McCullough and I represent the Irish Haemophilia Society.
A. Good morning.

Q. And just on a brief look at your article, it seems to be very interesting, on the article on haemophilia, and I'm going to read it over lunch. But just with regard to your statement and your evidence this morning, you said that in -- if I understood you correctly, in 1983 your -- 1983 onward, your policy in regard to treating children under your care with cryoprecipitate is directed towards preventing the development of non-A non-B Hepatitis. Was that in respect of the dangers you perceived from non-A non-B Hepatitis, and what were those dangers at that time?
A. I think it's quite difficult to remember exactly what I had in mind. I think it's fair to say that I'm a relatively conservative physician and I was aware that patients who had been treated with cryoprecipitate remained healthy; and when we looked at their liver function tests, most of them had normal liver function. I was fully aware that Hepatitis non-A non-B could be transmitted by the large pooled concentrates. That had been very obvious. And it's also the case, of course, that the cryoprecipitate was a very cost-effective way of treating haemophilia, which is another way of saying it was cheap. So I suspect that some of my colleagues thought that I was being too conservative, particularly in other hospitals; and I think that I perceived that, yet, it might be safer for patients to have the cryoprecipitate. But I think it rather -- it tends to illustrate a rather innate conservatism in my nature. My experience over the last 20 years is that the conservatism that perhaps I -- that perhaps I chose, had advantages and disadvantages. And some of my colleagues who perhaps were more modern in their thinking or more ready to embrace the latest advance, gained and lost as a result. So I think that what we were trying to achieve was very often based on really the sort of nature of Haemophilia Centre Directors. I think it's difficult to say this, but, as in many forms of treatment for patients, sometimes the outcome for patients are based not just purely on science and evidence, because the amount of science and evidence in medicine is often relatively limited, but can be based on the way people feel about the world. So I think I was a rather conservative physician.

Q. Was that conservatism promoted or -- were you conservative because you had fears that non-A non-B Hepatitis would have serious consequences or did you consider it to be a relatively minor condition at that time?

A. Well, I think, if you'll forgive me for saying so, both, in a way; I did perceive that it wasn't a huge problem, and I also perceived that it might be.

Q. So you erred on the side of caution, as it were, in your treatment?
A. Well, maybe. But then, as I've explained, the caution that I displayed, it might have had bad consequences for patients. For instance, you might be able to demonstrate - I don't think you could - but you might be able to demonstrate that my children with haemophilia had more joint disease, perhaps, than some of the children who were treated with large pooled concentrates at that period, if they were treated with greater enthusiasm in terms of dosage and frequency of dosage. And I've already acknowledged that for many of the patients I was trying to treat with cryoprecipitate, I actually failed and felt I had to get on to use a large pooled concentrate. So it's important that the Tribunal doesn't think that I'm in any way pleased with myself, because I'm certainly not. I mean, I think that the way I behaved at that time, I hope was honest to myself and to my patients, but I think that there were advantages and disadvantages to the way I saw my practice.

Q. During that time, from 1983 going on into the 1980s, was there a growing development and awareness of the risks posed to patients by contracting non-A non-B Hepatitis?
A. Well, I think that's evident. And for instance, in the brown -- sorry, in the black folder that I was presented with earlier, there's the paper from Dr. Hay, who was then in Sheffield but now in Manchester, in which he illustrated the potential importance of liver disease in haemophilia. On the other hand, there are other papers in that bundle and there are other publications not in the bundle which illustrated the great difficulty people had in assessing the severity of non-A non-B Hepatitis. Even now, as I've explained to you, the number of my patients who are HCV-positive, HIV-negative, and don't drink alcohol who have been in trouble at a physical level, is very small. Now, we're now looking at 20 to 30 years' experience, but, of course, it's possible that in five to ten years' time, many of those patients may become ill, I don't know. But the overall natural history of this condition is quite clearly up to 30, 40 or even conceivably 50 years before the liver fails or before there's a problem. So I think it's still quite difficult to judge how important, at a physical level, the epidemic of HCV is for HIV-negative teetotal patients.

Q. Just in your statement you mention that when modern viral inactivation techniques were introduced, that new infection with HCV ceased. And that would have -- I take it from that that "modern viral inactivation techniques" refers to the 8Y and 9A BPL superheat-treated product?
A. Which page are we at?

Q. I beg your pardon, Dr. Colvin, page four. And if you look at the third paragraph on that page.
A. So that's the -- is that the page, beginning of six, AIDS, or -- I think your pagination may be different from mine.

Q. It begins -- begins "the introduction of freeze-dried concentrates."
A. Sorry. I think that may be my -- sorry, that's my page three. I've already realised there was a slight discrepancy which can be sorted out later, but I got to the page now.

Q. It's the paragraph then which starts, "by 1985 it was known that all patients treated with large pool --"
A. Yes. So can you just repeat the question to me again?

Q. Yes. With respect to modern viral inactivation techniques, does that refer to the 80 by 72?
A. Yes. I think that -- what I mean by "modern viral inactivation techniques" is that the initial treatment with heat at 60 degrees Celcius clearly didn't altogether inactivate Hepatitis C. It was only when 80 degrees Celcius for 72 hours was introduced - and of course the use of solvent/detergent, which was a separate but also effective viral inactivation process, was introduced - that the HCV was controlled. So I think the reason I mentioned -- I used the word "modern" was to distinguish it from those viral inactivation processes, the early ones with heat treatment that weren't effective.

Q. Yes. And that was introduced in 1985, would that be correct?
A. Yes.

Q. And from that date onward, in your centre and those who were using that product, was there any further Hepatitis C, non-A non-B infection?
A. I'm not aware of any infection in my centre after -- I don't think I'm aware of any after '85, or certainly '86.

Q. So the situation you're facing even now would be entirely different from a situation where that if HCV infection was not prevented in 1985, and if patients continued to seroconvert for Hepatitis C, into 1990, for instance, you would be expecting -- the number of patients coming to you with Hepatitis C now would be greater?
A. I'm sorry. I -- I got lost in that sentence.

Q. If you had -- if you did not have a viral inactivation technique for Hepatitis C until 1990, would the patients that you're seeing now, would you have -- would you expect to see more Hepatitis C than you are seeing in your own patients?
A. My understanding is that the vast majority of patients who develop illness from HCV, is the illness, that comes in the long-term, after perhaps 20 or 30 years infected. Clearly there are those patients who get an acute illness when they fall ill with the active initial Hepatitis C infection, then there's usually a long period of relative health. I know very well that many patients with Hepatitis C infection who are apparently physically well feel unwell and feel tired. I'm aware of that. But then it's usually 20 or 30 years before anything else happens. And so in a sense we're still in that window. If patients had gone on not being infected until 1990, then I don't think we'd see patients getting ill now. We'd be looking at people getting ill in 20, 30, years if it was...

Q. But there would still be a cohort of patients presenting with Hepatitis C rather than the actual illness that followed?
A. If we hadn't had -- if we hadn't had viral inactivation processes from 1985 to 1990, I guess all those who were treated with concentrates between '85 and '90 would have seroconverted to antiHCV and would then be at risk of long-term disease.

Q. So the situation that you're facing in your own centre would be somewhat different to a situation that would prevail here?
A. I -- I don't --

THE CHAIRPERSON: Well, Mr. McCullough, Dr. Colvin is giving evidence about his own experience in England, I think that is his function here today; whereas I've heard evidence in relation to the Irish situation. And then it's up to me to draw the conclusions from both series of evidence.

MR. McCULLOUGH: Thank you, Madam Chairperson.

Q. MR. McCULLOUGH: Just with respect then, Doctor, to the viral inactivation properties of the superheat-treated product, there was no further HCV or HIV seroconversion on that product, is that correct?
A. That's to the best of my knowledge. And in fact, in the bundle of papers I was presented with this morning, there's a letter that I wrote some years ago, I think in the late '80s, confirming that when we looked at the patients who had been treated as part of the study, the antiHCV tests were negative. Because when we were doing the initial work with the superheat-treated products in 1988, there still wasn't a virus for non-A non-B Hepatitis. So we then retested those patients and confirmed - with one exception which was explained in the letter that they didn't -- they hadn't seroconverted.

Q. But even with that and with the knowledge that there was no further -- didn't appear to be further seroconversions to Hepatitis C, was it still your practice to have a regime in place to protect previously untreated patients?
A. Well, the previously untreated patients were treated really from April '85 with a superheated product. I think this was a bit of an act of faith. I mean, we'd been giving the youngest patients cryoprecipitate until '85, April, and then I had to make a decision whether to continue with that practice or whether to go over to the superheat-treated material. And I think by that time the correct advice from the UK CDO was that whatever the benefits of cryoprecipitate had been up to the period to April '85, it was now a greater risk to go on giving cryoprecipitate because of the risk of contamination of individual donor units, than to use a concentrate. So I had to take a very clear decision in April '85, which fortunately was the right one: To change from cryoprecipitate to the superheated concentrate. As I've indicated, I didn't know that the 8Y would be the right concentrate to use. So, as I think I indicated to counsel, I did do some studies in adults using heat-treated Profilate for those who had never been treated before. And so I didn't know until perhaps '86 to maybe '87 that I really could rely on the 8Y. And it was only when I knew I could rely on the 8Y that it seemed sensible to use 8Y for previously untreated patients. Now, some of my colleagues in the United Kingdom would have still taken the view that I was being a dinosaur, because by that time Monoclate P and the high -- monoclate -- or perhaps monoclate, the high purity concentrates were becoming available. And many of my colleagues were saying, we should move on to those high purity products. Now, as it turned out, they are excellent products and they didn't transmit any virus infection. But I think there are those who would say that it would have been 'better,' in inverted commas, to use a high purity product to treat new patients from '85 onwards. But my own approach was to use 8Y from the middle of '85 until we changed over to recombinant two or three years ago.

Q. But there was still in your view a necessity to have such a regime in place for previously untreated patients?
A. I don't know that I thought there was a necessity to have a specific regime in place for previously untreated patients. What we were very aware of was that previously untreated patients obviously must be given the best available treatment; that goes without saying. That's the whole basis of modern clinical ethics. But that if we didn't know what was the best treatment, then the previously untreated patients were very suitable for inclusion in scientific studies to establish what was the best treatment. And that, of course, also was an important part of medical progress; that where you don't know the difference between one treatment and another, and you believe that both are potentially the best treatment, then it's permissible, with research ethics' approval, to study such a patient. And indeed to one extent one has such a duty to examine such a patient, if appropriate clinical trial is available. And the patients under my care were very willing to enter into such trials with informed consent. And although the number of previously untreated patient trials have now tended to dry up, it is still the case that people with haemophilia who have never been treated before are an important -- when I say research, I don't mean resource. I don't mean that to sound impersonal, but, I mean, people in these circumstances are able to make a contribution to medical science whilst receiving the best possible treatment.

Q. Yes. Just in regard to that, Dr. Colvin, if you will look at reference six that you have given to the Tribunal. It's an article from The Lancet of the 8th of October, 1988?
A. Yes.

Q. And it's the study group of the centre directors --
A. Yes.

Q. -- on the surveillance of virus transmission by concentrate. And that sets out I think the effectiveness of 8Y and 9A?
A. Yes.

Q. As regards NANB?
A. Yes.

Q. It's just the last sentence of that on the internal page 816 states that "physicians should continue to prescribe as if all blood products still carry a diminishing but finite risk of transmitting blood-borne viruses, particularly the agents for NANBH." And it's just with regard to that observation in the study: Did you still think it was necessary at that point, even though you had the 8Y and 9A and you appeared to be escaping non-A non-B Hepatitis, did you still think it was necessary to have in place and to observe a protocol for previously untreated patients?
A. Well, I don't think we had a protocol for previously untreated patients as such. I think, as I've indicated to you, we were certainly very keen to enter patients into studies of what might be the most appropriate treatment, but I think in the period between 1985 and 1988 when the study was published, we didn't know what the best treatment for such a previously untreated patient was. And that's why we could enter them into the study. If we'd known the correct treatment, we could have had a protocol for it.

Q. Your study seems to reveal this particular treatment was effective and was working?
A. That's perfectly true. We didn't know the result of the study before we designed and published it.

Q. Of course. And but when you did know it and you did publish it, you were still saying prescribe with respect to non-A non-B H.
A. My personal view was that because of the 8Y study, it was appropriate to give previously untreated patients 8Y. Some of my colleagues I think felt that the 8Y treatment was a little bit old-fashioned by the sort of early -- by the early '90s, but my view was that here was a tried-and-trusted product that actually worked and was safe. And I had occasionally sort of drawn the parallel that -- I was down at the Haemophilia Society last week and drew the parallel between -- of Volkswagen and a Ferrari. The 8Y, if you like, was a sort of Volkswagen and would get you from A to B safely and sensibly and at a reasonable cost. It might be that the monoclate, high purity products that were state-of-the-art and were monoclonally purified, were if you like a sort of Ferrari, but they wouldn't necessarily get you where you wanted to be any faster. Now, I know that that analogy is perhaps a flawed one and could well be criticised, but the point I think I'm trying to make was that if you've got something that you had clinical scientific evidence works, is safe and is effective, then, you know, maybe you need to have a pretty good reason to change your policy.

Q. Yes. Thank you.

THE TRIBUNAL THEN ADJOURNED FOR LUNCH.

THE TRIBUNAL RESUMED AFTER LUNCH AS FOLLOWS:

CONTINUATION OF EXAMINATION OF DR. PETER COLVIN BY MR. McCULLOUGH, AS FOLLOWS:

THE CHAIRPERSON: Good afternoon, Doctor.Mr. McCullough, please.

Q. MR. McCULLOUGH: Good afternoon, Doctor.
A. Good afternoon.

Q. If I could refer you to I think it's page -- my page five, I think it could be your page six of your statement, please.
A. Yes.

Q. And just in the last paragraph of that, Dr. Colvin, you say: "For Haemophilia B, heated British source concentrates were not available until the autumn of 1985." And that, "It was known that by the beginning of 1985, that comparatively few patients with Haemophilia B were infected with HTLV-III." Just in regard to that, you mentioned to Mr. Durcan this morning that you had a Factor IX patient who was unfortunately positive for antiHTLV-III at the end of 1985, having been negative at the end of 1984?
A. Mm-mm.

Q. Had there been other Factor IX infection in the UK at that time, when that -- when that person was reported positive?
A. I think -- we don't know, Madam Chairperson, the exact date of seroconversion of this patient. As you may be aware, the number of seroconversions in the United Kingdom for patients with Factor IX was relatively small, compared to those with Factor VIII deficiency. So I can't pinpoint the date of seroconversion of my patient. And the point that I wanted to make was that there were seroconversions in the United Kingdom community; that those seroconversions were comparatively uncommon events; and that, by and large, we didn't know exactly when they had taken place. But I think the implication must be that the seroconversions that did take place were as a result of NHS Factor IX concentrate.

Q. And can you remember yourself when you would have had the first Haemophilia B person reported positive for antiHTLV-III?
A. I can't remember -- give you the exact month; but my memory is that by the time that seroconversion had taken place, we had, by then, already gone on to the use of NHS heat-treated product. But to the best of my recollection, I did use a small amount, as I explained this morning, of commercial heated Factor IX at one point. And it's possible that what that means is that I became aware of the seroconversion before the NHS Factor IX heat-treated material became widely available. I can't -- I can't be sure of that, but my recollection is that I did, in that particular case, use some heated commercial Factor IX concentrates. And the implication of that is that I realised that we had to use the heated material. And if I hadn't got heated material from the United Kingdom, then I was going to have to use commercial material. So I suspect that my policy was originally, as I explained to the Tribunal, to use NHS Factor IX unheated. Then I think I must have become aware that my patient had seroconverted. Then I think I used a small amount of commercial heat-treated material before moving on as fast as I could to the heat-treated National Health Service material. That is my recollection.

Q. And when that happened and you did have a patient who was -- Haemophilia B patient who was antiHTLV-III positive, did you conduct any sort of inquiry or investigation into the treatment he had been using?
A. Not to the best of my knowledge.

Q. Would you have informed any of your colleagues or centre directors that that that had happened?
A. I don't recall having done so.

Q. Would you have received information from any of your colleagues in 1985 about that -- about a similar-type situation?
A. I have inspected my memory on this topic and it's quite difficult to be sure of the events. But I don't recall a clear system in the United Kingdom for the notification of individual cases of HIV seroconversion at the centre of the United Kingdom Haemophilia Centre Directors Organisation, and I have asked myself what the reason for that might be. One possibility is that I simply don't remember something that actually did happen, so it's possible that there was some system which I don't recall; and that is a little bit unlikely. I think what's more likely is that there was a perception by the time -- by the time we began to understand exactly what was happening with HTLV-III infection; when you consider that it was only in November 1984 that we

were actually testing people, that really by the time that we had got a handle on who was positive and who was negative and why, we'd already, for VIII-deficiency , changed over to heat-treated concentrate, because it was only three or four months - perhaps four or five months later that we changed over to heat-treated concentrate entirely for Factor VIII deficient patients. And certainly it's my recollection that by the autumn of '85, as I have stated, we were on to, for Haemophilia B, Factor IX heated concentrates. And therefore, the timescale is really quite short. So my recollection is that we did not have a clear system of notification. The other reason why perhaps we didn't have such a clear system of notification is that the majority of severely affected patients with Haemophilia A and B were treated with more than one batch of Factor VIII or Factor IX, and therefore, it was usually impossible to identify exactly which batch had caused the problem. It's also important to remember that the fact that a batch had not caused HIV infection in any particular patient didn't mean that it wasn't potentially infectious for HIV. And I can draw your attention to a paper published from Edinburgh by Dr. Ludlum in August of 1985, in which he describes a cohort of patients with both Factor VIII and Factor IX deficiency who were exposed to a batch of Factor VIII and Factor IX concentrate derived from what is presumed to be a single infected HIV donor. And the consequence was that not every patient with Haemophilia A became infected when given that particular batch, and none of those given the Factor IX concentrate from that particular batch became infected with HTLV-III. And I'd already mentioned earlier this morning that there was a perception that the risk for infection with Hep -- with HTLV-III with Factor IX concentrate was perceived to be lower than that for Factor VIII concentrate. So I think that the answer -- the answer to your question was that we didn't have, to the best of my memory, a system for specifically identifying individual batches that we thought to be infected. In retrospect, as I indicated this morning, there were patients of mine who I now know were infected by a particular batch, but by the time we knew that information, it was too late to do anything about it.

Q. Do you remember, Dr. Colvin, earlier in that summer of 1985, Dr. Craske publishing information about Factor IX patients seroconverting, and recommending that heat-treated products should be used?
A. I don't recall the exact incident. I would be happy to review the paper. But I think -- though I have already indicated this morning that people like myself had to make a judgement about what was the safest product to use. And rightly or wrongly, some of us made the judgement that we suspected that commercial Factor IX concentrate that had been heat-treated might still infect with HTLV-III. But I'd be happy to look at such a paper if it was given to me, and it wouldn't surprise me if that was the case.

Q. Just moving on from that, Dr. Colvin. You say that there was fears about Factor IX in that summer, various reasons why people wouldn't use heat-treated Factor IX, one of them being thrombogenicity and the difficulties that might arise from that condition. But just looking at the paper that you gave the Tribunal this morning at reference number 15 -- that's paper from Haemophilia --
A. Yes.

Q. -- 2001. And the diagram that was opened to you by Mr. Durcan at page six of the paper. That is figure 3. The consumption of Factor IX in the UK, 1969 to 1996.

Just, if I'm correct in my interpretation of this, it seems to indicate that commercial heat-treated Factor IX was available in the UK --
A. Yes.

Q. -- at that time. And indeed, it was used, and there is a rise in the use of that product between -- is it the end of 1984 and the start of 1986?
A. That's correct.

Q. And corresponding decline in the National Health Service Factor IX?
A. That's quite right.

Q. Would that seem to indicate that that concern about thrombogenicity was, therefore, not a universal concern; some of your colleagues obviously used the heat-treated commercial -- commercial heat-treated Factor IX?
A. Yes. And I made that point this morning, and I entirely agree with the point that you make. It would perhaps be useful to explain the level of anxiety about the thrombogenicity, because I think it's fair -- it's fair to say that the main concern about thrombogenicity is in patients having orthopaedic procedures. And I think all the patients that I have looked after who have had venous thrombogenicity or pulmonary embolism following the use of Factor IX concentrate have had this following orthopaedic procedures or major surgical procedures. And that means that, for everyday use, there was nothing wrong with the standard Factor IX product, whether heat-treated or unheated, from the point of view of clinical efficacy and coagulation safety. And for the unheated product, the concern was that it might be thrombogenic for orthopaedic surgery or major surgery. What was unknown, and this was I think an entirely unquantified risk, was if you heated the product, would it become more thrombogenic? Because there is no doubt, as I have explained, that the unheated product - although perhaps dangerous in orthopaedic surgery - wasn't dangerous in everyday life, from a thrombogenic point of view. But there was a fear that, since it was known to be thrombogenic in large volumes during orthopaedic surgery, if you heated it, that might make it more thrombogenic. And of course, the consequences of thromboses of a severe degree, had they been realised, would potentially have been coronary thrombosis or cerebral thrombosis or conditions that could have led to severe disability or death. Actually, I don't think we have ever demonstrated that that was - looking back - a serious risk, but at the time there was some concern that a heated concentrate might be more thrombogenic, to the point of danger. But that was speculative and wasn't based on anything other than the knowledge about dangers of unheated concentrate at the time of orthopaedic surgery.

Q. It was a potential problem but it wasn't something that impinged upon everybody's consciousness to the same extent?
A. I think all of us in the field at that time were doing calculations on relative risk based on extremely inadequate information. So it was anybody's guess, if one could use such a crude word, as to what the correct thing to do was. I mean, I don't have any doubt in my own mind now, looking back 15 years later, that the -- a better strategy would have been to have used a commercial Factor IX concentrate from the beginning of 1985, except that I still feel that it's possible, and indeed maybe even likely, that some patients would have seroconverted as a result of being given heat-treated Factor IX concentrates, had they been sufficiently contaminated with HTLV-III. Because at the beginning of '85, as we know from the Armour experience, the

heat treatment might not have been effective in dealing with the very large amount of contaminating virus present. And of course, the result of that might have been that the different patients would have become infected. So that it might be that one person might not have not have become infected, but another person might have been. So I think that although in retrospect I probably regret that we didn't use the heated Factor IX concentrate earlier, I still maintain that the -- that the decision that we took was based on, or is -- decision I took was based on reasonable data at the time. And really there is no proof, even now, that to have used commercial heat-treated concentrate from the early part of '85 onwards would necessarily have saved any particular person's life.

Q. But just to be clear: Both heat-treated and nonheat-treated Factor IX concentrate, commercial heat-treated and unheat-treated BPL concentrate, were in circulation at the same time?
A. That's perfectly correct.

Q. Dr. Colvin, could I ask you to turn -- to turn -- my page seven, probably your page eight of your statement, please. And you say there on the third paragraph: "It is important to appreciate that between October 1984 and the middle of 1985, haemophilia treaters were faced with a difficult dilemma: If they used locally-produced unheated concentrates, then there was a risk that any contamination with HTLV-III would result in new infection. On the other hand if they used heavily-contaminated American concentrates, which had been heat-treated, there was a risk that the viral inactivation might not have been successful and previously uninfected patients might become infected." Just in relation to the evidence that you gave this morning, do I understand correctly that, in fact, what was -- what was used in the UK was a combination of US-imported, heat-treated concentrates and locally-produced, unheat-treated BPL --
A. Correct.

Q. -- Factor VIII?
A. That's true.

Q. And the -- so that -- so I'm just wondering where the dilemma arises, in that since both were used at the same time? I think from what you were saying this morning, the -- this policy or this mechanism that you put in place was designed to eliminate the use of unheat-treated imported concentrates. I am just wondering where the dilemma arises?
A. The dilemma arises in that there were those in the UK who took the view - and I think it's a perfectly understandable view - that we should immediately stop using any form of unheated concentrate, and that the NHS unheated Factor VIII and Factor IX should be withdrawn forthwith. And for those -- for those who took that view, there were sufficient world supplies of heated, large pool commercial Factor VIII and Factor IX concentrates to allow that switch-over to take place, to the best of my knowledge.

Q. But this wasn't, if I understand you correctly, this wasn't a dilemma which you yourself entertained because you were using both?
A. No -- on the contrary. It was very much a dilemma for me because I can remember sitting in my office in December 1984 talking to Peter Kernoff on the

telephone - because I always tried to discuss with my colleagues where we were going, and, by and large, tried to remain in the same sort of general policy position as my colleagues in the Royal Free Hospital that was close by. I remember saying to Peter, what do we do next? And what was done at the Royal Free I think - obviously Professor Lee could explain this better than I could - was similar to what I did, which was to continue to use NHS Factor VIII unheated concentrate. Now, you could argue that such a policy was just sort of using up what was available and not wanting to spend the money. That is certainly a point of view that you could adopt. But it's not, in my view, what we were actually talking about. What we were talking about was our anxiety about what happened if the heated American concentrate was so heavily contaminated that the heat treatment didn't work and that we then transmitted HTLV-III to all those patients who had previously been on NHS unheated concentrate who, to the best of our knowledge, had not yet been exposed to the virus. So that we -- if the scenario that I have just indicated had been the case, then of course a large number of new seroconversions would have taken place. Now, the material we had available to us in the NHS, which was the unheat-treated material, was not sufficient to meet our needs. And therefore, we had to source the rest of our needs from somewhere else. And we understood very clearly that when we were sourcing our needs from elsewhere, we had to use heat-treated American products. Because it was quite clear to us that the heat treatment had some influence on or was likely to have some influence on the level of viral contamination; or therefore, it would be sensible, if we had to use commercial material, to use heat-treated commercial material and not unheated commercial material. The difficulty was that heated NHS material was not available to us. So that I think that whether -- whether people were using exclusively heat-treated commercial products or whether they were using a mixture of NHS unheated and commercial heated products, they were still facing the same dilemma.

Q. But I just want to be clear: You used both - both the unheat-treated BPL product, Factor VIII; and imported American concentrates - when there was a shortfall of the BPL product, is that correct?
A. Yes, that's correct.

Q. So both were being used?
A. Yes. The -- there was a limited supply of unheated NHS product. There was a greater demand for Factor VIII than could be supplied by the NHS unheated product. There was no NHS heated product available, therefore, if we were going to stop the bleeding, we had to use a commercial product. And that commercial product was heat-treated. But, the dilemma was: I could, if I had chosen to, as of, shall we say, December '84, given up using all NHS unheated product. And I could have sourced all my -- all my treatment from commercial heat-treated material. And it was my perception that if I did that, then if the commercial heat-treated material was capable of transmitting HTLV-III, I would then give HTLV-III infection probably to all those who I had so far kept free of HTLV-III infection by giving NHS material, which had been our preferred option.

Q. Thank you for that, Dr. Colvin. Just with regard to -- just excuse me for one moment. Yes. This situation that you found yourself in where you had this dilemma and the various choices that you had to make at the time, would you have informed your patients of these questions that were arising; would they have been kept abreast of these developments?

A. I think the fair answer to that question is no. And I think the reason for that answer is that the situation was moving extremely rapidly; that I as a physician didn't know what to do, and had very inadequate information. And it was my perception, rightly or wrongly, that the patients wouldn't know either. Now, I think that one could enter into a debate - I'm willing to do so - on the issue of what we tell our patients and why. But it's a very big -- very big question that covers the whole of modern medicine. I think there is no doubt over the 30 years of my practice, there has been a growing awareness of the importance of discussing with patients what the plans are. And that growing awareness has led to an improvement in patient care. And I think we were going through such a process in the '80s, and I have already indicated that we really didn't, for instance, get patient consent to the analysis of the antiHTLV-III samples. So, I think that, looking back to '85, it actually wasn't the case that we were involving our patients closely in the decision about what to do next. And maybe we were at fault in that. But now that we have a much more patient-orientated approach and we consult with our patients widely, regularly and deeply about what is best for them, it doesn't always lead to happiness and clarity and easy decisions for either us or our patients. And very often these days I go through with my patients all the options that they might choose. And they say to me, "what do you think, Dr. Colvin?" And I'm afraid it is the case that doctors quite often have very, very considerable power; because rightly or wrongly, the patients, not infrequently, trust them to do the best they can and will often wish to give to the doctors the responsibility and the -- and if you like, the power to do their best, as they see it at the time.

Q. But would you agree that it's probably a better system that they have patients informed of a situation that confronts them?
A. Well, I am absolutely committed to securing and validating information for my patients. As I have indicated to you, I'm not sure it always lead to happiness for everybody, but of course I am absolutely committed to openness with my patients. But I'm not sure that, in 1985, that best medical practice was exactly what it is in 2001.

Q. Thank you, Doctor.You mention there, just in respect of counselling and testing, that your patients weren't informed prior to tests being drawn, is that correct?
A. Mm-mm.

Q. Was -- was any representative of the patients informed, like local haemophilia society, or was there any -- was there anybody told that this was happening?
A. I don't think there was. And I think, in retrospect, that is regrettable. But one has to look back and see how the ethics of HIV testing developed quite quickly over a period of time. And we certainly were aware by the -- by a few years later, that there was a need always to ask permission before doing HIV testing, but that need was one based on, I'm sure, patient requirements and perhaps a better perception of the importance of the test. If you look at it from a theoretical point of view, as opposed to an ethical or pragmatic point of view, I think that the -- there are very few circumstances, even now, where doctors consult patients very deeply about every single investigation that they do. And by and large, they have tacit consent to the usual run-of-the-mill investigations. And that means that although there is clarity for the fact, you should now ask your patient if you are going to do an antiHIV test, and not do it unless they consent; and if you are going to do a hemoglobin, you can probably do it without consent because everybody -- there is tacit consent. As you go

through, there is no point at which you can really draw a line and say 'thou shalt not do something.' there is a quite a sort of spectrum. It's a rather sort of grey area as to what does and doesn't constitute something that a doctor has got permission for. I think the issue of consent is quite a complex one, even now.

Q. Yes. When you did draw those tests and got the tests -- and got the confirmatory results that you needed, were the patients whose results you had just obtained, were they promptly informed of those results?
A. I certainly hope so. I mean, maybe it's worth saying - and I know this isn't evidence perhaps, but maybe it's worth saying - is that for all the distress that my patients have suffered and for all the difficulties we have had over the last 20 years, I don't believe that I have ever had one of my patients saying to me, 'you shouldn't have tested my blood. You didn't tell me fast enough. And you didn't give me any support.' they have -- I don't believe said that to me. Now, maybe they said that to somebody else, but I don't believe that's ever been said to me.

Q. Could that be, Doctor, because you did give them support?
A. Well -- I hope so. But, I mean, again, I'm not trying to say that we did it better than anybody else because I don't think we did. But it certainly is my perception that if you are willing to talk to your patients even -- if maybe you have made what later proved to be errors in either their information or their management or their -- or their treatment, patients will listen to you and will, if you like, be sympathetic if they feel you are doing your best.

Q. Just so -- would it be correct to say, then, to say there was a reasonable sense of urgency attended to that particular task of telling people the results?
A. Yes. That's a word I feel very comfortable with; "a reasonable sense of urgency" I think is a very appropriate way of describing what we went through.

Q. How did you actually do that?
A. Well, my recollection is that I asked the patient to come and see me, sat them down in my office with my nursing staff and tried to explain to them what I knew about HTLV-III; what I thought it meant and what we were going to do next. Certainly in the early part of this period, say in 1985, there was a tremendous lack of understanding as to what an antiHTLV-III test meant. To begin with, of course, we had no information at all. We didn't know who was at risk. We knew who was at risk, but we didn't know who was positive and negative. And we knew that people with AIDS were dying from 1982 onwards, and people with haemophilia were affected shortly afterwards, but it really wasn't at all clear what the outcome of HIV infection was going to be, for the majority of patients. It was thought that maybe only a few patients would actually get ill. Then it was thought really that everybody who was infected would die quite quickly. And then of course even that was proved wrong, because here we are in 2001, and of my 40 patients, 15 remain alive and, generally speaking, pretty well in a way that I wouldn't have dreamed possible ten years ago. So I think that the natural history of this condition has been played out in front of the patients and in front of the doctors. And I'm not sure that all that often the doctors are very much ahead of the patients in knowing what was going to happen next. This uncertainty was a source of enormous anxiety for the patients. There were occasions, and I have had this experience myself, when patients who were anxious actually felt better when they'd had their first attack of pneumocystis pneumonia.

And the reason for this was they knew they were going to die. And when they were actually suffering from the anxiety of knowing they were antiHIV positive but not knowing if or when they were going to get ill, that created huge anxiety; and then the actual business of being ill sometimes - and I am not saying, always but sometimes - created a sort of feeling of resolution where patients knew what the deal was. And that, in a strange way, sometimes made them feel more comfortable.

Q. Yes. Just with respect to Hepatitis C, when that -- when you were able to test for Hepatitis C, was that reasonable sense of urgency repeated in informing people who had been tested of their condition?
A. Well, I think that that -- it's a question of what you mean by "reasonable"; in the sense that the level of urgency I think was a lower level of urgency, and I think appropriately lower; and, hopefully, was reasonable but with a lesser sense of urgency.

Q. But they were told with -- in a reasonably prompt way?
A. As I have indicated this morning, that we tried to give them reasonably prompt information, but the uncertainties with Hepatitis C were perhaps even greater than those with HTLV-III, HIV; because we still don't know, generally speaking, what's going to happen to people with Hepatitis C infection, even though we are 20 years, often, into the epidemic. So that it's quite difficult to counsel a patient when you say, 'I have got a blood test that shows you have had a virus infection. We know it doesn't make you feel ill to begin with, and perhaps one in five people, after 20 years, might get ill, but we don't know which one in five. And it could give you liver cancer, but we don't actually know how likely that is, or when, if at all, it's going to happen. So that the level of uncertainty, if anything, was greater with HCV than it was with HIV; although the level of urgency and sense of disaster was rather less. Because I think it was understood for all: HCV being a very serious condition, it wasn't as immediately life-threatening as HIV. Again, I think it's reasonable to say with reasonable urgency. There is no doubt that the level of urgency was less, and the process took a lot longer because there were more patients with HCV than there were with HIV. And those patients were often not terribly severely affected and therefore took a lot longer to gather together.

Q. Just on a matter of detail, Dr. Colvin: How many patients did you have in total, haemophilia patients at that time in the 1980s?
A. I think there were probably 600 or so on the books, but as I have indicated, we had about 100 who were regularly seen in my centre every year, because we spent a lot of time in the '70s trying to gather all the patients in my area with haemophilia so we had a register of them. And many of them of course didn't need much, if any, treatment. So, I think for many years it's been -- probably throughout the period we are talking about, it's been about 100 patients a year that I see, although a different hundred patients. And as I indicated, about 40 were HIV positive, and that roughly represented two-thirds of those who were severely affected by haemophilia.

Q. So they would be people with severe haemophilia; that two-thirds would be two-thirds of your patients?
A. I had about 60, if you like, about 60 patients with severe haemophilia. I mean, obviously some of them, some of the ones with mild haemophilia also got HIV-positive, but not very many of them. I mean, I have got figures on that which I don't

think I have got to hand today, but we had I think one patient with Christmas disease who was infected with HIV; no patients with von Willebrands disease who were infected with HIV; and then for the haemophilia patients, I think it was about eight or nine with moderate and mild haemophilia who were HIV-positive; and then 30 plus with severe haemophilia who were HIV-positive. And my recollection is that that worked out at about two-thirds of the severely affected Haemophilia A patients who were HIV-positive. And that meant that a third had, if you like, escaped.

Q. Just another matter that you mentioned to Mr. Durcan this morning: You said that with respect to those who did become HIV-positive, you carried the information about them around in your brain. Was that information written down anywhere?
A. Sorry, perhaps what I was trying to indicate was that I had in my mind the people who were most at risk. I certainly had written down and still have written down the actual results of my blood tests, and I keep a confidential file which is not electronically based. I do have a hard copy paper record of the Hepatitis C and HIV results. And I was referring to my brain as really as saying that I got in my mind the patients that I thought were mostly at risk, and whose sera I looked at when the time came to perform the antiHIV tests.

Q. But you kept --
A. A written record.

Q. -- detailed record?
A. Yes.

Q. Of all the tests and information that you had regarding those patients?
A. Yes, that's true.

Q. Thank you very much, Dr. Colvin.

THE CHAIRPERSON: Thank you, Mr. McCullough. Mr. McGovern?

THE WITNESS WAS THEN EXAMINED AS FOLLOWS BY MR. McGOVERN:

Q. MR. McGOVERN: Dr. Colvin, my name is Brian McGovern and I am acting on behalf of Professor Temperley and Dr. Daly and Dr. Jackson, who are three haematologists here in Ireland. I have just a few questions to ask you, Doctor.
A. I know all three of them very well, if that makes a difference.

Q. I see. Well, time will tell. On the question of heat treatment, you said at one point, and I think you were talking in the context of the mid-'80s, that you knew what was happening in vitro but you weren't certain about what would happen in in vivo tests?
A. Mm-mm.

Q. Can I ask you, as a haematologist, were you depending on the expertise of the fractionators and the virologists and people like that to keep you right, as it were, on what products you should use?

A. Well, I think that the -- we relied more on UK CDO, which had quite - that is the United Kingdom Haemophilia Centre Directors Organisation - which had quite a tight system of a virologist, Dr. Craske, who was particularly interested in haemophilia care; and people like Terry Snape, who were involved in the fractionation industry and who gave us advice about what was happening in the field of fractionation. So I don't think as individuals -- certainly I, as an individual, didn't so much relate to the fractionation centre and to my own virologist for policy; I relied on the United Kingdom organisation and its publications and the work that Dr. Craske did in coordinating the virological profile and the work that the fractionation people did in trying to keep up-to-date with what was -- with what was going on. I think this was a huge challenge for the fractionation industry because it had started up in a way which I think was very much part of the old NHS. And if you talk to Ethel Bidwell, who was one of the first people to prepare concentrates in Oxford in the '60s, she used to go on her bicycle with bottles of blood through the city of Oxford to go and fractionate. So it was very sort of amateur efforts; although, of course, very much pathfinding and vital scientific research; but it wasn't done on an industrial scale in those days. And even when I joined the NHS in the late '60s /early'70s, there was still this rather sort of amateur - the best sense of the word perhaps - approach, to what was going on. Then of course the big American commercial companies came into the field in the early '70s with a much bigger organisation, and the NHS in a sense had to compete with very adequate resources to -- with these very large American firms. I think it was -- the whole service, as I expect you'd understand, was underresourced. And lots of promises were made in the '70s that seemed never quite perhaps to have been fulfilled in terms of self-sufficiency in factor concentrates. And eventually, when we'd been through this terrible period in the '80s, the British fractionation industry I think turned over quite a new leaf and became a much more professional organisation. But I think its origins were, as I have indicated, quite sort of parochial. And so it may be that the whole organisation wasn't really equipped to deal with this catastrophe that people hadn't really expected.

Q. When Dr. Snape was giving evidence the other day, he referred to the fact that the haemophilia treaters, they would have -- the BPL would have looked on them as people who would give them feedback on products?
A. Mm-mm.

Q. And I think his own expertise was in chemistry, and you have mentioned Dr. Craske who would be a virologist. I take it as a haematologist you would be looking to these people and their respective areas of expertise to assist you in your choice of product?
A. That's quite true.

Q. And to evaluate the benefits of one type of heat treatment over another, or indeed whether you should use a heat-treated product as opposed to an unheat-treated product?
A. That is also true. But as I think I was trying to explain, their expertise was sort of fed into the United Kingdom organisation. And so, even in the sort of early to mid-'80s, there were some pieces of advice coming out of the UK Haemophilia Centre Directors Organisation which we tried to take notice of. As I have indicated and as you have heard today, there wasn't an absolute consensus about what was exactly the right policy at any particular time, because the knowledge was developing at such a

hectic pace and the levels of uncertainties were so great that it wasn't really very possible to judge exactly what the best thing to do was. I think in the black folder I was given to read this morning, there is a note from the UK CDO saying, here are all the products that are available and here are what we perceive to be their advantages and disadvantages. And there is a huge, long list of these products. Very long list. And although there are recommendations by UK CDO, it's quite obvious that we didn't really know necessarily what the best product was to use in a particular day. But you are quite right, people like Terry Snape and John Craske were advising the central organisation and that organisation -- that information and advice was being spread out to the users. And at that time, I wasn't a member of the inner sanctum of UK CDO because my centre wasn't a reference centre. I think I did receive the sort of information I needed in order to do my best to practice as well as I could.

Q. You indicated earlier, Dr. Colvin, that you felt that perhaps you were more conservative than some of your colleagues, and I think you were using this to illustrate there was no consensus as to how to proceed. And I noticed you used the word "dilemma" on many occasions, and the word "uncertainty". Is that how you perceive the position to be in the UK back in the mid 1980s, that there was this, A, lack of consensus; and, B, great dilemma and uncertainty for the treating physicians, haematologists in particular?
A. That's exactly the position.

MR. McGOVERN: Thank you very much.

THE CHAIRPERSON: Mr. McGrath, please.

THE WITNESS WAS THEN EXAMINED AS FOLLOWS BY MR. McGRATH:

Q. MR. McGRATH: Dr. Colvin, my name is Michael McGrath and I represent the BTSB. I just have a few questions for you and it's really following on on what Mr. McGovern has been asking you in relation to the dilemma and so on and the choice of products. But first, I'm just wondering how did the hospitals -- how did you purchase the product itself from the NHS, and was there a difference between the purchase of NHS product and commercial product?
A. Yes. There was a huge difference because the NHS product at least originally was provided free of charge; it was a free good. Later - and I can't remember the exact time when we began to pay money for it - it did -- it did come at a cost. But of course, there was always the perception, which I certainly had, that the money we were paying for it was being sort of ploughed back into the NHS. And as you are aware, there are many of us who have believed in the value of the NHS as an idea; and so I think many of us, including myself, and I freely admit it, favoured NHS products from an ethical and philosophical point of view, even when we were paying for them. Because we believed the money we paid would be ploughed back into making our fractionation industry better. So I think that although we never had good enough supplies, and it may be, to begin with, that the products may not have been of the very highest quality, when you relate them to the -- to the state-of-the-art in fractionation, at least to begin with, that there was this, as I say, philosophical belief in the NHS. Once one was purchasing commercial products it was a different story. There, the individual haemophilia centres would purchase Factor VIII concentrate from commercial suppliers, and obviously that money went into the commercial

suppliers rather than being ploughed back into the system. And I mean, some of my colleagues quite early on decided that commercial products were the best products technically, and therefore absolutely. And even some of them wouldn't have anything to do with the NHS. They thought the NHS product was inadequate; others, like myself, believed in the NHS, wanted to see it succeed, and its fractionation industry succeed, and felt that the right investment was in that area.

Q. Mm-mm. Does that mean that from centre to centre, the proportionate usage of concentrate, National Health Service as against commercial, could vary significantly?
A. It could vary very significantly. Of course, in most centres that had a lot of business, there would never be enough NHS product to go around for everybody. And I think really all the large centres were using at least some commercial material; but the proportion of NHS to commercial material being used would have varied quite a lot with one or two centres, perhaps one centre being unwilling to use NHS product.

Q. I see. And in relation to the overall usage, we have had evidence from Dr. Snape in relation to the fact that in the UK, you weren't self-sufficient in terms of Factor VIII concentrate. And indeed, there was a significant amount of commercial concentrate used. I am just wondering, in relation to your own particular centre, would you have any idea between 1985 and 1990 what the proportionate usage was between NHS and commercial concentrate?
A. I mean, it's a figure that I could produce quite accurately but I don't have it here today.

Q. Roughly?
A. I think that the -- it might easily have been sort of 50/50 or sort of 40/ -- probably 50/50, I would have thought. But it's certainly something I can provide to the Tribunal if it wanted to have the information. But at all times I think I had a very substantial reliance on both NHS and commercial materials, with my preference being towards NHS materials.

Q. Yes. And could I just ask you in relation to the commercial material: What commercial concentrates were used in your centre between 1985 and 1990?
A. Yes. I think we used really almost anything we could get our hands on for a while; certainly we used some Armour material for a while, although I have explained why I tried to avoid doing that. I have always been keen, where I could, to use one product; where it's possible, to keep a patient on the same product. So I think that the majority of the concentrates, to the best of my memory, was either 8Y or Profilate for Factor VIII use at that sort of period, '85, '86, '87.

Q. Yes.
A. And we may have used -- I am sure we did use some Armour, and I'm sure we used some Hyland and Cutter products. But I think the bulk of what I used was probably Alpha Profilate and NHS.

Q. Yes. I see from your statement that in the years 1993 to 1996 you were the Chairman of the UK Haemophilia Centre Directors Organisation --
A. Mm-mm.

Q. -- isn't that so? And I'm just wondering about your association with that organisation prior to 1993. I take it you would have been a member of that organisation for some time?
A. That is very interesting. It's a very interesting question which, if I may, I will expand on. I mean, I run a relatively small haemophilia centre in terms of its prestige, in that the running of the hospital is in a very poor area of London. We have been looking after people with haemophilia for a very long time. We have a rather poor fabric; we don't have a real haemophilia centre in terms of a centre. And we are on the doorstep of the Royal Free, which was, of course, created by -- the late Catherine Dormante (?) had a new palace built some years ago, and delivers an extremely high standard of care. But it's not that convenient to get to, being located in Hampstead, as it is. So the old system used to be one of so-called reference centres in the United Kingdom. And these were, if I may be permitted to say so, slightly self-styled centres of excellence. There was a limited number of people who were in the club, and we certainly weren't one of them. And the reference centre directors used to meet regularly in order to decide on policy. And I was minding my own business one afternoon in 1992, I think it was, when I was phoned by one of my senior colleagues in the organisation to say would I like to be chairman of the organisation? And I never actually attended a committee meeting of the organisation at all. I'd been to the annual general meeting; I was a member of UK CDO, and all haemophilia centre directors were. I had the unusual experience of chairing an organisation I had never actually been to. Now, there are a whole lot of reasons why that might have happened --

THE CHAIRPERSON: Well, perhaps -- perhaps -- perhaps it might be more interesting in the UK.
A. It illustrated I think that -- it illustrated I think that the -- that the organisation, like any organisation, has some tensions within it. But my own centre was quite a small centre, although we had a lot of patients, and I wasn't part of the policy-making group that worked from 1970 to 1993.

Q. '93, yes. The reason I was asking you that is we have included two documents - one is on page 37 of the black folder, and one on page -- slightly earlier on page 31 - and these were the UK Haemophilia Reference Centre Directors recommendations in the choice of product. You have already referred to these. I take it from the answer to the previous question that you had no direct input into what's contained in this document?
A. That's quite true.

Q. These documents. Would you have been aware of those documents at that time?
A. Yes, because I think the UK CDO has always had a good network of telling people what was going on. Although I didn't formulate policy -- and I apologise for the rather lengthy discussion on that topic --

THE CHAIRPERSON: Very interesting.
A. Although I didn't actually dictate policy, I was aware of what the policy was.

Q. Yes. Well, the two documents -- the first document, which is on page 31, and I can tell you by reference to page 36, that is dated the 16th of May of 1988?
A. Mm-mm.

Q. And the next document appears to be a document which came out almost one year later, on the 22nd of May of 1989?
A. Yes.

Q. Now, it's my understanding that these were general recommendations which were being issued to various reference centre directors --
A. Yes.

Q. -- as to the choice of product. Now, if I could just very briefly -- I don't wish to go through all the products that were there, but it would appear from these documents that between certainly 1988 and into 1989, that there were quite a number of different products available on the market?
A. Absolutely.

Q. And in terms of the first generation product, the Koate HT, that was the Cutter product --
A. Yes.

Q. -- which was dry-heated for 72 hours at 68 degrees. That was one such product which was available on the market in the UK in 1988, and I think you can see that on page 33?
A. Yes.

Q. And where you see it again, insofar as 1989 is concerned, it's on page 40?
A. Yes.

Q. And I think --
A. These are actually the same document, aren't they?

Q. Well, they are -- they -- there are some changes from year to year, but it's set out more or less the same.
A. Yes.

Q. What I'm interested in is, insofar as the recommendations and -- the specific recommendations are concerned, if you look at page 36 under paragraph 5.2, "specific recommendations." And at subparagraph one: "For patients in England and Wales with Haemophilia A who have received little or no previous exposure to blood products and who need treatment with concentrate," then we have the first choice, which is the National Health Service 8Y; we have the second choice, which is the Haemate P; and the third choice is the Profilate HT. And then we look at the multitransfused patients with Haemophilia A and it says "any of the products listed at 5.2.1 above plus Koate HT"?
A. Mm-mm.

Q. That would seem to be the first generation dry-heated product, 72 hours at 68 degrees, is that so?
A. Yes, that's right.

Q. Yes. And again, if we look at the previous page, at page 35, under "general recommendations," it states that "although it seems clear that --" 5.1.1. "Although it seems clear that different therapeutic products are associated with differing risks of contamination, it is not possible to quantitate these risks accurately. The data on which judgement should be based is to a large extent unavailable."And at 5.1.2: "Not all the products listed are currently easily obtainable"?
A. Yes.

Q. Now, that would tend to suggest that there was a process of evolving - of assessing products as you were going through the year 1988 and into 1989; is that a fair comment?
A. Well, I mean, as you have pointed out, I or -- I wasn't part of this process so I don't think I can really second-guess what was in the mind of the reference centre directors. At that time I was really still a general haematologist with general duties, apart from the care of haemophilia. So I don't think I can judge exactly what these people had in mind because they are mostly people who are reference centre directors who were perhaps only haemophilia...But I don't think that this information is necessarily very scientifically-based. I mean, I don't think we can say that these recommendations are what these days would be regarded as evidence-based medicine. I think that is really implicit in what they say. They don't really know what to say precisely, although the advice is fair.

Q. Yes. I see. Just one other thing that arises from the documents insofar as the NHS 8Y and the NHS 9A are concerned, in terms of its availability and in terms of the manner in which it seems to have been placed on the market. If I can ask you to look at page 41, and again, this is outlining the products which were available and recommended: 4.2.5, the NHS 8Y; that is the dry-heated product.
A. Yes.

Q. And it says: "Clinical trials exemption certificate for VP study;" -- virgin patients study -- "otherwise used on a named patient basis only." I am just wondering what that actually means in terms of the 8Y. And we have a similar type description under -- for 9A as well. Does that mean that the 8Y and the 9A were not, generally speaking, available, but were available for clinical trials and on a named patient basis, or what does it actually mean?
A. I think what it actually means is they -- I am fairly confident of this - I think probably Terry Snape would be better placed to answer -- I think it means they didn't have a product license. If you have got a product license, it's freely available; if you hadn't, it's on a named patient basis only. In reality, we used named-patient-basis-only products as if they had a license, but I think the word "named patient" just means there wasn't a product license.

Q. I see. And finally, just before I leave that topic, again, in relation to the specific recommendations which were issued in 1989, if we look at page 44, the "specific recommendations". 5.2.1: "For patients in England and Wales with Haemophilia A who have received little or no previous exposure to blood products and who need treatment with concentrate: NHS 8Y or Monoclate P. And underneath that: "It should be noted that neither of these two products is licensed for general clinical use, only products which have a CTX for VP studies are recommended for use in this type of patient. Wherever possible, and appropriate, patients should be formally registered

for inclusion in a VP study." That seems to follow on from what you have said earlier?
A. I mean, I think there was at that time a growing awareness of the importance of clinical studies, research ethics committees, and the whole business of regularising the process of clinical trials. And I think this text is really to do with UK CDO recognising the niceties of the theory of what they were doing. The reality I think was that from April '85 we used 8Y as if it had a product license.

Q. Yes. I see. And just finally, on that, 5.2.2; again, this deals with the general use in multitransfused patients with Haemophilia A: "We regard any of the products listed in section 4 above as being acceptable from the point of view of safety." Now, I have been looking at section 4 and it doesn't appear that there is a huge difference between what was being recommended in 1989 from what was being recommended in 1988?
A. Mm-mm.

Q. And it goes on to state: "While preliminary evidence suggests that 'super' dry-heating, heating in solution, solvent/detergent treatment, vapour heating and monoclonal purification, may all result in greater degrees of viral inactivation than conventional dry-heating or heptane slurry heating, we do not feel that this evidence is currently sufficiently wrong to recommend general adoption of unlicensed commercial products for routine treatment. It remains our view, therefore, that unlicensed commercial products should only be used outside formalised clinical trials if the need is considered compelling by the prescribing physician who must accept and understand the constraints of using therapeutic products on a named patient basis." I am just wondering, would you have seen that at that time in 1989?
A. I very likely would have done, but I think it's sort of -- it's formula-speak, rather.

Q. Yes.
A. I don't think that -- I can't really judge, I suppose, all these years later what he really meant by that. I think what they really meant to say was 'it was an unlicensed product and don't forget it, even though I know you are using it for everyday use'.

Q. Yes. I see. Now, insofar as theHepatitis C transmissions were concerned, I just have -- there is one document I would just like you to have a look at, and that's at page 54. I don't know when the precise studies were carried out for this, but I can tell you that this is a page from The Lancet of 7th of July of 1990.
A. Yes.

Q. I think if you look at the previous page, you will see it actually follows on?
A. Yes.

Q. And the studies I think - in fact, one of your communications is mentioned at paragraph one of the -- I should say note one, which I think was suggesting that there was not transmission or there was no evidence of transmission of Hepatitis C using the NHS 8Y?
A. Yes.

Q. But just -- I'm just interested in the actual table on -- in the first column, which seems to suggest that wet heat-treated 60 degrees /20 hours, that -- patients treated,

seven, and antiHCV-positive, three. My understanding is that that would be the Alpha Profilate product?
A. Mm-mm.

Q. Is that so?
A. Yes. I think that the -- that if you look at the paper - which I think is somewhere in the bundle here - from Peter Kernoff, of the first lot of treatment with Profilate, then you will find that about half of those, roughly speaking, who were treated with the original Profilate seroconverted -- sorry, developed non-A non-B Hepatitis. So I think that the United Kingdom was probably very lucky that the superheated 80 degrees Celsius for 72 hours product actually didn't transmit HCV. I mean, I don't know how much luck it was but -- shall we say, I think it was fortunate for us, for our haemophilic community, that that particular product in the end turned out to be very safe.

Q. Mm-mm.I just -- those figures seem to be based on a particular trial of a number of different -- testing of a number of different patients. I'm not quite sure, you may have touched on this earlier in your evidence with Mr. Durcan; is there any central recording mechanism in the United Kingdom for recording HCV infections?
A. There wasn't at the time because, of course, there wasn't an antiHCV --

Q. Of course, at that time, yes.
A. -- test. But when we knew about HIV, there was a very close and careful review of HIV results which were centrally held and from which a lot of important research on the natural history of HIV infection has come. But I don't think that we have ever had a register of that kind for HCV infection. The reason we know roughly how many people with haemophilia are antiHCV-positive is we do know how many have received large pool concentrates. And as we have discussed this morning, for those who received large pool concentrates before 1985, we know they are all just about antiHCV-positive. So that the organisation has really interpreted the number of antiHCV-positive patients from a number treated with large pool concentrates before '85.

Q. I see.

MR. McGRATH: Thank you, Dr. Colvin.

THE CHAIRPERSON: Thank you, Mr. McGrath. Ms. Cordial?

MS. CORDIAL: No questions.

THE CHAIRPERSON: Before I come to Mr. O'Brolchain, I will just rise for five minutes.

AFTER A SHORT ADJOURNMENT, THE TRIBUNAL RESUMED AS FOLLOWS:

THE CHAIRPERSON: Mr. O'Brolchain?

THE WITNESS WAS EXAMINED AS FOLLOWS BY MR. O'BROLCHAIN:

Q. MR. O'BROLCHAIN: Thank you. I have just one or two matters, just to clarify a few points. Doctor, I think up to 1993, you were a general haematologist, you told Mr. McGrath?
A. Yes. In fact, I was really a general haematologist a little bit longer than that, but certainly my training is in general haematology and I perform the sort of usual functions of a haematologist/oncologist and general haematologist as well as being a Haemophilia Centre Director. Some of my colleagues were exclusively dealing with haemostasis and haemophilia; I was acting as a general haematologist with an interest in --

Q. So that the haemophilia aspect of your practice was a portion of it, but not all of it?
A. Exactly so.

Q. Yes. In the course of your acting as a haematologist, did you tend to use DDAVP, or what is known as DDAVP?
A. DDAVP, or Desmopressin, was described in 1977 by Professor Mannucci and his colleagues as a potential means of treating patients with mild Haemophilia A and von Willebrands Disease. And it allows the level of Factor VIII, for those who have some Factor VIII in their blood, to be raised by chemical means. Unfortunately the effect often doesn't last very long and can't be repeated more than two or three times. Really, DDAVP is only suitable for managing very mild problems; for people with mild haemophilia and von Willebrands Disease. There is no doubt it's resulted in many patients' lives being saved. But it really isn't, and wasn't, a solution to the problems of patients with severe haemophilia. And it's my recollection that we were reluctant to use DDAVP for big events in mild haemophilia or von Willebrands Disease in the early '80s. Although the treatment was described in '77, it wasn't really until the late '80s we began to get a bit braver with the use. DDAVP certainly had some treatment failures with it. Although DDAVP has been a very important discovery and has benefited people with haemophilia immensely, we weren't using it in the early '80s very much for surgery or for dealing with serious bleeds, even in mild haemophiliacs.

Q. And in your own experience, did you use DDAVP to any large extent?
A. I used it from time to time, but again, I emphasise that where there was a surgical procedure or where there was a significant bleed, then I didn't use it. We used it mostly for rather minor dental extractions or quite small events that we wanted to cover with something which would provide haemostasis for a brief period of time. Once you were dealing with a significant bleed or significant surgery, you need haemostatic cover for longer than DDAVP will allow.

Q. Yes. In relation to Hepatitis C, you have, I think, 80 patients under your care who have Hepatitis C, is that correct?
A. That's correct.

Q. And of those, I think 40 are - approximately - are HIV-positive?
A. Forty were HIV-positive, but sadly, 25 of my HIV-positive patients have died. So of the -- of the 70 or 80 patients left, then 15 are HIV-positive.

Q. Yes. Now, in the early '80s, or coming up to between 1980 and 1985, what was your perception of Hepatitis C as a disease where the person did not have HIV and did not have any other difficulties?
A. I mean, the perception of it as a disease was that I'd seen very little consequences of it, and have still seen very little consequences of it; I mean my personal experiences of a number of my patients developing acute hepatitis when treated for the first time, so developing jaundice and being unwell with an acute attack - that is perhaps in, I don't know, four or five patients over the last 30 years. So the majority who did develop Hepatitis C infection developed asymptomatic infection. I am also aware, as I mentioned earlier in the day, that some patients with Hepatitis C infection feel ill. And we did a study recently which was - so far unpublished - looking at patients with haemophilia who were HCV-positive and HCV-negative, and trying to establish whether they felt ill or not in an objective way. I perhaps can't go into the detail of the study, but it was designed to find out whether or not people with Hepatitis C infection actually felt ill in an objective way; and the evidence is yes, they do. So my patients do seem to feel unwell, tired, listless with their infection. But the actual consequences of chronic liver damage leading to illness I have hardly ever seen outside the groups that we have discussed.

Q. Yes. So that in -- in the early '80s, if someone was found to be Hepatitis-C-positive, was there any treatment available for that patient?
A. Of course the virus wasn't discovered 'til 89. By definition, there was nothing that we could have done because we didn't know who they were, although we knew their abnormal liver function tests. Interferon was introduced as a treatment for Hepatitis C infection not that long after it was described, but sadly, Interferon alone very rarely improves Hepatitis C infection; it's not until the last sort of five - four or five years, when we have had the combination therapy within Interferon and Ribaviran, that we have been able to improve any significant number of Hepatitis C infections in people with haemophilia.

Q. Yes. Thank you. And then I think you confirmed, just lastly, to Mr. McCullough, that when you had your own seroconversion Factor IX patient in 1985, there was no system in place for notification to anybody else, isn't that the position?
A. I don't recall telling anybody specifically that my patient had seroconverted to HTLV-III positivity, other than the notification to Oxford that such an event had occurred. There was a system of notification to Oxford as the HTLV-III seroconversions took place, so they knew how many people we had who were antiHTLV-III positive. But I certainly wasn't -- I certainly didn't notify the central laboratory in terms of trying to establish which batch had caused the infection.

Q. Yes.

MR. O'BROLCHAIN: Thank you very much, Doctor.

THE CHAIRPERSON: Mr. Durcan, please.

THE WITNESS WAS FURTHER EXAMINED BY MR. DURCAN AS FOLLOWS:

Q. MR. DURCAN: Just two matters, Doctor, and they are both in regard to what Mr. McCullough asked you about. Firstly, you told us about thrombogenicity and

Factor IX. And firstly, if I confine my question to unheat-treat -- unheated Factor IX. Was I correct in understanding that you felt that, in practice, the concerns about thrombogenicity were in regard to orthopaedic surgery?
A. That's correct. I mean, the vast majority of the thrombogenic events that have taken place in people with Factor IX deficiency who have been treated with the old intermediate purity Factor IX concentrate, the vast majority of those events were related to surgery, orthopaedic surgery; and the reason for that I think is that the level of thrombogenicity is moderate and you need quite a big stimulus in order to reveal it. And obviously when orthopaedic surgeons go around doing the things that they do, they create a lot of damage, which they quickly repair, but it's quite a sort of traumatic business having an orthopaedic surgical procedure. It seems as though that big stimulus to the haemostatic -- together with the thrombogenic factor of the Factor IX concentrates, result in the trouble. To give you an example: Many years ago I had a patient with Factor IX deficiency who was having a knee operation, and we'd, I think rather unwisely in retrospect, put a long line into his arm because he had rather poor veins - all thrombosed up; that is when I became aware of this in the late '70s. We had another patient who had an ankle operation who developed a pulmonary embolism - that is a blood clot in the lung - following an operation under Factor IX concentrate. The patient who had the trouble with the arm had, on another occasion, a pulmonary embolism. Until high purity Factor IX concentrate became available, we didn't know that these intermediate purity concentrates of Factor IX were likely to cause thrombogenic events, but usually, in the context -- perhaps almost exclusively in the context of large doses being given to patients who we were doing things to, particularly orthopaedic procedures.

Q. And were the concerns about thrombogenicity in heat-treated Factor IX, equally were they in regard to the sort of events you have been telling us about; surgical intervention where large amounts would be used?
A. Well, I think that -- it's fair to say if we had been doing such a procedure, that would have been our area of greatest anxiety. But of course, if we knew that a concentrate was thrombogenic and, to put it crudely, we then cooked it, it might be more thrombogenic, because by damaging tissue you increase thrombogenicity. So perhaps the anxiety was by damaging deliberately the viruses, then the tissue, in inverted commas - that is the factor concentrate - might also be, in some way, modified and damaged, so therefore, thrombogenicity might be greater. And of course, if thrombogenicity was greater, then it might be expressed in everyday life with smaller doses than with the bigger doses that were used in orthopaedic surgery.

Q. I see that. But it's -- one has to look at it, I suppose, in this way: The concern, the main concern would have been about use in surgery, but the heat treatment might have caused it to become -- have greater difficulties with thrombogenicity, and therefore, it might have come into other areas?
A. Yes. I think I was -- I was anxious to point out that these were concerns, and they are clearly written down in various places, but I didn't want to overdo it. Really, there was an anxiety; I don't think it was fulfilled, but it was a factor that we took into account and the fractionation laboratory took into account when they were deciding what to do about heat treatment of Factor IX concentrates. And it's one of the reasons it took longer to produce Factor IX concentrate that was heat-treated, because there was the process of trying to establish whether or not it was thrombogenic. And there are some laboratory tests you can do by, for instance, perhaps administering the

concentrate to either laboratory animals or even to human beings, and then measuring the amount of thrombogenic potential in the blood. There are blood tests that you can use for measuring how much thrombogenicity is happening in the blood, and the sort of processes that might have been gone through by the fractionators would have resulted in a bit of a delay between saying 'this is a good idea and this works and it's reasonably safe'.

Q. The other matter I want to ask you about is you have told us about the concern there would have been in perhaps early 1985 about using heat-treated products. And that, in effect, the concern would be that if there was a heavily-infected donor pool, the infection might break through in any event, notwithstanding the heat treatment, is that correct?
A. That is perfectly true.

Q. Yes. Now, in fact, in regard to Factor IX, is there any evidence that infection did break through in any heat-treated Factor IX?
A. To the best of my knowledge and belief, no.

Q. And I think you have already told us that in 1985, and certainly at the beginning of 1985, that there would have been a belief that the method of making Factor IX; the manufacturing process, in fact, reduced the possibility of infection, that it was less factor -- Factor IX was less likely to carry infection?
A. That's true.

Q. Doesn't it follow then that heat-treated Factor IX was less likely to carry infection?
A. I mean, I think that's a possibility. And I mean, I make no secret of the fact that when I discovered one of my Haemophilia B patients had seroconverted on NHS unheated concentrate, I was deeply disappointed.

Q. Yes. Now, the -- the only thing I was -- you were telling us in the course of your evidence that you felt that people would have had concerns about the breakthrough of infection in heat-treated Factor IX. But because of the fact that people felt that Factor IX was less likely anyway to cause infection, that concern in regard to Factor IX must have been of a lesser order?
A. Of course that's true, but also, the other side of that coin is that our perception was that our -- very few, if any, of our patients with Factor IX deficiency were HIV-positive. And therefore, to expose them to the possibility of HIV from a heavily contaminated batch that had been heated but was still infectious, could have led to a greater disaster. It's got two sides to that coin.

Q. I think, in fairness, one could put it this way: If one looked at either possibility, the possibility of infection was perhaps of a lesser order?
A. Yes.

Q. Yes.

MR. DURCAN: Thank you.

THE CHAIRPERSON: Thank you, Mr. Durcan.

THE CHAIRPERSON: Thank you, Dr. Colvin. Thank you indeed for coming.

THE WITNESS THEN WITHDREW.

THE CHAIRPERSON: We will adjourn then until Monday morning at 10:30.

THE TRIBUNAL THEN ADJOURNED TO MONDAY, 16TH OF JULY, 2001, AT 10:30 A.M.