Thursday, 5 November 2020

(10.00 am)

SIR BRIAN LANGSTAFF: Good morning, professor.

A. Good morning.

SIR BRIAN LANGSTAFF: Let me just say a couple of things first, if I may, before Ms Richards starts questioning you again, because we're meeting under new conditions, as we all know, given the restrictions which were introduced as from today. Those who are watching remotely won't see, they never do see, the audience which is here. Nor do you. You just see the same faces. But for those who are watching out there and for your information, the only people who are present in the hearing room are the legal team supporting Ms Richards, your own counsel, some technicians, and a couple of members of Inquiry staff. There's no public here. But they are watching online.

So this is the conditions under which we are currently meeting. I'll continue to wear a mask because that's what we ask people to do in these premises, though it does interfere with talking sometimes, which is why I take it down when I'm talking to you.

Ms Richards.

and Adults and the Royal Free Hospital are all still using large amounts of BPL products and continuing to order them. I suspect that these 3 centres all use significant amounts of 8Y, which may present them with a financial problem. I was able to implement our policy rapidly because there were essentially no attached revenue consequences. I hear that Frank Hill will be wanting to move straight to Recombinant but I worry that the other 2 centres were basically not fully sold on the policy. If they don't implement this policy it significantly undermines our position."

Do you know whether the anxieties expressed in that letter, the concerns expressed in that letter, continued, or did other centres implement the UKHCDO recommendation?

A. Well, I think that at some point BPL withdrew their products, and then there was a gap, substantial gap, until they started to manufacture the same products, using imported American plasma. I can't remember exactly how long that took.

And the financial problem I'm alluding to is because those centres that continued to use a lot of 8Y, 8Y was quite cheap, but it was also very popular, it had a good viral safety record. It was also reasonably all right on von Willebrand's disease. So

CHARLES RICHARD MORRIS HAY (continued)

Questions by MS RICHARDS (continued)

MS RICHARDS: Professor Hay, I want to pick up the picture in relation to vCJD and the response to the risk of vCJD and the various notification exercises.

We looked yesterday at your letter in November 1997, and the meeting you described following that. Your statement tells us that at some point after that, at Manchester you were able to switch products to those manufactured from US plasma fairly quickly; is that right?

A. That's correct.

Q. There is also evidence to suggest that that may not have been the position universally for all centres.

Soumik, could we have on screen, please, HCDO0000133_188, please.

This is a letter you wrote January 1998, it's addressed to Dr Ludlam, and it's "Implementation of our Recommendation on CJD". That is presumably a reference to the UKHCDO Committee's recommendation which you discussed yesterday afternoon?

A. It is.

Q. Then you talk about:

"The commercial grapevine tells me that some centres, particularly Oxford, Birmingham Children's

some centres were genuinely quite attached to the product, it wasn't just because it was inexpensive.

But the fact that it was inexpensive meant that for them to change to American products would have incurred a considerable cost.

For me, that wasn't a problem because I had already switched all my patients to high-purity products so I was using more expensive products in any case. I can't honestly remember how long the situation went on.

Q. Okay. We move, then, I think, to -- just before we get to the national notification exercise in 2004, you had an exchange of correspondence with BPL in 2003.

Soumik, if we could have HCDO0000254_117, please.

This is a letter that you wrote, in May of 2003, to BPL, and it says that you were recently notified by the Transfusion Transmitted Working Party that your centre, Manchester, had received batches manufactured from plasma pools contaminated with plasma from patients who subsequently developed vCJD, and you're expressing here displeasure at not having been informed of this directly by the manufacturer and having learnt of it through this route of the Transfusion Transmitted

Disease Working Party rather than directly from BPL.

What had actually happened that gave rise to this correspondence?

A. Well, it just struck me that there were various other routes of communication that could have been used that would have informed me much more quickly. It was perfectly reasonable that they should inform the TTI Working Party and they were coordinating the whole thing. But had I been informed earlier I would have acted earlier to identify the recipients of these products.

And they had supplied these products to the Manchester Centre through the Transfusion Service, and either the Transfusion Service or the manufacturer would have known that it had been supplied to me and should and could have informed me earlier.

Q. The next I think key event in relation to vCJD and Haemophilia Centres and haemophilia patients was the 2004 national notification exercise.

Now, as I understand it, this was triggered by a case of vCJD reported in the recipient of a blood donation in December 2003, and then a second possible case in July 2004. Is that correct?

A. That's correct. I mean, this was obviously a game changer because up until this point, the possibility

of a transmission through blood transfusion was a theoretical possibility, and there was a lack of concrete proof that it could occur.

Q. And then if we go, please, Soumik, to WITN3289110, we're going to look at some of the documents, professor, from the 2004 notification exercise.

So this is a letter of 7th September 2004 from the CJD Incidents Panel, which your statement tells us had been set up in 2000, and we can see from it, it's setting out recommendations of the panel for tracing and assessment of patients exposed to plasma products using donations from individuals who subsequently developed vCJD. We're told in the second paragraph it was based upon a blood risk assessment carried out by an external consulting firm or organisation which had then been considered by the various committees who we see described there, including the Committee on Safety of Medicines. And then it reads:

"Batch specific manufacturing data from the fractionators concerned has been used with the Risk Assessment to estimate the potential vCJD infectivity in each batch of implicated product. For each of the major assumptions underlying the Risk Assessment, the most precautionary option was chosen."

Then we can see the panel has identified what

it means by being "at-risk" for public health purposes. And then there are three levels identified: high, medium, and (over the page) low.

We're told, in the third paragraph:

"The uncertainties underlying the assessment of 'risk' are great, and several precautionary assumptions are involved. Therefore the 'at-risk' threshold for public health purposes is not a precise guide for advising individuals about their potential additional risk of developing vCJD."

Then we can see in the bold print, there's a recommendation of action to be taken. In relation to those who fall within the high category:

"These batches should be traced and the individual recipients considered 'at-risk' of vCJD for public health purposes. The extent of individual exposure to these batches should be documented.

"Medium: Efforts should be made to trace these batches and assess the potential additional risk to individual recipients to determine if special precautions should be taken for public health purposes. The extent of individual exposure to these batches should be documented."

Then:

"Low: These batches do not need to be traced

and the individual recipients do not need to be informed."

We will look at some of the other documents in a moment but can you perhaps provide us with an overview of what the response to this then was by UKHCDO and individual Haemophilia Centre Directors.

A. Well, we were informed one way or the other, mostly by the database and through the Transfusion Transmitted Disease Working Party, of the batches that had been implicated, and these changed with time, as further patients presented with variant Jakob-Creutzfeldt Disease, and we did our best to trace the ultimate destination for all those products, who had received them.

We -- obviously all the patients were written to, including those who had not received British blood products. The initial notification was to all patients with bleeding disorders, not just those who had had British products, because it was felt that they would hear about this in the press and they might worry that they would be affected in any case. So we felt we had to write to everyone.

We had to speak to our surgical colleagues and the hospital administration, because the measures included, amongst those patients at high risk, certain

types of surgery had to be done with disposable instruments. Endoscopes had to be quarantined if they were used in high-risk individuals, so the notes had to be noted in that way. And if the patient required surgery, this became a consideration that had to be dealt with. And we had to report back to the database the risk level of each of our patients.

There are forms in the exhibits that show the returns to the database which show the amount of each batch that the patients had received, if they had received any. And if they had not received any implicated batch, that's also recorded. And the outcome of the discussion with the patient is also recorded, because this was a very unusual situation, and in the Advisory Committee we had lengthy discussions about how we should approach this, because this was a condition for which there was no test and there was no treatment. So we couldn't test the patients to discover whether they had been exposed or not. And even if we knew for sure that they had been exposed, there was no treatment and we were unsure of the likely natural history. Because, as things unfolded, recipients of implicated blood transfusions had developed variant Jakob-Creutzfeldt Disease as long as eight and a half years after exposure. And

they were all homozygous. So there was the theoretical possibility that had been raised that heterozygotes might also develop variant Jakob-Creutzfeldt Disease but perhaps after a very prolonged period.

Now here we are 30 years down the line and that hasn't happened, but it was in those early days raised as a possibility. So far only homozygotes have developed a problem and no recipients of pooled blood products.

Q. This was a national exercise organised centrally by the CJD Incidents Panel with the notification, the information we see here, the assessment, the strong recommendation to recipients of this letter, which included UKHCDO, to take the steps there set out?

A. And the National Haemophilia Database collating the data and, amongst other things, reporting it on to the HPA, which continues on a six-monthly basis to this day.

Q. If we just look at some of the documents that were also provided by the CJD Incidents Panel at the time of publication of its recommendations on 7th September.

We've got, please, Soumik, at WITN3289113.

We're not going to need to look at the detail

of every document but just to see the broad nature of the accompanying documents.

So, again, dated 7th September, this was a table of the vCJD implicated batch numbers. So that information identified the source in terms of manufacture, PFC or BPL was identified. And then if we go over to the third page, we can see -- we don't need to go through the details of it -- the specific batches. That information had all been gathered and collated nationally, had it?

A. Yes.

Q. And then if we go, please, Soumik, to WITN3289114.

Again, we don't need to go to the detail of it, but this is a clinical information sheet produced by, amongst others, the Health Protection Agency. We can see the date from the bottom of the page, 7 September 2004.

So this was, as it were, information for clinicians to accompany the recommendations.

A. Yes.

Q. And then if we go, please, to WITN3289115. We can see here there was also -- same date, 7 September 2004 at the bottom of the page -- again, a centrally prepared patient information sheet. We'll just look briefly at the various headings.

So 1, "What is variant CJD?" Then if we go over the page, "What's this about?" So it sets out what has led to the exercise, the first case reported: the death of a person from vCJD who had received a blood transfusion from a donor, so the first case of transfusion associated vCJD, and then a second probable case.

We can see the bottom half of that page talks about "Why am I being contacted?" So it explains to patients the purpose of communicating with them.

If we go to the next page, we can see a description of what measures are already being taken. And then point 5, "And in relation to blood?"

"Because it is uncertain whether vCJD can be transmitted by blood, the UK blood services have taken a number of precautionary measures."

Those are then set out from 1997 onwards.

We can see the bottom of the page the CJD Incidents Panel there referred to; it's established in 2000.

And then if we go over the page, we can then see under point 7 an explanation to patients of what has changed in terms of policy.

The next page, "Who is affected?" So it identifies the groups of those who may be affected by

this.

And then "How does this affect me?" It talks about the practical implications for patients.

And then if we go over the page, we can see it continues by giving patients information about the extent to which they face a risk, that's point 11. "Does this mean I'm going to suffer from vCJD?"

"Can I be tested? What happens if I develop strange symptoms? Will this mean I won't be able to get life insurance?" We can see from the top of the next page that that's an issue that's already been addressed. Insurers will not refuse insurance because someone is categorised at risk for public health purposes. And then it continues.

This was obviously a national leaflet prepared for the benefit of patients.

A. Yes.

Q. Did Haemophilia Centres send this information sheet to the patients whom they were notifying, as far as you're aware?

A. As far as I'm aware, yes.

Q. Then if we go just to WITN3289118, please, Soumik.

This is described as the "Patient notification exercise enquirer handling protocol."

If we go to the second page, at the bottom of

the page under the heading "timing", we can see a timed plan of action: 9 September, information will be sent to haemophilia doctors, immunologists medical directors of trusts. Then the plan for haemophilia doctors and consultant immunologists looking after patients with primary immunodeficiency to send out patient letters on 20 September. And then a full press briefing by the Department of Health planned for 21 September.

Certainly, the letters we've seen, Professor Hay, sent to patients, many of them are dated 20 September 2004. Again, as far as you're aware, was the expectation of UKHCDO and the VCJD Incidents Panel that all Haemophilia Centres would send those communications to their patients at the same time?

A. Absolutely. Absolutely. I mean, the timing of this was determined, as far as I remember, by launching of a Parliamentary question which was going to alert the press the following week, so the whole thing had to be rushed along. And it was strongly emphasised to centres that this matter had to be dealt with as a matter of urgency.

Q. We can see that from the UKHCDO letter to directors at WITN3289111. So this is 9 September. At this point

in time, you were Vice Chair, Professor Hill was Chair, and this letter was sent by him. But we can see it's to all Haemophilia Centre doctors. It's for urgent and immediate attention. And then we can see in the first main paragraph reference to the toolkit which I think are the documents that we have just been looking at.

A. Yes.

Q. And then the actions are:

"To brief Centre staff to ensure we can get letters out to all patients so that they're given comprehensive information at the same time. The letter to patients needs some insertions, telephone numbers, et cetera, and should go to all patients or parents of children with haemophilia and other bleeding disorders. If possible, use the letter as sent. Some may wish to adapt because of local reasons. Ensure you file copies in each patient's notes."

Then this:

"It's felt that all patients need to be informed, even those not affected so that they are informed about the events and understand the implications."

Does it follow from that that UKHCDO, in

relation to this exercise, had decided to go further than the, as it were, minimum requirements of the VCJD Incidents Panel because your proposal was to communicate with every patient, whether or not they'd ever received British products within the relevant time frame?

A. That's an interesting question. I think -- I can't remember whether the Incidents Panel wanted us to write to everybody, or whether it was a UKHCDO decision, to be perfectly honest. But I think, whether it was or not, we certainly felt that we needed to inform all patients because the patients would not necessarily know whether they'd had British blood products or not, and they might think they were involved. And so when we spoke to the patients, we gave all of them a certain amount of core information, whether they were affected or not, and then put it into a personal context.

So if we, for example, knew that they had not been exposed to UK products during that period, we could tell them that and say, "Well, now you know all about -- all that we know about variant Jakob-Creutzfeldt Disease, but it shouldn't affect you". And with the others who had had British blood products at that point, we were still in the process

of working out which batches were affected and assessing the level of risk. And so, you know, you wouldn't be able to attribute a level of risk at that point, but you would be able to tell them whether they'd had British blood products and might be involved. And so I don't really know the answer to your question, but that was our thinking.

Q. And we can see the exposure assessment form that you referred to at WITN3289116.

Again, we can see this is part of the 7 September 2004 production of documents, the date at the very bottom of the page.

This is a form to be completed for all patients with bleeding disorders. And then a copy should be sent to the National Haemophilia Database. There's the start question:

"Did the patient received any UK sourced pooled factor concentrates or anti-thrombin between 1980 and 2001?"

"Yes" or "no" gives the answer to whether the person is at risk of vCJD for public health purposes.

There's then an exposure assessment, so that's an analysis undertaken by reference to each individual patient.

Then over the page, we can see the last box

asks the question:

"Has the patient asked to know if they received the implicated batch? When was the patient informed if they'd received the implicated batch?"

The purpose of that last box was presumably to ensure that patients received the information that they wanted to but were allowed to choose not to receive information if they didn't want to.

A. That's right. I started to explain that earlier but didn't really finish. Because it was such an unusual situation in that there was no test that we could offer them and there was no treatment, we realised that some patients might prefer not to be told. So they were all provided with the background information about variant Jakob-Creutzfeldt Disease, transmission by blood transfusion, at the very least theoretical risk of transmission through pooled blood products, what we thought the risk was, the business about it having only affected homozygotes who made up about a third of the population and so on.

But in relation to their own exposure, they were offered the choice of being told or not. But it was important to document that choice, both in the notes and centrally, so that you could continue to respect that choice or, at the very least, if there

were overwhelming reasons to tell them, put the choice to them again.

Q. Your statement tells us that not all patients could be traced.

Do you know what steps were taken, first of all at Manchester in your capacity as Director of the Centre, to trace patients, or was that not a problem that affected Manchester?

A. I don't remember it being a particular problem at Manchester. There are always some patients, particularly those with mild bleeding disorders, who are lost to follow-up and need a lot of chasing. I can't remember whether it was a particular problem in relation to this.

There were also problems, of course, tracing who had received the implicated batches; I detail in my Section 9 response.

Q. Then if we move from 2004 to 2006. Could we, Soumik, have ABMU0000053, please. So if we just going a little closer.

This is an email from you at 14 November 2006:

"VCJD and plasma products: look back and patient notification."

This is being sent by you now as Chair of UKHCDO to Centre Directors and you refer in the body

of the email to:

"... two further batches of concentrate which include donations from patients who subsequently developed vCJD, relating to products released in 1988 through the Transfusion Service in Tooting, Wales, Colindale and Birmingham, not previously notified because it was not possible at that time to trace their distribution. If you received these products, you may have to notify your patients."

Then if we go over the page, we don't need to go through the detail of it, but we can see this is a letter explaining that there have been these two further batches identified that weren't included in previous notifications.

And is this right: essentially, what Centre Directors were being asked to do in 2006 was to check their records to see if they had received these batches, and if they had, to then go through the same exercise in relation to those batches as had been done in 2004.

A. Yes, and we were also trying to stir up some centres that had not responded, in our view, adequately to the first request.

Q. We then, I think, next see vCJD in 2007.

Soumik, could we have HCDO0000131_006, please.

So again, this is an email from you. This is January 2007. And then we see, if we go over the page, a draft press release. So this tells us that there's been a fourth and therefore presumably a third case, because we'd previously looked at cases 1 and 2 having triggered the 2004 notification -- a fourth case of vCJD associated with blood transfusion. So this is a draft press release from the Health Protection Agency.

And then if we go, please, Soumik, to HCDO0000131_007. And zoom in on the top half of the page.

This is an email from you in your capacity as Chair of UKHCDO, 16 January 2007. You were, I understand, in this email, notifying all UKHCDO members about this fourth case. The second paragraph explains that:

"The case contracted vCJD from the same donor as the third case."

And then refers to the patient having been still alive and manifesting clinical signs of suspected vCJD eight and a half years after receiving the blood.

"This is the longest incubation period reported so far in relation to this mode of transmission.

Then the second paragraph explains that:

"This patient had been treated in the '90s with several batches of UK sourced clotting factors, including one batch of Factor VIII that was manufactured using plasma from a donor who went on to develop vCJD."

Then it explains that:

"The haemophilia patient was in his 70s when he died of a condition unrelated to vCJD, 11 years and 1 month after receiving the batch of implicated Factor VIII."

Then the significance of this, we can probably pick up from the last two lines of this page:

"This is the first time that vCJD abnormal prion protein has been found in a patient with haemophilia or any patient treated with plasma products."

Then if we go over the page, we're told that the case doesn't change the public health vCJD "at risk" status of any patient, but then doctors, directors, are asked to take these actions:

"Send the enclosed letter to all patients with bleeding disorders (including those not at risk of vCJD). Please do this as quickly as possible."

And then:

"It remains the case that vCJD has not been reported in recipients of non-cellular pooled blood products. This does not, therefore, change the advice that we would offer our patients, and we were not planning a mailing to patients."

Do I understand this to be you communicating news of the fourth case to Directors, but because there were no new implicated batches, there was no further notification exercise to patients; is that right?

A. Yes. It strengthened the evidence that variant Jakob-Creutzfeldt Disease could be transmitted by a whole blood transfusion, but it didn't actually change anything that we would have advised the patients, or any of our actions. And so it was felt that a further notification exercise would be superfluous.

Q. Then there was then a further national notification exercise in 2009. Soumik, could we have WITN3289130, please.

We can see this is a letter from the Health Protection Agency's CJD section, February 2009, to all UK Haemophilia Centre doctors informing them of:

"A post-mortem finding of asymptomatic vCJD, abnormal prion protein in a person with haemophilia."

"Make arrangements for appointments with any concerned patients."

Then we can see it encloses information leaflets for both patients and for healthcare staff.

I don't think we need to go through the detail of those leaflets -- you've exhibited them to your statement -- but can you give us, again, an overview of what triggered this 2009 exercise and how it was implemented by UKHCDO and by you in Manchester?

A. Well, the significance of this particular case remains uncertain, but it was certainly potentially evidence of possible developing variant Jakob-Creutzfeldt Disease in a patient with haemophilia, presumably secondary to exposure to an implicated batch. The patient did, in fact, die from carcinoma and had no neurological signs or symptoms, and prion protein was not found in any other parts of the autopsy. So there's no evidence of abnormal prion protein in the patient's brain, so it was just one little corner of his spleen.

So the significance of this wasn't known, but there was certainly the theoretical possibility that had the patient not died of cancer and, say, lived another few years, he might have developed variant Jakob-Creutzfeldt Disease. We'll obviously never

know.

I seem to remember that the patient was atypical also in that I don't think he was a homozygote for prion. I think he was heterozygous, which was also a little odd. And, of course, it was 11 and a half years after his exposure to the implicated batch.

So whatever the uncertainties surrounding the interpretation of these findings, it was felt reasonable to inform the patients that this was perhaps evidence of transmission. So we wrote to all our patients again.

Q. And so, as with the 2004 notification, this was a nationally organised and directed notification, to the extent that there was actually a template letter which we won't look at the leaflets but we'll look at the letter. WITN3289132. This is the letter you were being asked to send to patients.

We can see at the bottom it says it doesn't change the way in which the patient will be treated. So the purpose of this national notification presumably was to ensure that patients had the maximum, up-to-date information for them to understand the position and apply it to their own personal circumstances?

A. That's right.

Q. And then we can see the UKHCDO letter from you to your colleagues at WITN3289133, please, Soumik.

This is a letter dated 16 February 2009 from you:

"Dear colleagues ..."

And it says:

"Unfortunately, due to circumstances beyond our control, this notification exercise has to go live on Monday, February 16, 2009."

And you go on to explain there that the timing has had to be accelerated because the matter's being picked up in the national press.

A. Yes. We preferred them to hear from us.

Q. Can you recall the kind of responses that your patients at Manchester showed in relation to this second notification exercise?

A. Well, it varied. Some were distressed. Some were philosophical. Most of them thanked me for telling them. It did vary. Because apart from everything else, this was a little different from HIV and hepatitis C in that, you know, we had at this point been following it for a long, long time already. And, you know, we had been looking out for it, and frankly when Jakob-Creutzfeldt Disease presents clinically,

although it's very rare, it's a pretty easy diagnosis, and we hadn't spotted anything. So it seemed likely, at that point, that even if some patients did become affected, the numbers affected were likely to be quite small.

And so I do not remember very much distress. I don't suppose the patients were very happy about it, but most of them seemed philosophical, and there wasn't much they could do about it, to be honest.

Q. There's a follow-up letter, then, in April 2009 from you and Professor Hill to directors. WITN3289120, please.

We can see it's a letter to update on the current position. Point 1:

"The index patient investigation is continuing, and risk assessments are awaited on the four potential routes of acquisition of vCJD prion."

What does that refer to, please, if you can remember?

A. Err ... I'm not quite sure what that means.

Q. Don't worry.

A. Potential routes of acquisition of variant CJD prion. I mean, there is always the possibility, of course, that the patient had not acquired this from blood products at all but from a beefburger, which you also

can't exclude. And I think that they may be referring to that.

Clearly, the patient had been in receipt of an implicated batch, and you would not be able to exclude that as the route, but there were other possibilities.

Q. And then the second point in the letter is about the notification exercise. And you record here that:

"Many centres wish to only contact patients in the 'at risk for health purposes' group. Some Centre Directors, including some appointed since 2006, realise the 'at risk' status of their patients had not been determined, and patients who had received implicated batches had not had their notes identified as at risk for public health purposes. In some instances, there are contaminated instruments that need identification and public health follow-up to identify other patients who have been put at risk."

So what is it that you, in your capacity as Chair of UKHCDO and/or in your capacity as director of the National Haemophilia Database by this time, what had you learnt about the notification exercise that gave rise to the need to write this letter?

A. Well, a number of Centre Directors had retired and replacements had taken up post and, of course, were not necessarily familiar with the previous

notification exercise since they had been juniors when this took place. And the most recent notification had alerted them to all this and then they had gone away to find out which of their patients were implicated, and realised that the previous instructions had either not been followed or not followed adequately. And they had notified us, the Database UKHCDO, of this, and there was a catch-up necessary.

They would also realise that if that was the case, then, since at-risk patients had not been identified, and had maybe had surgery, that they might have had the sort of surgery that was listed as a risk: gut surgery, that sort of thing, lymphoid surgery, with non-disposable instruments, which would have to be traced.

Q. Then if we go over the page, we can see in the top paragraph, you set out that you're aware:

"... there have been no notifications of at risk patients from some Centres to the [National Haemophilia Database] ... [or some] Centres have not accounted fully for the total units of implicated products they received."

Without going through the detail of the rest of the letter, as I understand it, the proposal here was that the National Haemophilia Database would tell each

centre what information the database currently held in relation to patients at that centre insofar as relevant to this issue, so that centres could effectively work out what data was missing and what they needed to submit to the database. Is that an accurate summary?

A. Yes, that's accurate.

Q. There's a follow-up letter. I don't think we need to go to it, but there's a follow-up letter from this that you sent out in June 2009, that you've also exhibited to your statement.

There was then, in 2010, an issue with a mistaken or false notification. Can you outline what happened there, please.

A. What happened there was that some of -- when we originally worked out the period of risk, it was expressed in terms of years. And the problem with that is that towards the end of that period of risk, BPL were beginning to manufacture products using imported American plasma so that you had circulating at one and the same time BPL products that had been manufactured from British or American plasma. And as a result of that, some of the patients who had been notified that they were at risk, it turned out had been treated with US-sourced BPL products rather than

UK-sourced BPL products. So this applied to a very small number of people using specific products. So it applied almost exclusively to two centres: the Royal Free and Oxford.

The Royal Free in particular because it related to Factor XI concentrate, and the Royal Free looks after possibly the largest group of Factor XI deficient patients in the country, and they used concentrate to treat those patients rather than plasma. I've probably got the second largest group in the country, but my treatment practice is different, so it didn't affect us.

So we realised that some patients had been told that they were at risk but were not, so we had to identify those, and notify them.

Q. And we can see from WITN3289134, this is the letter that was then sent out by you on 7 April 2010 to all UKHCDO Centres and all haemophilia nurses. It reads:

"I have been told that a centre [that was in fact the Royal Free] has mistakenly identified and notified a number of patients that they were at an increased risk of vCJD for public health purposes. These patients had, in fact, only been treated with BPL products manufactured from American sourced plasma. I am writing to all Haemophilia Centres

asking that all past vCJD risk notification are checked because I suspect that this error may have been repeated in other centres."

So the matter having been raised with you, as I understand it, from other documents that you have exhibited to your statement, by the Royal Free, all centres were asked to do a check on their notifications. Do you know how many centres or how many patients turned out to have had the same problem as the Royal Free?

A. Well, the main other centres that are mentioned that were affected was Oxford. Most of the patients affected were at the Royal Free. I can't remember the precise number that were affected, but I think it was something like 20 patients.

Q. Then in 2013 there was what has been referred to in the materials as a "de-notification exercise".

So if we look, please, Soumik at WITN3289136.

We can see this is letter from the Health Protection Agency dated 24th January 2013 to Dr Dolan, who by now had taken over as chair of UKHCDO.

"Reassessment of vCJD risk from UK produced plasma products and de-notification of certain recipients."

We can see there's been a review by the Health

Protection Agency of the risk assessment which has led to recommendations that:

"... individuals who received Factor VIII and Factor IX between 1990 and 2001 should remain notified as 'at ... risk of vCJD for public health purposes'

...

But:

"(ii) Individuals who only received plasma products between 1980 and 1989 should now have their treatment history reassessed to confirm this fact and if it is confirmed, they should be de-notified."

Then if we go to the letter sent out by Dr Dolan to Directors, it's WITN3289137.

This Dr Dolan, enclosing the HPA letter, the recommendations. It says:

"Please do not take action immediately. What we have agreed is that NHD [the National Haemophilia Database] will review the records and generate lists for each Centre. These lists will then be sent to each Centre to be verified. There should be formal communication between each Centre and [the National Haemophilia Database] to confirm the risks and discuss any errors.

"In the meantime the UKHCDO Executive, NHD and Morbidity and Mortality Working Party will work on

producing information which will be of help in discussions with patients who are to be 'de-notified'."

And without going through the detail of the remaining documents on this issue, can you set out what then happened in terms of the de-notification exercise, from your perspective?

A. Well, we produced spreadsheets based on their previous returns from each centre, which had lists of patients that we considered could possibly be de-notified. There was then a dialogue between each centre and the database to fill out any missing data, and produce a final corrected list of patients who should be told that their risk had been reassessed and they were no longer considered to be at public health risk.

This took a little time. I think it was quite a lot of work for the database and for centres, but we wanted to get it right, as you can imagine, given the history of this exercise, and its complexity.

And then the patients were notified by the centre. It was not clinically urgent. I think most centres would have discussed it at the next patient appointment.

Q. And then in terms of the current position, does the --

A. I forgot one important thing. The other thing is that

they changed the policy in relation to endoscopes and disposable instruments. And so we all had to take these out of quarantine.

Q. I'm going to ask you about that in a moment, but just in terms of this information, in this letter, does it remain the case in terms of the current position, as at 2020, that individuals who received Factor VIII and Factor IX between 1990 and 2001 are regarded as at risk of variant CJD for public health purposes?

A. Yes.

Q. Then in terms of the practical consequences of being so regarded, could we have, please, BART0000924.

This is an annual general meeting of UKHCDO, 13th October 2005. If we could go, please, to the fourth page. No, sorry, that's the wrong document. I think on my note it's the wrong document.

Well, we can look at this and pick up the picture from this, I think.

Could you just go back to the front page, please, Soumik. and could we go on --

So this is a meeting on 16th May 2005. There's then a second meeting in October that we'll look at.

If we could go on to the next page, please. And the next page. Yes.

So under the heading "vCJD Issues", the second

paragraph reads:

"Endoscopies: Charles Hay reported the trouble Manchester is having with endoscopies. From an ensuing discussion it was clear that different policies are being pursued in different centres."

Then there's a reference to updating information on the website.

What was the trouble that Manchester was having with endoscopies and how was it resolved, if at all?

A. Well, the problem was that endoscopy, because there's a lot of lymphoid tissue in the gut, was considered a potential risk for transmission. So the worry was that an endoscope could transmit variant Jakob-Creutzfeldt Disease to the next patient that used it, for example. I mean, endoscopes are obviously cleaned in between use, but prion protein is quite sticky, and we didn't have any evidence to know whether the cleaning procedure for an endoscope would get rid of prion protein were that instrument to be contaminated with it.

There eventually emerged evidence suggesting, for example, that metal instruments used during surgery, if they were also cleaned several times, probably would be safe, but that evidence wasn't around right at the beginning.

So the instruction was that if you used an endoscope in a patient that was considered at high risk, you should quarantine that instrument and only use it for that patient.

So we had a growing number of endoscopes with my patients' names on them, that couldn't be used for anybody else. And in fact, I had one patient with type 3 von Willebrand's disease who required repeat endoscopy using a double-balloon endoscope, which is a particularly expensive instrument, costing £50,000, and we actually brought one just for him.

Eventually my hospital had something like three-quarters of a million pounds' worth of endoscopes in quarantine. And that was at least three-quarters of all the endoscopes in the hospital and was threatening the endoscopy service with collapse through lack of instruments.

Now, the situation was eventually improved because the Department of Health made money available for the purchase of additional instruments.

I think some other centres were perhaps not following this policy as assiduously, but my understanding is that it was a problem in most really large Haemophilia Centres, like the Royal Free, because if you have a large number of patients, you're

bound to need to endoscope some of them on a fairly regular basis.

Q. And you said, I think a few moments ago, when we were talking about the 2013 de-notification exercise, that there had been a change of policy in relation to endoscopes.

A. Yes. Well, there was a change in policy overall, because that reassessment was more wide ranging than merely reassessing the period of risk. It reassessed the level of risk.

Now, if you remember right at the beginning, they admitted that when they assessed the risk of transmission through blood products, way back at the beginning of this exercise, the vCJD Incidents Panel always used their most pessimistic assumption. Now, I remember at the time wondering how they could make any assessment at all because so little was known. There were so many variables. And I saw the calculations and the assumptions themselves ran to two pages of A4 single-spaced ten point type. So the only way that they could make any sort of assessment at all was by making educated assessments and lots and lots of assumptions.

Now, it became clear by 2009, far less the later period, that these assumptions had to be far too

pessimistic, because if they had been correct, we would have seen tens of patients with variant Jakob-Creutzfeldt Disease, and we had seen none. And so when they made the reassessment, they had to take into account what we observed in the previous decade, ie, zero, so they changed their assumptions and they revised their assessment of risk downwards in general.

So we changed the period of risk and we also revised downwards our assessment of the risk to those who continued to be considered a public health risk.

So it was no longer felt necessary to quarantine surgical instruments, to use disposable instruments, and/or to quarantine endoscopes at all.

Q. You referred to "they" reassessing the risk in that regard, was that the Health Protection Agency?

A. Yes, and the variant Jakob-Creutzfeldt Incidents Panel. Yes. It wasn't our -- not our assessment.

Q. We have heard both from individual patients and through the statements of some clinicians that there were centres where the practical implications of the policy over the years that it was in place was that there were occasions where surgery was deferred or cancelled, often at short notice, because of the concern about instruments. Was that a problem in Manchester?

A. I think it was a problem everywhere. It was a problem that we tried to mitigate. Operations got cancelled sometimes when people seemed to realise at the last minute that the patient was at risk. You could minimise cancellations by planning the whole thing, so that you should identify who was and was not at risk in advance of surgery, so that appropriate disposable instruments would be available, for example.

Q. Before we leave the topic of vCJD completely, there's just one issue I wanted to ask you about arising out of some of the exhibits to your statement and the vCJD surveillance study. I'm not going to ask you about the detail of that work because we have that covered in documentation elsewhere, but if we have WITN3289148, please.

This is a letter, it's from Professor Hill, dated 22nd June 2007, but you've exhibited it and it relates in part to the database so I'm hoping you can help us with it.

It refers to Professor Lee having obtained ethical approval for a number of studies relating to vCJD, haemophilia and implicated products.

And then below the two numbered paragraphs there's a paragraph that says:

"With regard to the post-mortem studies, we

have obtained a list of patients with haemophilia whose Death Certificates indicate that there may have been a post-mortem or a post-mortem may occur. These names are being linked on the Database and I will be writing separately to enquire if you can check if a post-mortem has taken place and whether or not material is available. James Ironside has indicated he will be prepared, as in the original submission, to look at relevant material."

So there appears to have been a proposal to study material obtained either from post-mortems that have already taken place or from post-mortems that may take place prospectively.

I just want to show you two further documents and then ask you questions about it.

If we have please, Soumik, WITN329150.

So this is a draft consent form for seeking consent from the next of kin for results of post-mortem examination. Reference is made in the bold print to the concern about vCJD and the proposed prospective and retrospective surveillance study that was being undertaken.

It contains provisions for the relative to agree to the post-mortem examination being performed. It explains samples will be sent to the National CJD

"In the period 1985-1998, at least 88 postmortems were performed out of a total of 1,300 haemophilic deaths (as reported to the UKHCDO Database). Wherever possible, centres should establish the extent of their postmortem material and refer relevant sections to the CJD Unit following liaison with the study coordinator. Help with the tracking and retrieval of specimens may be available.

"No additional consent is required for this.

"In the case of biopsy material available in deceased patients, similar action should be taken. Where the patient is still alive [presumably in relation to biopsy material] consent would be required for such an examination using the retrospective analysis consent form".

It would appear that in relation to the retrospective study of post-mortem material and, indeed, biopsy material from deceased patients, there was no intention to notify relatives or seek their agreement. I'm seeking to establish this as a matter of fact. Is that your understanding from this material?

A. That's my understanding. I know that they took this question to the Ethical Committee, and it was discussed also with the CJD Unit in Edinburgh. And it

Surveillance Centre in Edinburgh, where they will be examined, that the results will be available to the relative. And then it provides:

"It is ... your decision as to whether you wish to be informed specifically of the results of the tests for vCJD."

And then provisions made for the relative to sign.

As I understand it, that addresses the question of obtaining consent from the next of kin for post-mortems postspectively, so any post-mortems that might be undertaken following the production of these documents.

If we go, please, Soumik, to WITN3289151. We can see this is a further document relating to the proposed vCJD surveillance study. We can see data is going to be collected through the National Haemophilia Database.

If we go to the third page, please, Soumik.

We can see, under the heading "Prospective study of postmortem material", provision is made for consent to be obtained from relatives, and we've just looked at a sample form.

In relation to the "Retrospective study of post-mortem and biopsy material", it says this:

was the Ethical Committee's opinion that we didn't need to. I wasn't involved in that, but I know that this issue was examined.

Q. Do you know whether in your capacity as director of the Manchester Centre or in your capacity as director of the National Haemophilia Database, the extent to which centres hold post-mortem material that would have been covered by this study?

A. Well, that's part of the problem because I don't think that they do. You know, after the Alder Hey scandal, retention of material was dramatically reduced. The Human Tissue Act has a lot to say about the retention of material. And so retrospectively there is little or nothing available.

And the sort of deposit, tiny deposit, of prion protein in the spleen of that patient that we reported in 2009 would not have been picked up by a standard autopsy. A standard autopsy would have completely missed it. It's not a microscopic appearance that we're talking about. It's carefully slicing up the spleen and using a very specific stain to see what you're looking for. So you have to be looking for that specifically.

So frankly, the chance that this would have picked anything up was relatively slight anyway. So

I don't think there were large amounts of retained material.
Q. Do you know what the position is in relation to Manchester specifically when you became director in '94 --
A. I'm sure we had nothing. I know that I -- as a centre, we contributed nothing to this study.
MS RICHARDS: Sir, I note the time, and I'm about to move on to another topic, so would this be the right moment to take the break?
SIR BRIAN LANGSTAFF: Yes, it would. We'll take a break for half an hour as usual, allow you to get a cup of coffee, and we will be back at quarter to 12.
MS RICHARDS: Thank you, sir.
SIR BRIAN LANGSTAFF: Quarter to 12.
(11.16 am)
(A short break)
(11.46 am)
SIR BRIAN LANGSTAFF: Yes.
MS RICHARDS: Professor Hay, I'm going to ask you next a handful of questions about the functioning of UKHCDO, to your knowledge, in light of the roles you've held within UKHCDO, and about the National Haemophilia Database.
Could we please have on screen, Soumik,

WITN3289082.
This is a constitution for the United Kingdom Haemophilia Centre Directors Organisation dated September 1991, and if we go over the page we see what was there being set out, it's:
"... non-profit making. It exists to promote the provision of the higher standards of care for patients with Haemophilia and other Inherited Bleeding Disorders.
"Its functions and purposes also include -
"a) the collection and analysis of statistics;
"b) the initiation of research;
"c) the provision of professional advice to other bodies;
"d) the diagnosis and treatment of inherited thrombotic disorders within those Centres which elect to participate in this activity."
Now you became a member of UKHCDO in 1987, so about four years before this. As far as you know, was this the first time there had been some form of written constitution?
A. Yes, this corresponded with the organisation becoming a registered charity, and we took advice and decided we needed a constitution partly for that reason.
We also reviewed the membership. When I became

a member, it was a member of Haemophilia Centre Directors. So although the initials of the organisation have remained the same throughout this period, it's at this point that the membership was widened to include all doctors involved in haemophilia care. So it becomes the UK Haemophilia Doctors Organisation.
Q. Prior to this, and if you don't know the answer to this, because it may predate '87, then please say so, were there any materials that set out the way in which UKHCDO was organised or would function in any written materials?
A. Not as far as I'm aware.
Q. Sorry, professor, carry on.
A. Well, you know, I might have missed something but I have read a lot of the older minutes, recently.
Q. Then if we go to page 6, we can see here there's a list of regional centres. Now previously we've -- I've been referring to, and they were referred to in the minutes, as "Reference Centres". This seems to include what were the Reference Centres but add a handful of other centres such as Liverpool, Newcastle, Norwich, Truro, and Lord Mayor Treloar College. Was this the point at which the concept of Reference Centres changed to a concept of regional

centres and became slightly broader?
A. I think that had happened already, at an earlier stage. The Reference Centres were only ever about five centres. I think they included Sheffield, Manchester, Oxford, the Royal Free and St Thomas', and that was about it. Maybe Cardiff, I'm not sure.
Q. Cardiff and Edinburgh --
A. Yeah ... well, yeah. They were centres of reference and the Organisation of Haemophilia Care in the UK changed from time to time. There was a health service circular -- HSC197630, I think -- which described the Organisation of Haemophilia Care in the United Kingdom, and I think at that stage divided Haemophilia Centres into Reference Centres, Haemophilia Centres, and Associate Centres.
And that was subsequently changed with HSG9330 -- 93, I can't remember the second name -- the second number -- which introduced the concept of Comprehensive Care Centres and Haemophilia Centres, depending on the level of service that they provided, and giving criteria for the designation. And that was subsequently audited, so that if you wanted to become a Comprehensive Care Centre you had to have an audit, and the level of service you were able to provide was audited anyway.

Q. And in terms of the chair of UKHCDO, this constitution provided for an elected chairman with a three-year office that could be extended to six years.

Do you know, prior to this, what the arrangements were for selecting the chair even?

A. I think they were more informal. This formalised things. I think the chair -- I'm not entirely sure, to be honest, because I couldn't come across anything written.

Q. That's all right. In terms of -- I'm sorry, carry on.

A. I think the chair would be elected by affirmation in the past. It can still happen, because what happens is that the chair sends out an invitation and anybody can apply, and if there are more than -- if there is more than one applicant, and they have to have a proposer and seconder, then an election takes place, of the entire membership. So all the members vote.

If there's only one applicant, and they are agreed, then they may be elected unopposed.

What people frequently do is they canvas to discover what their support is and then they may or may not apply, depending on how much support they feel they've got. Similarly for the other post holders, the treasurer, the vice-chairman, the secretary.

Q. Over the time of your involvement with UKHCDO, so

either the period from '87, since you've been a member, or '92, since you've been an officeholder, how has UKHCDO been funded as an organisation?

A. Well, it has very little funding. It's a registered charity. Charities are not allowed to trade. Before that, its only source of income was the annual general meeting, which generally generated a profit of something of the order of £20,000 to £30,000. When this new constitution became into being it was also decided that the members should pay an annual membership fee of £20. That brought in something of the order of £1,500 to £2,000. It was recently abandoned because it was considered that it was more trouble to collect than it was worth.

Q. Again, over the time that you've been involved, to what extent has the organisation received funding from the Department of Health?

A. Well, the charity hasn't received very much funding. After it became a charity, the organisation had to form a trading arm. This is very common amongst learned societies and so on, if they're registered as a charity, because the source of the profit for the annual general meeting would be industry and BPL coming along with a stall and giving sponsorship for the meeting.

And prior to being a charity, that was fine, but once we were a charity, you couldn't continue in this way. And so the UKHCDO limited company was formed, initially to deal with the membership fees and to deal with the annual general meeting, and, at a later date, also took under its arm the National Haemophilia Database.

Now, in the very early stages of the organisation, shortly after being formed, the organisation did receive some funding from the Medical Research Council, predominantly to look at hepatitis, but I don't know that it received very much direct funding from either the NHS or the Department of Health.

Latterly, during my involvement, we did receive funding from the Department of Health, partly to support our involvement with national procurement and various other projects.

Q. So is this right, and please correct me if I'm wrong, that the Department of Health does not provide a regular ongoing amount of funding to UKHCDO, but has funded UKHCDO to undertake or work on particular projects? You mentioned national procurement; I think I've seen some reference in the papers to UKHCDO's work in relation to recombinant, there having been

possibly some funding in relation to that.

A. Yes, yes, that's correct. When I took over the database, the big problem was it had previously run with no funding per se but had effectively been supported by the Oxford Health Authority in that they had paid the salary of Rosemary Spooner and a part-time secretary who helped Rosemary Spooner. Those were the only paid staff running the database back then.

Now, when I took it over, it appeared to me that the database is withering on the vine and for it to be sustainable it would have to be brought up to date and to produce more interesting data, because we produced an annual report at that point, but it wasn't producing very much research, and the data wasn't timely enough to be of interest to the Department of Health.

As far as I could see, the data would be of use for Department of Health planning purposes, which would benefit the patient group as a whole. And so I approached the Department of Health and had conversations with, amongst others, Julia Stallibrass to talk about the potential for getting funding from the Department of Health, and she very reasonably said to me what I've expected, and that was, "Well, you've

got to produce something of interest, and we would think about it."

And so at that time we passed the hat around industry and for a year or so we funded the database through unrestricted grants from various suppliers.

Then there were these project grants that came along, but funding was insecure, which is, to be honest, the fate of disease databases, many of which fold after a short period of time, through lack of funding, and we clearly wanted a regular income stream so that the database could develop and become more useful. And the Department of Health did facilitate this. Apart from providing us with project funding for various projects that were obviously important, they facilitated discussions with the commissioners so that the commissioners now provide us with a lot of funding, which we charge them on a pro rata basis according to the population served, so we get funding from NHS England, the lead purchaser, which I think is the London Consortium, NHS Scotland, and NHS Wales.

Q. You referred to there being, in the early stages of the establishment of the new database, your words I think were "unrestricted grants from various suppliers".

A. Yes.

Q. First of all, by "suppliers" you mean pharmaceutical companies?

A. Yes, that's exactly right. Yeah.

Q. What do you mean by "unrestricted grants"?

A. An unrestricted grant is an unconditional grant. I've always felt it was -- they're always described as "unrestricted grants". I've always felt that it was probably the wrong word to use, but there you are. These are grants that are given without conditions, which would be an absolute prerequisite for the organisation.

Q. And other than funding from pharmaceutical companies towards costs of the National Haemophilia Database, what other funding has UKHCDO received from pharmaceutical companies, to your knowledge, over the years you've been involved. There's the sponsorship of the AGM.

A. Yes.

Q. Has that continued to receive pharmaceutical company support?

A. Yes.

Q. And what other kind of matters are funded by pharmaceutical companies?

A. Well, sometimes we get unrestricted grants from industry to fund non-commercial research, for example

the -- several companies shared the cost to support research into risk factors for Factor VIII inhibitor development. Sometimes they come to us with a request for an analysis, for example of how their products are used, and we would provide them with an anonymised aggregate report focusing on the use of their product, which is useful market data, and we would charge them for that.

Sometimes they need this to deal with an argument we had with NHS England, for example, in which case the data is provided to NHS England and to the pharmaceutical company, exactly the same data, but the pharmaceutical company will have to pay for it.

An example of that is the recent discussion between Sobi and NHS England about the relative efficacy of their extended half life Factor VIII, and whether, because of its extended half life, you may need fewer units, and whether their product reduces the annualised bleed rate in the patients using it, for example.

And that's the sort of question, to be honest, we welcome, because it's a question that's of interest to everybody. And it helps NHS England to make its own planning decisions.

Q. Do you know whether there is any record of amounts

received by UKHCDO, either from pharmaceutical companies or the Department of Health, prior to 1987?

A. I don't know of any such record. The organisation was running on a far more amateurish basis compared with now. I mean now the database has a manager. Obviously since we've been operating as a company, we have had a board of directors. Their accounts are all audited and have to be submitted to Companies House, and we have detailed financial records from them.

Q. I want to ask you a little more about the National Haemophilia Database itself. In what year was the database formally established and management transferred from Oxford to Manchester?

A. Well, the database was established about the same time that Haemophilia Centres were established, way back in 1968. And it started under the leadership of Rosemary Biggs, who was the then Centre Director in Oxford and an international authority on blood clotting in the UK. In fact, I think the first clotting textbook I bought was written by her. And Charlie Rizza worked with her. He took it over when she retired, and initially they were attempting to address simple basic questions that were not known. For example, how many patients with haemophilia are in the UK?

And initially, it was very much focused on

haemophilia A and B. And in the early years of the database, they didn't consider any other diseases, not even von Willebrand's disease, for several years. I'll give you a history of all of this in the final chapter of UKHCDO's rule 9 response.

The database developed a little bit over subsequent years. And then in about 1999, I became more involved with the database because it needed to be upgraded technically, and I employed a software engineer who had written the Haemophilia Centre information system that I used in my centre, amongst other things. And we went down to Oxford to assess its technical requirements and, from that point on, liaised closely with Miss Spooner, who was running it.

And then in 2001, she retired. It might have been 2002. But her imminent retirement precipitated a bit of a crisis because, as was the case right across the UK, Oxford Health Authority reviewed all its posts as they felt they could and resisted attempts from outside organisations to get them to pay for what was a national function. So, you know, this is a little district Health Authority, and it's employing one and a half people for a national function, and it didn't want to continue to do that. So her post was threatened with not being refilled.

So the organisation had to consider the future of the database, and so I was the chairman of the Data Management Working Party at that point. And we put up a proposal. The organisation summoned Oxford and Manchester to put rival proposals to the executive and the Advisory Committee, and then they decided that they preferred my proposal, and so the database was moved to Manchester.

Q. Now, one of the issues that has arisen in relation to the database over the years in the various minutes that we have amongst the Inquiry's materials is the question of patients' consent to information about them being provided to the database or being held by the database.

In some of the materials that you have produced over the years, what appears to be said is that prior to 2000, there was no consent process in relation to the collection of that material, and it was the Data Protection Act coming into force that then triggered a series of debates that play out through the minutes of various meetings about what form that consent should take. Is that an accurate summary?

A. I think that is an accurate summary, but I think a little context might be helpful.

Like many historic databases, the database

started in a very different climate. And back in 1968, there was no data protection legislation, and since we were not conducting interventional research, I think it was felt perfectly reasonable to collect and hold this data.

There was some data protection legislation prior to 1998, but the 1998 Act harmonised this legislation across Europe and tightened things up considerably. And I was a member of the Information Technology Working Party and then chairman of the Data Management Working Party, both of which fulfilled the same role as a sort of oversight committee for the database.

And the Information Technology Working Party, chaired by Brian Colvin in the late '90s, began to address this question. And I think we began to think, well, we weren't keeping the database a secret; the Haemophilia Society knew about it and so on, but we suspect that many of the patients did not.

I think you've taken evidence from previous medical witnesses who have told you that they don't think that patients were being asked about the database back at that time, and I think that that is probably correct.

So, you know, as with so many historic

databases, it was a matter of catching up and taking advice on what was reasonable, and opinion on what was reasonable did change with time. So we established around 2000 -- our opinion was that the patients needed to be actively informed about the database, the data that was being held, the uses to which it was being put, and of course their rights under the Data Protection Act of 1998. Although the Act is dated 1998, there is always a gap before the conditions come into force. But we needed to inform the patients that they had rights under the 1998 Act, and that these included the right to have their data withdrawn.

Now, my personal starting point to take advice was to go to the Information Commissioner. Now, the Information Commissioner was based in Data Protection House, which is on the main street, or off the main street in Wilmslow, about three or four miles from where I am now. So it was particularly convenient to make an appointment to go and speak to a case worker to outline our situation with them, and to outline our proposals for addressing it. They were extremely helpful.

They felt that the NHS purposes to which we were putting our data, any reporting to the NHS that took place -- of course, at that time, there was very

little -- did not require any form of consent. Just as you don't give consent when you go along to a hospital or the GP, but it is assumed that they will handle your data and that they will handle your data securely. But any further purposes, for example research or sharing anonymised data with third parties, would require consent.

There then followed a debate about what the nature of that consent should be. Should it be -- and of course a lot of this consent would have to be obtained retrospectively because we had held those patients' data for a considerable period of time anyway.

Should that consent be written consent, or would implied consent be adequate? Now, implied consent is informed consent, as for written consent, but with an opt-out. And that was the pattern that was adopted by disease databases right across the UK. And the Data Protection Registrar considered that that was adequate, and so that was the form of consent that we had. But we had to have a process whereby we made sure that the patients were aware of the database and their right to an opt-out.

So we produced a series of leaflets. I have included all of the leaflets as exhibits to my rule 9

response. And you will see that they were reviewed at irregular intervals throughout that period and reissued, and each time we would print something like 30,000 copies, distribute them to centres, centres could request further copies if they ran out, and we recommended that they should not be posted to patients because you don't know if they've been received or what response there should be, but should be given to them in an opportunist way. By that I mean when opportunity arises.

This was another specific point that I discussed with the Information Commissioner and, indeed, subsequently with the NHS Research Authority and Ethics Committee because patients, particularly with mild bleeding disorders, are not seen very often. So getting this information to the patients could take quite a long time, and I had to know that that was acceptable.

In general, both the NHS Research Authority and the Ethics Committee did not favour posting these things to the patients, and that's a position I entirely agree with because you don't know if it's been received, and perhaps most importantly, the recipient doesn't have the immediate opportunity to have their questions answered, because they may read

this and then they may have questions.

So when we sent the leaflets out, and you'll see this also in my exhibits, it went out with a protocol, "How to use this leaflet", basically. And they were asked that either the nurses or the doctors give this leaflet to the patient to read before they're seen so that they can read it, digest it, take it away, and they've got an immediate opportunity to ask either their haemophilia doctor or their nurses anything more that they might want to know about the database.

We also put this leaflet on our website, on the website of the Haemophilia Society, and we have a hyperlink between the Haemophilia Society website and the UKHCDO website. And we have, for a number of years now, included a complete list of all the data points that we collect on our website so that everyone can look at that. You can go on our website and explore it if you wish. And you can see from the minutes that this whole process was reviewed at regular intervals.

From 2013, we recognised that we had a problem in that NHS Digital, who provided us with death certification data, became more difficult to deal with in a number of different respects. They questioned

whether our consent process was adequate. That's one thing. And we sought advice from them. Now, I know from my conversations with other disease databases that our experience with NHS Digital at that time was not unique; it was par for the course. Our problem was that you couldn't get consistent advice from them. We had difficulty contacting the same person twice in a row. We had difficulty contacting anybody, so we didn't know which path to take. And they stopped sending us death certification data, and they suggested to us eventually that, rather than dealing with them, we should go to the NHS Research Authority.

So I had a correspondence with the NHS Research Authority Confidentiality Advisory Group, which are based in Skipton House, Elephant & Castle, and this culminated in a meeting that I went to with their Confidentiality Advisory Group, in 2017, and we discussed this for an hour-and-a-half.

Now the other thing that was happening in the background was that GDPR was looming, and that would also change the Data Protection Act in certain fundamental ways, one of which was that an opt-out was no longer considered adequate. Consent had to be affirmative. And therefore you needed an opt-in. So that clearly would change our approach.

The meeting with the NHS Research Authority Confidentiality Advisory Group was very constructive and they confirmed that they didn't think that we needed to have any form of consent for the NHS purposes to which we put our data, ie, the increasing number of reports that NHS England, for example, were requesting of us.

They asked whether I thought it would be possible to get written informed consent from all our patients. Now, there are 30,000 of them. I made it clear that we clearly couldn't get consent from patients who had died, and we didn't want to cull the database of patients who had died, because their data was nevertheless very useful, in all sorts of ways, not least for the patients, many of whom have requested data on their deceased relatives, as is their right. And we have sent at least 500 reports out, and it would be unfortunate if we'd had to cull that data.

I made it clear to them that some of the patients were not seen frequently. They asked me over what period I felt I could obtain written informed consent from the whole group, and I told them, given the frequency with which patients were seen and the fact that some were lost to follow-up, it would be

five years and it would probably never be complete.

Now, they accepted that, and the reason for them questioning me so closely about the process and the difficulty, actually, getting the patients face-to-face to get consent was that they said at the time that if I had told them that it was impossible to get consent, as is sometimes the case with databases, then that would form the basis of an application for exemption from our common law duty of confidentiality and we could get exemption under Section 251 of the NHS Act of I can't remember which year. But we concluded that we could get written consent, and we set up a process for doing that.

Now, entirely reasonably, the NHS RA CAG also wanted an annual progress report of where we were up to, and we felt at that point that the central record of who had given consent and who had not would be useful, and of course it would be absolutely required for us to give an annual progress report.

So we wrote a series of age-appropriate information sheets, which are included as exhibits in my Rule 9 response, age-appropriate consent forms, which you'll notice have a QR code on them which is unique to the patient. We wrote software on the database for centres to access -- to get the

appropriate paperwork for each patient. So there's a button that they press and it will produce a patient-specific consent form, and package of information, which is appropriate and personalised. That enables them to upload the whole thing, once it has been dealt with, to the database, so that we have an electronic record of each consent.

We went to the Ethics Committee and they gave us ethics approval for the database as a research database, and that was the situation. And we were busily getting consent when Covid struck and that has obviously reduced the number of face-to-face interactions quite dramatically and slowed down obtaining consent.

But the other thing that changed was we are still going through the process of sorting things out with NHS Digital to start sending us death certification data. Not least because clearly mortality data forms an important element of the UKHCDO response to their Rule 9 request. There's a whole section on mortality.

And we got to the point we wanted to make an annual report to NHS RA CAG, and at that point, they sort of indicated to us that their opinion had changed.

So we organised a meeting with NHS RA CAG. It wasn't a meeting with the whole committee as it had been before. The whole committee is a very large room lined with people, it must be about 30 or 40 individuals, I never counted them. We met with, if you like, the executive of that committee earlier this year, and they indicated to us that they had revised their opinion. Not just in relation to UKHCDO, but in relation to other disease databases. And they felt that partly because of Covid but also because of the numbers involved, and because of several aspects that I had discussed with them at earlier meetings, including the fact that you can't take consent from people who have already died, you have a problem with people that are lost to follow-up and who refuse to come along. They had concluded that it was impractical to obtain written affirmative consent from all the participants in the database, and that we would be eligible for section 251 exemption, which they strongly encouraged us to apply for.

And they suggested two separate applications in relation to, firstly, the NHS purposes to which we put the data, and secondly, the research purposes to which we put the data.

So we submitted two separate applications.

I think they had also changed some of their procedures, both with NHS Digital and with the NHS RA CAG. Since we first dealt with them, they have realised that a lot of the difficulty that they have with applications is that we are trying to work out what they need and we don't necessarily know. So they have caseworkers who offer advice as you're developing your application to make sure that you're addressing the right questions --

Q. So, what --

A. -- in the right way.

Q. What is then the current position if -- if -- for the period from 2000 until recently, the database operated on the basis of implied consent with an ability to opt out, and that information was disseminated to patients through the various situations of the leaflet that you produced?

A. Yes.

Q. You then, in the way you've described, started to move towards a written informed consent in relation to the holding and use of data, interrupted by the current pandemic. What is the UKHCDO's intention, then, from now onwards, in terms of whether it obtains some form of express consent?

A. Well, the situation is that we submitted our two

applications for Section 251 exemption. The Committee considered those on August 3 of this year, and subsequently -- and this has to be confirmed by the Secretary of State for Health or their representative, with the weird title of a "decision-maker", and they have confirmed that this has the approval of the Secretary of State for Health, and so we now no longer have to obtain written consent. I'll be describing this to the membership of UKHCDO at the AGM tomorrow.

Q. Are there any purposes for which data held by the National Haemophilia Database is put for which you will be seeking express written consent, or express consent of any form, or is the position going to entirely revert to the 2000 to 2019 position of implied consent with opt-out?

A. With this exemption, we do not need the patient's permission, though the patients still have the right to have their data removed, and we have removed one patient's data at his request only last week, despite this. So the patients can still opt to have their data removed, should they wish to do so. Although we don't have to ask for permission, we have always felt, at least since we started to think about this around 2000, that the patients should know what we're doing, why we're doing it, and what we hold.

So we will -- we're in the process of again revising our patient information, because although we revised it only last year, it has rapidly gone out of date. We don't anticipate that we will ever share named data, so I don't anticipate that there will be any exemptions.

Q. There's one discrete issue arising out of the operation of the database I wanted to ask you about.

Soumik, could we have, please, HCDO0000002_066, please.

So this is a meeting in November 2003 of the UKHCDO's Data Management Group. If we go to the last page, please. This is in the context of patients' request to access information held about them.

The minutes received read as follows:

"Dr Hay continues to receive such requests. Patients do not really know what data is being held on the national database. Dr Hay has not prepared a leaflet to let them know what type of information they can expect, but he sends them a letter explaining this, together with an invoice for £10 instead. This often is sufficient for them to abandon their request."

Now, that reads, Professor Hay, arguably, as seeing the abandonment of a request for data as

an advantage to which the --

A. I can see where you're coming from, and that is not the impression that I would wish to give, because I think early on, I think a lot of people thought that we held far more data than we did. So we would let them know what we did hold. In fact, although it may be a little scanty, particularly in the older -- in the earlier period, it is sometimes more useful than we think. And the £10 invoice was the fee that is set out in the Data Protection Act of 1998. Since we've gone to GDPR, there is no fee at all. It's a nominal sum in any case.

I deprecate the impression that is given here that we wanted to discourage anybody from making a request. We get a lot of phone calls from patients. We try to be as helpful and friendly as we can. It's clearly their right under the Act to get data. Sometimes, although the data from the early years is not extensive, it nevertheless tells them the brand of concentrate they were first exposed to and which year they were exposed to it. And for people that are trying to find out about the origin of their hepatitis C, that is a key piece of information which may have already been lost from their notes.

I think a lot of the patients thought that we

held as much information as the hospital might, and that we were an alternative source of really detailed data. And, of course, that was never the case.

Q. A separate issue but still relating to records is the subject of my next question.

Soumik, could we have NHBT0091224_008, please.

So this relates to the approach taken by the Skipton Fund to applications, and there are various communications between you and the Skipton Fund in the materials that we have. I just wanted to ask you in particular about this one.

You wrote on 5th July 2011 to Mr Stevens as chair of the Skipton Fund along with the chief executive or the then chief executive of the Haemophilia Society, Mr James.

And you say:

"We are writing to you jointly to express our concern and to question the approach currently being adopted by the Skipton Fund to a number of applications from the dependents of the deceased.

"A number of cases have been rejected even though the deceased relative can show that they were treated with concentrate during the period of risk, because the notes have been destroyed or the patient died prior to the advent of HCV testing. We have

heard of one case refused even though liver disease was mentioned on the death certificate. Some applications have been refused, even though evidence of chronically abnormal LFTs was also provided. In many cases, the notes have been destroyed because of the passage of time, but either the centre or UKHCDO can provide evidence of treatment with concentrate during the period of risk. Had this group been included from the inception of the Skipton Scheme, as both UKHCDO and the Haemophilia Society argued, it is far more likely that the documentation would still have been available to support their application.

"These refusals are causing considerable distress."

Then you go on, on the second page, to set out in the first paragraph of that page your concern that Skipton, rather than applying a test on balance of probabilities, was applying a higher standard, of beyond reasonable doubt, in reaching decisions, and then you say:

"On the balance of probabilities, all patients treated with clotting factor concentrate during the period of risk will have contracted hepatitis C, given the 100% infection rate documented in the literature. On the balance of probabilities they will also have

developed chronic hepatitis C, given a 25% spontaneous remission-rate and should therefore be eligible for a part 1 payment, even if the documentary support for this has been destroyed and/or they died before the advent of HCV testing."

Professor Hay, the Inquiry will be examining the operation of trusts and schemes for financial assistance in more detail in the early part of next year. What can you tell us about this particular issue, and the extent to which it was resolved or not following this communication?

A. Well, we never sent data directly to the Skipton Fund. I don't remember this. I think at some point the Secretary of State for Health stated that these cases should be settled on the balance of probabilities, which seemed the only reasonable basis on which it should be decided. And we wanted to do whatever we could to support the applications to the Skipton Fund.

What happened in reality, was that patients who were scratching around for evidence would turn to us and ask for an extract of the data we held on their relative, or the patients themselves would. And we would provide that. And I think, after this, they did take that into account to some extent, because -- these were very often deceased patients whose notes

had been destroyed after death, and they were left with very little documentation.

But the data we held, scanty though it was, we felt should be adequate to support an application at least for a part 1 payment and, if they had a death certificate, perhaps part 2.

Q. I want to move, then, to your involvement with -- or the involvement of the Haemophilia Database in an HCV look-back exercise.

Henry, could we have, please, WITN3289157.

So we can see this is a proposal submitted by you on behalf of UKHCDO and the database entitled "Hepatitis C Look-back Exercise in Patients with Bleeding Disorders: 2009/10".

If we go to the third page, please, Soumik.

You set out in this proposal the objectives. (1) was:

"To document patients with bleeding disorders already tested."

And to identify how many had hep C, whether they'd been offered treatment, what was the outcome, how many patients had died.

Then (2) was to identify patients who had not been tested for hepatitis C, so that they could be offered advice, testing and, as necessary, treatment.

Then if we turn on, please, Soumik, to page 6. Thank you.

We can see here what you set out in the first main paragraph is that:

"All patients with bleeding disorders treated with blood products during the period of risk (before 1987) should have been tested in 1992 or soon after. All should also have been tested for hepatitis B from the late 1970s or early eighties."

Then you say, skipping over a sentence:

"Those untested are most likely to have been mostly mild bleeders, reviewed annually or irregularly and then subsequently lost to follow-up."

Then you go on to explain how it was arisen that patients were not tested, in the bottom half of the page, at (a), (b) and (c), you say:

"(a) Many Haemophilia Centres did not follow up mild bleeders regularly at all once the diagnosis had been made ...

"(b) Many such patients will have moved house ... and will thus have become lost to follow-up. In this way they may have fallen through the net and not have been screened.

"(c) Some patients may have moved or registered with a new centre. The new centre may be unaware of

their previous blood component or blood product treatment history and therefore may not have identified the patient at being at risk for hepatitis C."

Then the top of the next page, at (d):

"An unknown but significant number of mild bleeders may have been treated by non-specialist centres. These patients are often not followed systematically and are less likely also to be registered with the [National Haemophilia Database]."

Then if we go on to page 9, you set out there a proposed approach using the database to generate lists, sending them to centres, asking the centres then to scrutinise those lists, effectively, and to work from there.

So that was the proposal which was, as I understand it, then put into effect. Can you underline for us how the look-back exercise was then undertaken?

A. Well, we provided centres with spreadsheets, giving them the information that we held and asked them to fill out the blanks, effectively. There were a number of objectives. We focused on the identification of patients who were untested, but the Department of Health added a lot to this, which was unfortunate in

the end because it became overwhelming.

They wanted information about treatment provided to patients and the outcomes, the number of patients with severe liver disease, and various other things for the purpose of healthcare planning and also to help them to work out how much funding they needed to put into the Skipton Fund. And that made this an extremely involved exercise.

And so we asked centres for all this data. We asked all the centres that the patient had been registered with to provide us with data because we knew that the most recent centre might not know what the patient had been treated with, say, two, three, four decades before in some other centre or maybe even district general hospital.

So we approached this whole thing making no assumptions about anything, other than if they had been diagnosed outside the period of risk; ie, after 1991, they would not have been exposed to an at-risk product. So we were looking just at patients who had been diagnosed before 1991 and making no assumptions about the treatment that they might have had.

Unfortunately, that led to us asking for data on something like 28,000 patients, some of whom -- about a third whom had died because of the long

timescale we were looking at. And we were asking in some cases multiple centres about the same patient to get the whole picture because, you know, we have some patients recorded on the database against seven different Haemophilia Centres because they'd moved around the country during their life.

And the centres were quite honestly completely overwhelmed by this. They did try. We told them that this data had been requested by the Department of Health, but I don't think they were staffed to do it. The patients who were lost to follow-up or who had died, obtaining their records was sometimes difficult, and sometimes the records had been destroyed. And that sort of collecting them together was quite difficult.

And this was primarily a problem for the non-severe bleeders, because the severely affect patients are seen very regularly; they're well documented, and pulling their data together wasn't difficult. But they are a small minority of all the patients who were potentially at risk. So it rapidly became apparent that we were not -- just not going to get all the data. The testing data was just a small part of that.

So we had to go back to the Department of

Health and revise things, and we pointed out to them that we would be able to extrapolate from, say, 10% of the data. And they agreed a modification to the protocol whereby we would still request the testing data on everybody, but the more detailed data, such as the severity of their liver disease, the treatment history and so on, would only be requested from a randomly selected 10%. For planning purposes, we could extrapolate from that.

Whilst it was entirely understandable that the Department of Health might have wished to ask those questions, this was the element that just completely overwhelmed the centres and made it impossible for us to pursue it. I have actually included as an exhibit to my section 9 response a copy of the final report which gives you a flavour of how far we got. But after a period of about three years, we had to abandon this because we weren't getting any new data in.

Now, since that time, we have obviously launched a less ambitious, deliberately less ambitious hepatitis C look-back exercise which will be reported in our UKHCDO section 9 response to the Inquiry, which includes all the data that we got from this 2010 look-back but also any further information that we had subsequently obtained.

Then in terms of extrapolations, if we go down to the bottom half of the page, you say:

"We strongly suspect there was under-reporting of occasional treatment of mild bleeding disorders and so suspect that far more of such patients were treated than had been reported to NHD over the years."

So you:

"... felt obliged to consider all patients not included above but registered with a bleeding disorder during the period of risk ([approximately] 18,000 ...) to be potentially at risk of HCV exposure unless the centre could confirm that they had never been treated with blood products or concentrates."

And then you report:

"Of the 9,090 patients whose previous treatment history was reported as 'unknown', HCV status was also reported as 'unknown' in 7,567. Of the 1,523 patients whose treatment history was reported to us as 'unknown' but who had been HCV tested, 398 had evidence of active HCV and 21 of past but cleared HCV. Thus 27.5 per cent of those members of this group who were tested and had a test result reported to us had evidence of previous exposure to HCV."

Then you say this:

"Were this to be found in the whole of the

I should add, incidentally, that prior to these look-back exercises, UKHCDO issued and indeed published several liver disease guidelines, including recommendations on testing. So, you know, these patients should all have been tested anyway. And I anticipate that you're going to ask me, "Well, how many untested patients did you identify?" And the answer is: not very many. I think people continue to come out of the woodwork in small numbers.

Q. We'll await with interest the UKHCDO response to the Inquiry's request, but for the sake of completeness, I'll just ask you to look briefly at the report of the 2010/11 exercise.

Soumik, it's WITN3289162.

We can see it's a report that's said to be up to 31 March 2014. It's headed "Hepatitis C look-back report".

"This report is comprised partly of data imputed from the treatment records of NHD collected over many years and partly from data collected specifically in an HCV look-back exercise conducted from 2010. Centres found the look-back exercise burdensome and in some cases difficult, and the data is consequently incomplete. Many patients were probably lost to follow-up."

18,000 patients for whom we have no treatment reports, we would expect about 5,000 additional patients whose exposure to HCV has not been documented or who have not been tested. It is likely that there is reporting bias, however, and that those treated are less likely to be lost to follow-up and that the true number of those exposed is significantly ..."

Top of the next page:

"... lower than this statement. However, unless this group are tested and reported we have no way of making an accurate estimate."

Then you strongly recommend that:

"... all patients diagnosed with a bleeding disorder before September 1992 should be tested for HCV because Centres and the patients themselves will frequently not know what their treatment history is."

So professor, subject to whatever is going to emerge in the further material you provide to the Inquiry, this, as I understand it, is the report that was produced following the look-back exercise commissioned by the Department of Health?

A. Yes.

Q. And --

A. This report is actually taken from one of our annual reports. As a supplement to that.

Q. Do you know what steps have been taken, if any, by centres in response to the recommendation that you set out there in bold and italicised and underlined?

A. Well, I think I know that centres have attempted to trace some of these patients. The database holds NHS numbers. It doesn't hold NHS numbers for all the patients, because we didn't collect NHS numbers for the whole history of the database. So there are some patients for whom we don't hold NHS numbers. Usually these are very early registrants, so they may be dead. But they are very difficult to trace, because some of the early registrations we may not even have the whole name. We mostly do, I hasten to add. This is a tiny minority. Because these days we wouldn't accept a registration of that quality. We would go back to the centre and chase them for the missing details.

Now the point about this is if you know the NHS number, and the patient is registered with a GP, then you should be able to trace the patient, or at least the GP. And I know that in my centre, and we have asked other centres to do the same, we need to trace all these people.

You will hear, with our response to the Rule 9 request to UKHCDO, that that's not always been possible, and in some cases when centres have asked

the patient to come up to the centre for review they have refused, but we can at least write to the GP and ask if they've been tested, and if not, ask the GP to arrange for them to be tested and explain the situation in a letter.

UKHCDO has no direct patient responsibility but in these exercises what we were trying to do is to facilitate and make it easier for Haemophilia Centres, whom we think do hold that responsibility, to follow these patients up.

I know that in my own centre there have been some patients who have refused to be tested, refused to come up. Fortunately, very small numbers of those. Yes.

Sir, I note the time, and I'm going to be moving on to a separate topic, so perhaps we could take lunch now.

SIR BRIAN LANGSTAFF: Yes. Let's take a break until 2 o'clock, shall we.

MS RICHARDS: Before we cease the transmission and the link with Professor Hay, just two matters, if I may, sir.

The first directed to Professor Hay.

Professor Hay, you've been sent a document by the Inquiry in the course of the morning which is

a report from Dr Biggs. It's essentially a precursor to the report from Dr Rizza that you referred to yesterday, and I may want to ask you some questions about it on the issue of life expectancy, so I would invite you to check your emails and perhaps read that over lunch. It's a fairly short document.

And then, secondly, addressed to recognised legal representatives who are not present in the room as they normally are but are listening remotely, this hour is the opportunity for the recognised legal representatives, please, to communicate by email to me and to Ms Scott any further questions in addition to those they've already submitted that they would wish us to consider asking Professor Hay this afternoon.

SIR BRIAN LANGSTAFF: Well, what I shall do, given that we're asking you, professor, to look at a report by Dr Biggs, we'll extend the lunch break for ten minutes.

So it's ten past two, please, and I look forward to seeing you all then.

A. Thank you.

(1.02 pm)

(Luncheon Adjournment)

(2.10 pm)

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: Professor Hay, a handful of questions next on the issue of consent, patient consent. And my questions are going to be essentially seeking to understand the factual basis for your understanding of current and previous practices.

In relation to blood samples, you've said in your statement, paragraph 80.3:

"One did not ask for consent to take blood samples. I think it is assumed that the patient has consented because they go along and allow the phlebotomist to take the sample. It is not normal to take verbal or written consent for blood sampling other than for the purpose of research."

I understand your point, professor, about the patient consenting by allowing the blood to be taken, but do you take that to mean, in terms of your own practice or your understanding of current practice, that the patient is consenting to any and every use of that sample, or is there some limit to the uses to which the sample can be put?

A. Well, I think if the sample was to be stored, that would be a separate matter. Although the Human Tissue Act doesn't apply to plasma, as far as I'm aware. But the patient wouldn't necessarily know that, probably wouldn't.

I mean, it isn't normal practice for ask for consent but you would -- and in a routine review appointment, you tend to take the same samples each time, and at some point you might -- well, the patient would often know what the samples were for, because the results would often be discussed. For example the HIV viral load, the CD4 count, the patients often want to know what those results are because they give them an index of their current status, so you discuss them.

If you're taking a sample for something new, depending on what it was, you might describe it in general terms. I know, for example, if you refer a patient with abnormal liver function tests to be investigated by a hepatologist, they won't describe every single test that they're doing but they'll say, "Well, we're going to test for some hepatitis viruses and some antibody tests and liver function tests". They probably wouldn't say more than that unless the patient asked, and if the patient asks, then of course you'd tell them.

But what I was trying to get across is that it is not normal practice to sit down and list every single test that's going to be done, every time, and say, "Is that all right?" Do you see what I mean?

Q. Yes. In a sense you've anticipated, I think, two of

my next questions.

Where you have a patient who is a new patient or you're doing something which is not the standard array of tests you may have done many times before, and then explained the results, and you may assume that the patient has some, therefore, understanding of the purpose, but would you accept that, in principle, different considerations may arise, depending on the particular circumstances, with a patient who has not previously been tested or a patient where you're doing something new?

A. Yes, absolutely. Because at the end of the consultation with a new patient, you would summarise where you think you're up to. They will probably want to know the range of possible diagnoses, and you will describe in general terms what the tests will be. You know, someone comes to me with easy bruising, I will give them an -- my personal evaluation of the bleeding history that I've just taken from them, and I will tell them, you know, "We're going to check a few clotting tests. We will probably have to get you back in on another occasion to check your platelet function tests", and you'll tell them they have to avoid aspirin and drugs like that for two weeks before the test, and so on.

Similarly, if I saw a patient with a mild bleeding disorder that had been long since lost to follow-up, who was new to me and might have been treated with who knows what, in another hospital, I would explain to them that we had to test them for hepatitis C. I would give them an evaluation of the likelihood of that test being positive, and say, you know, "It may well be negative but we really need to know one way or the other."

Q. And in relation to stored samples, could we look, please, Soumik, at WITN3289054.

If we go to the second page. Now, this is a specific form at Manchester Royal Infirmary in relation to genetic testing, but if we go on to the next page we can see it's -- it seems to be an information sheet for patients. It asks the question "What is the purpose of obtaining a blood sample?"

Then if we go over the page, it provides information about where the sample will be tested, how long the sample will be stored and then, if we go to the next page, "What else might be done with my blood sample?"

Now I appreciate this is a leaflet specifically concerned with the taking and storage of samples for genetic testing. But would you consider that those

kinds of questions, where will it be stored, how long will it be stored, what else might be done with it, are the kind of questions which patients should be given information about if samples are going to be stored?

A. Well, genetic testing was considered particularly sensitive, and this is the form that we actually give to them before we go through a formal consent process -- and this leaflet was submitted to you as one of the exhibits to my response -- as was the consent form. And as the consent form says: it is our plan to store your sample indefinitely, which is unusual, actually, because that means even after the patient has died, we may continue to store that. And the patients are asked to consent to that in writing.

Now that's not for research purposes. That may be to facilitate testing of relatives at some stage in the future. And this leaflet and the accompanying consent form were actually designed by the Genetics Working Party of UKHCDO. And again, it's considered -- I don't think this is really a very good example because the status of genetic testing is in general a little bit different.

I think if we were to store samples for potential research in the future, some form like this

would be appropriate, but UKHCDO certainly don't do that, and I don't have any research samples stored away either. Research repositories have to be regulated and a form like this would be appropriate for that sort of purpose.

Q. And what about -- it may be this is hypothetical if you don't do it -- what about storing samples to keep, essentially on the basis that there might come unknown viruses in the future that one might want to -- or other unknown issues in the future when one might want to take the sample out and test at some future stage? I mean, is that -- first of all is that something that happens at Manchester, in your --

A. No -- well, all our virology departments, as far as I'm aware, store samples for three years, and then dispose of them, and that's in case they need to investigate further. One of the other principles you will have noticed, going through the consent process in relation to genetic testing, is the principle that if we want to re-test the sample for a different condition, we would have to go back and ask the patient for consent again. Because the consent is extremely specific. And in the first -- the first part of the consent form, you explain to the patient that you are only going to test for the main

condition, which will be haemophilia A, B, or von Willebrand's disease, or whatever, and that you won't be testing for anything else.

So that they understand that you won't be digging it out and using it as a research thing without their permission. And we say quite explicitly to the patients, "If we want to do that, we are obliged to come back and ask you". Because, for example, once we have a stored sample of DNA, we could in theory test that sample for cancer genes, and -- just using that as an example.

And the implications of testing for something that might give you cancer are very different from the implications of testing you for a hereditary bleeding disorder. So the patient may be very happy, and has often volunteered, to be tested for the familial gene, but might prefer not to know if they have a gene that predisposes them to cancer.

So it's an important principle that applies to genetic testing.

Now, by the same token, I think if you stored a sample and you wanted to do research on it, you'd have to go back to the patient. I mean, I think that's the current view. I don't think it has always been that, but I think that, you know, even if you've

got a sample stored, you may have taken general consent that you have a sample stored for research purposes, and in some cases that consent includes consent to keep the result anonymous. That would be one way of handling, for example, testing for a new antibody test, where you may not know what the implications of a positive test are, or indeed how good the antibody test is. And then it's helpful to test a group of patients anonymously on the understanding, explained in advance, that the patients will not be told the result.

SIR BRIAN LANGSTAFF: By "anonymous" you don't mean without identifying the individual; you mean without telling the individual?

A. Yes, that's right, and keeping the report anonymous as well.

SIR BRIAN LANGSTAFF: Yes, well, I understand that last. It was just the use of the word "anonymous", I just wanted to clarify. Thank you very much.

A. Sure. All the reports would be anonymised but you clearly need to identify the sample.

MS RICHARDS: Moving on, then, to the question of hepatitis C testing, you say in your statement this:

"... it has never been customary, in any branch of the health service, to provide pre-test counselling

or obtain specific consent for hepatitis C testing, hepatitis A testing or hepatitis B testing."

Then you refer to information received from your hepatology colleagues that in 2020 if they saw a patient with abnormal liver function tests, they'd arrange a battery of blood tests which would include viruses such as HCV and would tell the patient words to the effect of "I'm doing a few tests, including tests for viruses."

Now I just wanted to explore with you what the factual basis is for that, your belief that that is the customary position.

Your own practice, as I understand it from your evidence so far and your written evidence, is that you -- I think you say almost invariably or invariably did tell patients that you proposed to test them for hepatitis C, thus affording them, presumably, an opportunity to decline.

A. Well, I can't remember anyone declining, although they have recently, when we've chased them up, the odd patient. Well, I think this circles around what you mean by "counselling", to be honest. Because my understanding of the questions being put to me in my Rule 9 request was that a comparison was being drawn between the situation of formal counselling for

HIV testing and hepatitis C, and my answer was in relation to that. Because whilst I would certainly tell people I was testing them for hepatitis C, the implications for that test are not the same as for HIV.

And indeed, the process of counselling people prior to HIV testing really only fully emerged a year or two after we started to have a test, because to be honest, back in 1984/85, when testing first became available, the implications of the test were not fully known.

So, you know, the conversation could be quite short and would include assertions such as just having HIV doesn't mean you've got AIDS. Because we didn't know the natural history and so on. We didn't realise that it would have major implications for getting a mortgage, for getting life insurance, and all of those have to take their place in the process of counselling to have an HIV test once those things are known.

Now, with hepatitis C we knew that the natural history was a prolonged one, that a significant proportion of patients would have a very good prognosis, whilst a significant minority would obviously get serious liver disease.

So it would be a different conversation. I'm not saying that you would -- I think in our practice we probably talked more to our patients about hepatitis C prior to testing even than the liver doctors do, because the liver doctors see lots of people with abnormal liver function tests. The commonest cause of abnormal liver function tests in the general population is obesity.

Now, in my group of patients, that's sadly not the case and, you know, if I see a bleeder, my concerns are slightly different. If they've got abnormal liver function tests, I would assume it was hepatitis C until proven otherwise.

Q. So if you were, in 2020, seeing a patient, perhaps one of the infrequently treated patients who'd been lost to follow-up who has now come back to the centre, and they either hadn't been tested for hepatitis C or you don't know whether they'd been tested for hepatitis C or not, and you thought it would be prudent for them to be tested for hepatitis C, what information would you typically now give that patient in advance of undertaking the test?

A. Well, some of these patients are already concerned because you've dragged them out of the woodwork, and they're worried that you might be giving them bad

news. And they may have very little awareness of hepatitis C because I think there is much less awareness in the general public of hepatitis C than there is, for example, of HIV. So you have to introduce to them the possibility, having taken whatever treatment history you can elicit, that there is a possibility that they may have contracted hepatitis C. And, you know, as I say, you would make some sort of calculation based on what you'd been told. You might not be able to assess the risk, but you have to put that to them, and then you would say, "I think we need to test you." And they will almost invariably say yes.

Q. And so that would be your practice in 2020. Was your practice in 1992, 1993, 1994, any different from that?

A. No, not really.

Q. And so the basis for -- if we leave aside pre-test counselling in the way in which you've described it, the basis for your -- the statement in your witness statement that it's never been customary to obtain specific consent for hepatitis C testing, are you there talking about written consent, or are you there talking about the practice that hepatologists, colleagues tell you that they just say, "Well, we're going to test for a range of viruses," without saying

any more?

A. Well, we certainly did get written consent. We do get written consent for genetic testing, but not for any other tests unless they're invasive, of course.

Q. In relation to HIV testing, and I just wanted to understand your understanding of the current position, you've said in -- again, I think it's the same paragraph of your witness statement, you say that -- you're talking about HCV you say:

"Unlike HIV, which almost uniquely requires pre-test counselling during the '80s, '90s and until fairly recently," and then the impression your statement gives is that the current practice in relation to HIV testing would not necessarily involve the patient being told they were being tested.

A. Well, that's my understanding. I mean, I personally haven't tested any new patients for some time. If someone came out of the blue and their last treatment had been during the period of this, I would still go through all of that business. But at the beginning, I'm sure you appreciate, different clinicians had very different approaches to imparting someone's HIV status to them. I felt that Professor Preston's approach was a very good one, and some of my colleagues not so good. And then it became universal practice to

carefully counsel people before they were tested.

And I only mention that because I think that the implications have changed with time because the treatment is very much better, and very few of our patients have died from HIV since 1995. Life insurance is also less of a problem.

I mean, at one time, if you had asked for a house loan above a certain level, the insurance company would insist you had an HIV test. I've been HIV tested twice myself on that basis, and my GP told me that half the residents in Lymm had had an HIV test for that reason. And he counselled me, despite the fact that he knew I was a consultant haematologist.

So I've seen both sides of this, shall we say. But all pregnant women are tested, and -- you know, so practice does change.

Q. I wanted to then ask you about some of your evidence yesterday in relation to life expectancy. So this, professor, was in the context of having asked you what consideration was given at Sheffield in 1983, 1984, to the possibility of reverting to cryoprecipitate more extensively, at least for a period of time. And you referred, when giving your evidence about increased risk of death and from haemorrhage and decreased life expectancy, to a paper by Dr Rizza, and I wanted to

check first of all that I've got the correct one.

WITN3289047.

A. "Haemophilia treatment in the UK from 1969 to 1974." British Journal of Haematology, 1977.

Q. That's the document we asked you to read over lunch which I'll come on to.

But first of all, yesterday, your evidence was that this was a potentially relevant piece of material, and this is one of the exhibits to your statement.

A. Yes.

Q. We can see it's by Dr Rizza and Ms Spooner. "Treatment of haemophilia and related disorders in Britain and Northern Ireland during 1976-80: report on behalf of the directors of Haemophilia Centres in the United Kingdom."

A. Yes.

Q. If we go to the second page, right-hand column, please, Soumik, under the heading "Age at death and causes of death". I wanted to check whether this was the material that you were referring to, Professor Hay, as relevant to the assessment being made in Sheffield in 1983 and 1984. So we'll see under the heading "Age at death and causes of death". Can we scroll down? Thank you. That's perfect.

You'll see it says in that first paragraph, in the last two sentences:

"The average ages of the patients who died were 46.7 years in the haemophilia A group, and 48.3 years in the haemophilia B group. Comparable figures for 69 to 74 were 42.3 years and 33.6 years respectively."

Then if we go to the next paragraph, please. It says:

"A more useful statistic was the median expectation of life."

I think it's easier if we just go back to how it was before. Thank you.

"This was calculated from life tables. Surprisingly, the calculations yielded a median life expectancy of 69.1 years for severely affected haemophiliacs, as compared to 72.8 for normal males. Those figures must clearly be viewed with caution since the numbers in the calculations were relatively small and also because of the possibility that deaths in haemophiliacs may not all be reported to Haemophilia Centre Directors."

Then there's reference to the number of deaths due to cerebral haemorrhage in the following paragraph, at 26 of 89 deaths (29%).

Now, first of all, is that the report or study

that you were referring to in your evidence yesterday?

A. Yes.

Q. And what is it that you drew from this report when this issue -- well, sorry. I'm going to start that again.

Was this something that was expressly considered in 1983 and 1984 when the question of how to respond to the AIDS crisis may have been being discussed in Sheffield?

A. Well, it was published in 1983, in March. And the perception certainly was that the introduction of concentrate had significantly improved life expectancy.

Now, in the paragraphs you've just quoted me, they compare the average age of death, which is not quite the same thing as life expectancy, but they compare it with the previous reports from Rosemary Biggs, which you suggested I should read over lunch.

And -- now, Rosemary Biggs doesn't use actuarial methods or life table, so the average age of death is the only metric for comparison, and I'm sure you're going to point out to me that it has gone up relatively modestly.

Q. Yes.

A. I think, though, the headline figure that people took

away was the median life expectancy of 69.1, which has been much quoted since.

Of course, Rosemary Biggs was not the only source of data. There were other studies showing the average life expectancy at that time was about 40, but -- you know, back in the '60s and very early '70s, but it's quite difficult comparing all these things because people use different methods.

I've recently written a review which is about to be published in the Journal of Thrombosis and Haemostasis on mortality and haemophilia, and this is a difficulty that besets the whole area. It's actually quite difficult to compare.

Now, one other thing I'd say about the comparison between these two is they report adjacent periods. And the second report from Charlie Rizza is reporting a period during which concentrate is being introduced and patients established on home therapy. So you would perhaps not expect a really dramatic difference because, in terms of the therapeutic approach, the two periods overlap somewhat.

What it's showing is a trend towards improved life expectancy that would not flower fully until the period after 1980, when most people were established on home therapy.

15 years, and so from the 50s they would have had blood transfusion and plasma, and cryoprecipitate was introduced in the mid to late 1960s.

SIR BRIAN LANGSTAFF: That's why I think Rosemary Biggs is referring here, in the first sentence, is it, to 1967 because that's when cryoprecipitate would have been introduced?

A. Yes, widely. I think it was described in '66.

SIR BRIAN LANGSTAFF: Yes.

So the first sentence she says -- is observational. It expresses an opinion. Is that an opinion you would agree with? That:

"Increasing amounts of cryoprecipitate and of Factor VIII and Factor IX concentrate have greatly improved the prospect for treatment of patients suffering from A and B."

A. Yes.

SIR BRIAN LANGSTAFF: Thank you.

A. Unquestionably.

SIR BRIAN LANGSTAFF: So unquestionably the introduction of cryoprecipitate, then, and later we know that concentrates, the NHS concentrate, from probably about 1970 onwards, we're informed, formed an increasing part of treatment, and then commercial concentrate, when there wasn't enough NHS to go round, from about

Q. If we just look at the Biggs report because you've got the benefit of it and I have, but others watching don't, so I'll just put it on screen.

It's PRSE0004645.

Soumik, it'll be in the knowledge of risk material, so you may have it stored in a separate location.

A. It was part of my submission, as an exhibit, actually.

Q. We now have on screen and I know you have a copy, professor, the Biggs report. So we'll see that covers period '69 to '74. And if we go to the fourth page of that, please, Soumik.

SIR BRIAN LANGSTAFF: Can we just stop at the first page.

MS RICHARDS: Yes, back to the first page, please.

SIR BRIAN LANGSTAFF: And underneath the summary, just the very first sentence, because before -- around about 1960, as one understands it, the life expectancy of a haemophiliac suffering from severe haemophilia was probably in the region of 20 to 25 years. It hadn't gone up very much since the 1930s. It had gone up a bit but not much. That's probably about right, is it?

A. Yes, it's about right. It's -- life expectancy was about 29 years. And it improved a lot from the no treatment era, when it would have been about ten or

1973 onwards. That, I think, is broadly the position, isn't it?

A. I agree.

SIR BRIAN LANGSTAFF: You weren't practising at the time so this all done by report so I'm putting a very broad picture to you. I'm not going to hold you to a point answer, but I think that is broadly the understanding --

A. No, no, I was a medical student at the time, but obviously I've gone into the history.

SIR BRIAN LANGSTAFF: So you were going to go to the fourth page --

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: -- Ms Richards, I'm sorry.

MS RICHARDS: And to draw attention in particular for the benefit of those listening -- Professor Hay has a hard copy -- to the top of the page:

"In the early statistics the average age of death of severely affected haemophilic patients was less than 20 years. Thus the age at death seems to have more than doubled as a result of Factor VIII therapy."

And of course, I think we know broadly that in the period she's here looking at, up until 1974, the majority of Factor VIII therapy would have been

cryoprecipitate, although, as you've just observed, of course, concentrates were starting to be used and were then used much more increasingly in the years that followed.

A. Yes.

SIR BRIAN LANGSTAFF: Yes, I mean, the precise amounts of cryoprecipitate compared to the precise proportion is -- will be a matter for us to explore elsewhere, but I think broadly what you've said must be right.

A. Yes, absolutely. And you should get those figures that we have in the UKHCDO statistical response to their Rule 9.

SIR BRIAN LANGSTAFF: Thank you.

MS RICHARDS: Then we can see reference in the table to the age at death of patients having haemophilia A or B, and for present purposes I'll just look at haemophilia A. And we can see there the average age at death: 42.3. And whilst we're looking at it, just to observe, we also see the number of deaths from intracranial bleeding, which -- the figures in both reports are fairly small, but it's 16 out of 62, which I think would have been approximately 25, 26 per cent of deaths from that cause in that period.

This is looking at it very broadly, Professor Hay, but is this right: before the

availability of any form of Factor VIII therapy, and so before the availability of cryoprecipitate, the average age of death was around 25 years or so. But according to Dr Biggs in this, it almost doubled during the period '69 to '74, when most of the Factor VIII therapy producing that result would have been cryoprecipitate?

A. Well, I think my interpretation of what she is saying is that it doubled from the period before cryoprecipitate to the period that she is looking at.

SIR BRIAN LANGSTAFF: Yes.

A. Because the use of cryoprecipitate was already well established in 1969, I think.

MS RICHARDS: Then when we look at the period covered by Dr Rizza's report, we can see that the average age of death increases again, but it's a much smaller margin, around two and a half years.

A. Yes --

SIR BRIAN LANGSTAFF: It's about 10%, isn't it?

A. -- I'd agree with that, and to be honest, I think that the actuarial calculation paints a much rosier picture but you can't use that to compare with the earlier period, because there isn't a similar calculation in Rosemary Biggs' report. And I think that the period that Charlie Rizza is reporting is a sort of

intermediate period, because it's a period during which some centres are quite well advanced in converting to concentrate, and others much less so. But I know from the history of the Manchester Centre that there were still patients being treated with cryo in the early eighties, and whilst I appreciate that they were unusually conservative in their approach to treatment in the Manchester Centre, it was a more gradual process than I had realised.

Yes.

Q. And so would this be fair: that these two reports don't provide any significant support for a conclusion that reversion to cryoprecipitate in 1983, particularly for a relatively short period of time, maybe a couple of years, would have led to a significant increase in deaths or a significant decrease in life expectancy?

A. Well --

SIR BRIAN LANGSTAFF: You're asking in the absence of HIV infection?

MS RICHARDS: Yes. Yes, we know, of course, as well established in later reports, including those co-authored by Professor Hay, that as a matter of fact, the greatest impact upon mortality in the years that followed was viral infection of HIV.

SIR BRIAN LANGSTAFF: Yes, but people would not have known that --

MS RICHARDS: No.

SIR BRIAN LANGSTAFF: -- at the time for the purposes of this comparison?

A. Well, I think that I would agree that the increment in life expectancy between these two reports is relatively modest. It's not insignificant. And you also have to recognise that the second report is an intermediate period when there's still a lot of patients being treated with cryoprecipitate, and not everyone has been established on home therapy.

You will see that if you look at the report of the Prophylaxis and the Home Therapy Working Parties from the seventies and early eighties. I was unaware until recently of the existence of this working party but they did actually audit their roll-out of home therapy, and it was slower than I had realised.

I think my view was rather coloured by my personal experience in Sheffield, and I had assumed that all other centres were as quick to do it as they were. But that is actually not the case.

MS RICHARDS: Sir, I'm going to move on to a separate topic. Before I do so, was there anything further that you wished to ask --

SIR BRIAN LANGSTAFF: Only this, really: I just draw your attention to the risk, I think, or the cause of death, proportionately, which Dr Rizza in his paper identified as being intracranial bleeding. I think it was about 29%, he said, of the cases that he was looking at, died of that, if they didn't die of other causes.

If one takes the 16 that we're looking at, it's table III, the first item, "Intracranial bleeding", then the total number of cases, 62, it's about -- just over 25 per cent, it'd be 25% if it was 64. So it is just over 25%. But there's not a great deal of difference in those two figures, for what it's worth; is there?

A. No, true, but -- I agree, and intracranial bleeding was the commonest cause of death during that period.

But I would come back to the fact that, you know, you wouldn't expect a dramatic difference looking at two periods when, in one case, everyone is treated with cryo and, in the second, you have a transitional period, they're not all on home therapy during this second period, or not for the whole of that period.

I can tell you that the number of patients dying from intracranial haemorrhage now is less than

10%. So treatment with concentrate, as currently practiced, and with prophylaxis -- which may of course be very, very important, because you will expect to prevent a lot of the bleeds that might have occurred with treatment on demand, but we have reduced that complication quite dramatically.

SIR BRIAN LANGSTAFF: I can full understand the significance of prophylaxis, but just comparing these two sets of data -- for what it's worth, as you've indicated, they're not exactly comparable -- this -- well, what you're looking at on the screen at the moment, the Biggs paper, is at a time when there was some but very little home therapy, I think. Am I right?

A. Yes, I think that's correct.

SIR BRIAN LANGSTAFF: So the two changes were -- it wasn't just a change from a little Factor VIII concentrate to a lot of Factor VIII concentrate, proportionately, but also a change from a little home therapy to a lot of home therapy proportionately. You still have a fairly comparable death rate in these two studies over the two periods so far as intracranial bleeding is concerned. It doesn't allow for a very dramatic distinction between the two, does it?

A. No.

SIR BRIAN LANGSTAFF: Thank you.

MS RICHARDS: Professor Hay, I've got a number of questions now that I've been asked to ask by core participants, and so we're going to dot about from topic to topic, rather than follow a chronological or thematic order.

The first arises out of a passage in your statement about research where you describe the difference between an interventional study and observational research, and your statement explains the different ethical requirements that might attach to each.

Is the distinction between an interventional study and observational research always clear-cut?

A. No, I don't think it is, actually. It may be a matter of opinion.

We recently conducted a study internationally -- not UKHCDO, by the way, but investigator-led study -- which involved applying a number of quality of life questionnaires to the patient at intervals. They had to give consent to this anyway because -- you know, written informed consent, but it wasn't regarded as an interventional study in six out of the seven countries. The seventh country was France, and in France they said, well, if

we'd asked fewer questions, it would have been an observational study, but they regarded it as an interventional study because it took the patients more than an hour to fill out the forms. And I think that illustrates a classical grey area, and I can see their point, but that came down to a matter of judgment.

There are other studies where you may have -- you may record the results of interventions that are clinically indicated, and that should make it an observational study because the intervention would have occurred anyway -- for example, an operation or a blood sample or whatever -- and the intervention has not been done for the purpose of research. Because it's not been done for the purpose of research, that would be an observational study. But if you were to test a new agent such as a new Factor VIII concentrate, to establish safety and efficacy, that's unquestionably an interventional study because the patient wouldn't be given that agent if they weren't participating in the study. But once that same agent is fully licensed and we start to prescribe it in the normal way, when they participate in, of course, marketing surveillance study, that's an observational study, because they would be having that agent whether they were participating or not.

Q. Is there a risk --
SIR BRIAN LANGSTAFF: May I just ask a question?
MS RICHARDS: Yes.
SIR BRIAN LANGSTAFF: Just going back to the start of your answer there, you were describing where the intervention would have been done anyway, and you're simply observing the effect of it. That would be observational.

One of the situations I've come across on a number of occasions in cases which I've had to determine in the past have been cases where there were two possible forms of treatment: one conservative, the other interventionist. Both were entirely proper as a matter of practice, but the choice was left to the clinician. If the clinician chose the interventionist and had in the back of his mind that this might be a benefit to research which he was particularly interested in doing, would that make it interventionist or observational?
A. Well, that's an interesting question that speaks to the intent of the person in question. And that's a really grey one because if he was influenced by the fact that it was being studied and that introduced bias, that is -- that's actually a problem because it affects not only the ethics of the study but also its

interpretation, because you want to avoid that sort of bias, you know? That is the advantage of a randomised comparison because then you have negated any biases from the operators. And randomised comparisons are always interventional by definition but can be difficult to conduct.

I conducted a randomised trial comparing high dose with low dose immune intolerance, for example, in 17 countries, and the biggest difficulty that we had there was that we were doing the study because so much was unknown, but nevertheless, clinicians around the world had very fixed views. They were all convinced that they were doing it the right way, and if they had, we wouldn't have needed to do a trial. So many refused to participate because they disagreed with our protocol. You know, what can you do? So ... yeah, it's difficult.
MS RICHARDS: And picking up from the Chair's point, professor --
SIR BRIAN LANGSTAFF: Well, it was a question, not a point.
MS RICHARDS: Sorry, question.

Is there a risk that observational research, the undertaking of observational research, the desire of a clinician to follow that through, might lead

a clinician to keep a patient on the same treatment, rather than changing to what might have been a safer treatment?
A. I think that's unlikely. That would be really unethical.
Q. And in the early and mid-'80s, and I think you were engaged in research from roughly 1983 onwards at Sheffield, but in that period of time in the early and mid-'80s, what were the safeguards against clinicians undertaking something that was unethical, or a safeguard that might address some forms of subconscious or unconscious bias?
A. Well, subconscious or unconscious bias is a problem in research anyway throughout which is why the strongest evidence is always considered to be the results of a randomised controlled trial. Not that that trial design has -- doesn't have weaknesses, because it's often criticised because the subjects that participate in such a trial are selected, but it's the most reliable way of excluding bias.

Occasionally, you can also exclude bias by following natural experiments. And one example of that is a trial -- well, not a trial, an observational study that we conducted between Scotland and England, looking at the effect on the immune system of

different types of concentrate.

Now, in those situations, the whole of Scotland used a Scottish high-purity product that had been prepared in one way because that was what was available to them, and the whole of England used different materials. So just through circumstance, you had two groups that were all treated in the same way, and that offered the opportunity to compare the two.

In a way, the next best thing would have been to randomise them. And incidentally, the participants were -- although it was an observational study, we had to collect a lot more data than would have been normally the case, so they were consented in the same way as they would have been for an interventional study.
Q. Do you know --
A. The thing to do, to be honest, and this is what we try to do currently, is to assess each case individually and to make a judgment: is this an observational thing? If you have to take additional samples, or are you doing something burdensome, then it becomes interventional, and you have to get consent for that.
Q. Do you know, in that period of '83 to '87 when you were at Sheffield, and I appreciate you were the

junior to Professor Preston and Dr Greaves in terms of your role at the time, but do you know what, if any, ethical approval systems or other safeguards there might have been in place at that time?

A. Well, the details have changed over the years, but the basic principle has been the same throughout this period. That is, if you want to do a clinical trial, you have to take it to the Ethics Committee. They have to approve everything, not least the patient information and the consent form. They have lay members on every Ethical Committee, and they take a particular interest in that area, as you might expect. They also have statisticians on an Ethics Committee.

So if, for example they consider that the trial design is inadequate, then they could -- that is an ethical issue. It's unethical to do a clinical trial that is inadequate to answer the question because it potentially puts -- in theory, it would possibly put patients in harm's way without having any hope of answering the question, and that would be considered unethical.

So if you want -- if you participate in a clinical trial of a new product, for example, the Alphanate trial that was conducted in Sheffield in

1984, all the participants would have been consented.

Q. That's, I think, the trial that you referred to yesterday, is it, with the heat-treated products?

A. Yes.

Q. Did you have any involvement in that trial yourself, in terms of selection of patients and what information was or wasn't given to the patients?

A. Well, I don't remember much about it because it covers a period when, for part of that time, I was at the Children's Hospital, partly because I was moving about, they got the other senior registrar to get more involved, and her name is actually one of the co-authors. But my recollection is that patients were given an information sheet and had to write consent.

Q. Moving to a different topic -- no, actually, sorry, before leaving that. That trial -- would that trial have gone before any kind of Ethics Committee for approval?

A. Oh, yes, yes. At that time, they would have all been hospital ethical committees. Much later, they introduced a system for national approval, so you go to an MREC, and they're arranged regionally for multi-centre trials involving more than four centres. But even when you get national approval, you still have to take it to your local Ethics Committee and

your local R&D department and get approval from both of them before you're allowed to start.

Q. And then moving to a completely different topic, in your capacity as hospital haematologist responsible for the blood bank, which I think was when you were at Liverpool, did you ever become aware of any ongoing issue about HBV infection and pools contaminated with hepatitis B?

A. No, I can't remember.

Q. This morning, I asked you about the notification process in relation to variant CJD. Do you know whether there was any, in earlier years, any notification system to UKHCDO of suspected contaminated batches -- contaminated with HIV or with non-A, non-B hepatitis, hepatitis C? Was that something that used to be drawn to the attention of UKHCDO directly?

A. We had an adverse event working party and an adverse event reporting system which I will be describing to you in greater detail in the final chapter of our UKHCDO Rule 9, and that collected adverse events, including any new reports of hepatitis from the early 1980s onwards. I was a member of that committee.

The data was collated by the National Haemophilia Database. We did -- we do report adverse

events that we think are specifically related to a product to the manufacturer so that they can satisfy their regulatory requirement to report it on to the regulators. That's the European Medicines Agency and the Food and Drug Administration.

This has result in the withdrawal of some batches, which seemed to be giving lots of reactions, for example. The investigation of new reports of hepatitis after about 1988 all proved to be false reports, insofar as it was genuine hepatitis but not a new diagnosis.

You can imagine that we were particularly keen in the years after 1985, when products had been introduced that were marketed as only hepatitis-reduced, to evaluate any further episodes of hepatitis sneaking through.

And there were certainly reports with some products in Canada as late as 1988 of some of the virally attenuated products transmitting hepatitis C. And hepatitis B seemed to be more difficult to eradicate than hepatitis C, but then, on the other hand, all the donors were tested for hepatitis B from probably the early 1970s. So the only patients who would have got through that testing net would have been those who were in the window period at the time

that they donated. That is to say, the period when they were incubating hepatitis B but had not yet become positive for the tests. The window period, which we haven't discussed so far, is a problem with the all viruses, and another one of the reasons why we wanted to get away from plasma-derived products.

If you go through this period, from the eighties through to -- well, the present day, really, you will see that donors have been subjected to more and more tests, of increasing sensitivity, to progressively reduce that window period. And of course, donor selection is also very important with all of that.

The other thing that's really important that we haven't talked about before is repeat donation, because the safest donor is a donor that repeatedly donates. If you go back to the early 1980s, 50% of UK blood donors were first time donors, and often the only time they donated. They may only have donated once. And if you test those for viruses, you'll find most of the positives will be in first-time donors. So they are the most risky donors. The safest donors are donors who come repeatedly. And of course they're tested every single time.

By the end of the eighties, at least 90% of

blood donors were repeat donors. And in the commercial sector, people encouraged that too. So these days, most plasma is actually derived from plasmapheresis donors, who can donate far more frequently, because they're only donating plasma, and they can donate as often as once a month.

Anyway, I think I drifted off the subject a little.

SIR BRIAN LANGSTAFF: May I just ask a question.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: You were going to back to the early 1980s, and you said 50% of the blood donors then were first time donors, and most of the positives were in that group. If you're talking in terms of positivity for hepatitis C, or non-A non-B, as it was, how do you know?

A. Well, that's a good question.

You'll see in my report, and in fact in some of the exhibits -- the exhibit you showed me earlier which has the proposal to the Department of Health of the hepatitis C look-back -- who reviews this evidence quite well, I thought, rereading it -- in the early eighties there were a number of studies trying to assess the frequency of non-A, non-B hepatitis. Obviously without a specific test. And the way that

they approached it was they saw how many recipients of multiple blood donations subsequently developed hepatitis. Now, these would be patients undergoing, say, open heart surgery, or some other surgical intervention that required a large blood transfusion.

So they would be exposed to a number of donors as a consequence of that. So you could evaluate how many donations they'd been exposed to, and then you see what percentage of them develop non-A, non-B hepatitis thereafter. And from that you derive a figure for the number of the donors that were infectious for non-A, non-B hepatitis.

Now, clearly, that methodology is relatively soft, and you'll find somewhere in my exhibits there is a table -- I know you're going to subject this to independent statistical analysis -- which shows the risk of contracting non-A, non-B hepatitis, based on the number of donations that you're exposed to, and it gives a range of percentage. The average is about 0.75% of blood donors being infectious for non-A, non-B hepatitis in the very early '80s, based on that methodology, but it varied.

There are a number of papers that looked at this from different countries, and of course, we do know that the incidents of hepatitis C varied from

country to country. It was higher in America than in the UK, and higher again in places like Italy and Japan, for some reason, also had relatively high rates. So the rate will genuinely vary from country to country. But based on that soft methodology, in the early '80s we think it would have been between about 0.5 and 1%.

Now, there are papers later on in that decade from Contreras et al which I also quote. Once they had a test, they were able to assess the prevalence in the donor population accurately, bearing in mind also that the donor population is not a cross-section of society. You know, there are certain ethnic groups that donate less, which is actually a practical problem because there are ethnic differences in the frequency of blood groups as well. So that does give rise to practical problems.

When I did my transfusion training, for example, blood donations from people from the Afro-Caribbean community were coded so you could identify them because they were particularly useful if you had a patient with sickle cell trait, for example, if they needed a transfusion.

Anyway, I'm drifting again. Um -- (overspeaking) --

SIR BRIAN LANGSTAFF: If I can --
A. -- (overspeaking) -- this paper --
SIR BRIAN LANGSTAFF: Sorry, you're going to talk to me about the Contreras paper. Sorry, I'm interrupting. My apologies. Please.
A. The Contreras paper showed a tenfold reduction relative to those early soft indication -- early soft assessments. And this was attributed to the introduction of donor selection.

Now, although donor selection -- you know, this is pre-donation exclusion. This is the process whereby all prospective donors have to read the leaflet, and if they fall into the following risk groups, not donate, please. Of course, although this was directed at the reduction in the risk of HIV, there is an overlap in the risk groups for HIV and hepatitis C, clearly. So donor selection dramatically reduced the risk of hepatitis C as well.

SIR BRIAN LANGSTAFF: Just going back to the start of your answer, the question really arising out of your comment that about 50% of the donors would have been one-time donors, and they were the ones who created more of a problem than the regular donors back in the early '80s.

Suppose that you had -- as your first example

has, as far as you know, no basis in the literature?
A. Sorry, I don't understand.
SIR BRIAN LANGSTAFF: It's all right, it's probably more of a comment than a question.

That's all I need to ask. Thank you very much.

MS RICHARDS: Sir, I've got some questions still, but I note the time and I think it might be sensible to have a break and then I can complete the questions.
SIR BRIAN LANGSTAFF: Yes, of course.

Counsel will -- she needs to field questions from people who aren't here, to talk to her and give her further questions, because you will appreciate that counsel to the Inquiry ask the questions in an inquiry, and, in general, core participant counsel don't. That's a generality, but it's likely, I suspect, to be true in this case, particularly when they're not here in any event.

So we shall take some time just to do that. How long do you think you need?

MS RICHARDS: I've got most of the questions, sir, there's only a handful I haven't been able to consider, so half an hour will be ample. But that will give Professor Hay an opportunity to take a break and those watching to have an opportunity to take a break as well.

was surgery, involving quite number of transfusions, suppose, let's say, ten bags: five from first-time donors, five from other donors. How would you know which bag contained the infection if the person who was having the surgery actually later on developed and showed signs of hepatitis non-A, non-B? That was the point I was trying to understand.
A. I see. Well, in the absence of a test, you wouldn't necessarily. You could go back to all those donors and test them for what you knew about, see if any of them had chronic liver disease and take a history.
SIR BRIAN LANGSTAFF: Was that done, do you know?
A. Well, there were latterly look-back exercises conducted by the Transfusion Service, but they did not occur until after hepatitis C testing became available, and they were really directed at people who were repeat donors who turned out to be positive for hepatitis C, then they went back and traced the recipients of previous donations.
SIR BRIAN LANGSTAFF: I understand the repeat donors, it's the one-time donor and their infectivity which I was really trying to understand.
A. The one-time donor, you couldn't do anything about.
SIR BRIAN LANGSTAFF: Does it come down to the fact that's an estimate, really, which you have given us, which

SIR BRIAN LANGSTAFF: Yes, so we'll have a cup of tea and come back at -- will four o'clock be all right?
MS RICHARDS: Yes.
SIR BRIAN LANGSTAFF: Will four o'clock be okay? Four o'clock.
(3.25 pm)
(A short break)
(4.00 pm)
SIR BRIAN LANGSTAFF: Yes.
MS RICHARDS: Professor Hay, you told us yesterday that in relation to Sheffield, there was no programme for prophylaxis and that that was formally introduced many years later. Were you aware of patients on home treatment administering treatment to themselves on a prophylactic basis?
A. There were patients during the 1970s and in fact there was a Prophylaxis and Home Therapy Working Party chaired by Dr Peter Jones. I have been unable to source any of the minutes of their meetings but they did report on an annual basis to the annual general meeting of the UKHCDO and their findings are of some interest.

I think that the -- I wasn't aware of this working party at the time, you understand, but Peter Jones was quite well known. He wrote a chapter

on comprehensive care in the first edition of Hemostasis and Thrombosis, which was one of the first textbooks of haemostasis I ever bought. And that chapter influenced me, and it did describe prophylaxis and prophylaxis was being practiced quite widely in his centre, and at Lord Mayor Treloar. And during that time, they published some papers on prophylaxis which you're probably aware of. So I was aware of prophylaxis, and it had been pioneered by Inga Marie Nilsson in Malmo in Sweden, and to some extent also in Holland.

So we knew about it, particularly in children, but it wasn't widely practiced for a number of reasons, not the least of which was the relatively inadequate supply of product, and then of course, when HIV came along, treatment intensification did not seem like a very good idea.

Q. I know there was no programme of prophylaxis in Sheffield, but were patients informally, and of their own initiative, using their home treatment on a prophylactic basis, to your knowledge?

A. No, I don't think that they were. Not at that time.

Q. Then moving from that to funding from pharmaceutical companies to UKHCDO, during your time as a member of UKHCDO, how were decisions made about which

pharmaceutical company would fund the annual general meeting?

A. Well, the manufacturers would approach UKHCDO and request to sponsor. It was very common, and still is, for pharmaceutical companies to offer sponsorship for meetings. That is all regulated. We would wish to have sponsorship from as many different sources as possible to avoid any accusation of bias.

Q. And what involvement, if any, in the annual general meeting would this sponsorship give the pharmaceutical company?

A. They would be allowed to attend certain parts of it. They would not be allowed to attend business meetings. And they would be allowed to set up a stall in an exhibition area. It's very common for scientific meetings of all sorts to have a commercial exhibition where manufacturers are allowed to set up a stall. That, again, is regulated in various ways, and the regulations will vary from country to country.

Q. And what, if any steps, were taken within UKHCDO to try to ensure that this sponsorship didn't influence members' decision making about which products to purchase for treatment at their centres?

A. I don't think UKHCDO felt that they had a part to play in that. Latterly, a lot of this is regulated because

we purchased these products through a national contract, and that has been the case for a number of years. On an individual basis, though, I don't think UKHCDO felt that it had a role to play, or indeed could. You know, in individual conversations, people would recognise that being dependent on a single manufacturer was probably a bad idea anyway, because it made you very vulnerable to issues of supply should that manufacturer have a problem, and it would also open you up to an accusation of bias. So it was normal and general practice to have two or more suppliers, mostly more.

Q. Would you have expected, in the 1980s, discussions about risks and the possible consequences of contracting non-A, non-B hepatitis or AIDS, if those discussions took place, to be recorded in a patient's medical records?

A. Well, um ... how should I put this? Certainly in my own medical records you'll get more from reading the letters than what I've written. It may only be mentioned in passing. It was commonly advised that any critical discussions, for example, discussions of Jakob-Creutzfeldt Disease, hepatitis C or HIV, should be noted, even if it's only a short note.

Q. Is the answer to the question, then, they should be

noted but they weren't always --

A. I think that's probably correct.

Q. -- in your experience?

A. I would say that the absence of a note doesn't mean that the conversation has not taken place, although I know that it would be a common legal judgment to the contrary.

Q. What role, if any, did lifestyle advice, with the aim of reducing bleeds, have on the treatment of patients under your care in the eighties, in particular mild and moderate haemophiliacs?

A. Well, it was well recognised early on that the patient's lifestyle affected their tendency to bleed, and the patients were certainly very well aware of it. They find out from experience the sort of activities that might cause them to bleed, and many of my patients have talked to me about the way in which haemophilia hangs over them like a cloud and they're constantly worrying that they might do something that might set something off. You know, something as trivial as stepping awkwardly off a pavement might cause an ankle bleed.

Not every patient is like that, of course, and, you know, it was early observed that, for example, you might have a pair of brothers, and one brother is

never out of hospital, and you hardly ever see the other one, and the other one's probably got his nose in a book, whilst brother number 1 is bouncing off the walls. And so personality does come into it.

There are also other aspects of the clotting mechanism that mean that some patients bleed much less. About 10% of patients with severe haemophilia have a relatively mild bleeding phenotype.

So early on, people would be advised to avoid contact sports, to remain physically fit if they could, because if they had good muscle bulk, they would be less likely to bleed, but not to go looking for trouble, essentially. So no rugby, no football, and no boxing, that sort of thing. But running, cycling, swimming were all good things to do and were encouraged, and we eventually started to encourage people to go to the gym as well. So lifestyle was quite important.

Q. And then if we could have on screen HSOC -- this on a completely different topic, professor -- 0005123, please, Soumik.

So this is a letter from you to Mr Barker at the Haemophilia Society in November 1994. If you could go down to the bottom half of the page, please.

You say this:

"I would very much like to have a chat with you about hepatitis C. I am obviously sympathetic towards increasing patient awareness, but I do not feel that the recent press coverage has been helpful in any way."

Then you talk about one specific patient, and I'm not going to ask you about the specifics in relation to that or any other individual.

Then you say:

"I'm rather worried that the whole thing is getting out of hand. If the Society wants patients who have contracted hepatitis C to obtain some compensation, I am not sure that encouraging them in their mistaken belief that they have a good case of negligence is the right way to go about it. I get the strong impression that although that's not the Society's official view, that some members of the executive are certainly encouraging this point of view, and a lot of the lawyers ... are doing so. I no longer have any very clear idea of the Society's position on this, despite the recent rather vague press releases, and I would like to talk to you about it."

What was the purpose of writing to Mr Barker in these terms and the purpose of asking to discuss this

issue with him?

A. Well, I wanted to know what the Haemophilia Society's view about litigation was. Because a lot of cases were being brought which had little chance of success, because to succeed, they would have had to prove individual negligence, and the patients in question had not been managed in an unusual way. There were patients who had severe haemophilia but were, nevertheless, claiming that they should have been treated with DDAVP, though they would not have responded to that.

Now, I had every sympathy with their desire to be compensated, because they had clearly been damaged by their treatment. And my feeling at that time was that surely this was a classical example of a situation where there should be some form of no-fault compensation scheme. But, in fact, I was told that whilst there was all this litigation going on in the background, no such scheme would be put together.

So, you know, a lot of the litigation that was going on at that point seemed unlikely to succeed. There was more and more of it. We then had the campaign where a whole series of patients from around the country reported the Centre Directors to the

General Medical Council, claiming various acts of professional misconduct, which were, as far as I knew, and certainly in relation to the two complainants against me, completely false.

And, you know, I was very sympathetic towards a campaign for compensation, but that was hardly calculated to get me on site. How would you feel if someone made a complaint to the Bar Council about you, for example?

So -- and I had gained the impression that elements in the Haemophilia Society were encouraging this. It was a slightly circular problem, though, because when I was a little bit more senior, a little bit further on, and was talking to the Department of Health, what they told me was, so long as there was litigation going on in the background, they couldn't put any scheme into place, because it would influence the outcome of the litigation.

And I think a lot of my colleagues and I felt as if we were slightly caught in the crossfire, because we were the closest target for the patients' ire, they blamed their medical attendants for their suffering, and we were not in any position to help with financial compensation. It was really the Department of Health that they needed to approach.

But we were the only outlet, and they sought to increase the profile of their campaign by suing us all and reporting us to the General Medical Council.

SIR BRIAN LANGSTAFF: Excuse me, can you just help and tell me who it was that you spoke to at the Department of Health who suggested that having a form of compensation scheme would in some way influence the outcome of the -- of a court case? In other words, I think the suggestion is it might influence a judge in favour of or against the case.

A. I can't honestly remember. The various people that I dealt with at the Department of Health were Charles Lister, David Kutowski, and William Connon, over the years. It was probably one of the earlier ones, most likely Charles Lister.

SIR BRIAN LANGSTAFF: Thank you.

A. And of course there was the class action that I was involved in.

SIR BRIAN LANGSTAFF: Yes.

A. Which was brought -- that was not claiming negligence, interestingly. That was brought under consumer protection legislation, which was a very interesting approach.

MS RICHARDS: Was this letter an attempt by you -- or, the meeting that you proposed follow it, an attempt by you

to persuade the Haemophilia Society to dissuade patients from bringing legal claims?

A. No, it was an attempt to clarify what their position was.

Q. To what end?

A. I never did anything, either individually or collectively, to try to dissuade people from litigation. I did have an exchange with -- what's her name? Well, with one patient, you sent me a letter, in evidence, on -- that was in response to an enquiry from her in general terms.

Q. You referred to a campaign to bring cases to the General Medical Council. Obviously, Professor Hay, you're familiar with the complaints that were made against you. But what's the basis for your assertion, the factual basis for your assertion, that this was part of a campaign as opposed to individual cases?

A. Well, it was well recognised at the time that that was the case. I was not chairman at the time. Professor Hill was chairman at the time. He actually knows how many of these have -- were lodged. I don't. But there were a number. At one point I was told that there might be as many as 50. There were certainly two against me, both of which were entirely false, but they took a long time to resolve.

Q. I'm asking not specifically about the complaints against you, and you've explained what the outcome of those were, that they didn't go anywhere. But in terms of it being part of a campaign, you've said it was well recognised. By whom? Do you mean that was the view of the Haemophilia Centre Directors?

A. Well, it was well recognised by Haemophilia Centre Directors, and I refer to it in correspondence with one of the patients who'd actually raised it with me. It's my understanding that this was done to raise the profile of their campaign.

Q. But the factual basis for that understanding is discussions between Haemophilia Centre Directors?

A. Yes.

Q. Could we have on screen, please, HCDO0000266_004, please.

This is another letter from you. This is a few years later, to the Haemophilia Society, to Ms Pappenheim, December 2002. You're responding to a letter from her, and it's about what are said to be difficulties of accessing medical records.

Let me just pick it up at the bottom of the page because this may be of more general interest. You say in the last paragraph:

"Medical record-keeping 20 years ago was not as

scrupulous even as it is now, and so patients should not be surprised or disappointed if they find that their records do not contain detailed records of batch numbers, et cetera, that may be medicolegally important with hindsight but had little apparent clinical relevance at the time."

Surely batch numbers would have had considerable clinical relevance at the time for two reasons? One is the single product batch dedication policy being followed at Sheffield and some other centres, and secondly, because that's the way in which you trace implicated batches.

A. Well, you'll remember yesterday we talked about ledgers. And every single unit of Factor VIII and Factor IX in the Manchester centre and, as you have already learned, in the Sheffield Centre is recorded, so we do record the batch numbers, but they are recorded in a ledger. Now, in Manchester, I think they may have had some other records as well before I came, but they are recorded in a ledger.

Now, the problem with showing the patient a ledger is that it's full of information about treatment for other people. You can't show that patient. You might extract it if requested, but that would obviously be a lot of work. But you can't show

one patient's information to another. So, yes, it is recorded, but not invariably in the patient's notes.

Q. If a patient makes an application for information that they believe is in their medical records wrongly, for the reason you've given, but the centre nonetheless holds it in another form, would the appropriate response of the centre not be to tell the patient that that information is held and provide it to the patient in some form, photocopying the relevant page of the ledger and just redacting out the irrelevant entries?

A. Well, if they make that request, but at that time, they were just looking for evidence that they'd been treated with one product or another, and the batch numbers were not relevant, frankly. They really wanted to know which supplier had supplied the product they'd been treated with for specific episodes, and that would be in the notes. Because, apart from anything else, that's on the prescription chart.

Q. But the point I understand to be being made here is that this information often won't be in the records. A patient can't know to request a copy of the information in another form such as a ledger unless they're told by the centre that the information exists in that form.

A. Yes, but the request that the patient asks for are

their clinical records, and those are provided. And to be honest with you, my involvement with that would be extremely peripheral. Because they make a request for the patient records, that goes to the medical records officer, they send me a form, which I have to sign, or the consultant that is looking after them has to sign, and we sign it, giving permission, and that goes back to the medical records officer, and they make the notes available. Or if the patient has requested a copy, they will arrange to copy what they have and present it to the patient.

Q. If we go over the page please, Soumik, to the second paragraph, five lines down it says:

"Unfortunately there appears to be a feeding frenzy amongst the patients at the moment."

Then you explain you don't have the time to go through the records of patients individually, and I understand the latter point. What do you mean by there being a "feeding frenzy amongst the patients"?

A. Well, at that point in time, there was a legal company, I can't remember which one it was, and they were trying to mount a class action. And as far as I can see, they were trying to do this relatively on the cheap. And by that, I mean they weren't going through the usual medical negligence process of

requesting the records and getting an expert to go through the records and providing a report. They were basically asking the patient to answer certain generic questions, and the generic question that the patient seemed to be interested in was: had they been treated with a certain brand of American concentrate during a certain period of time? Because the class action was against that manufacturer.

So lots and lots of the patients came along and they wanted to know that, and so they requested their notes. Their notes were made available to them. But then I think the problem often was that even though the information they were looking for was actually in the notes, they didn't know exactly how it was presented, and they weren't quite sure what they were looking for, and they might be presented with several thick volumes of papers, because these patients had been patients of the hospital often for many years, and so their notes were really voluminous. And, to be honest, when I got to Manchester, a lot of the notes were not in great shape.

One of the reasons for that being that if you sent them to the Medical Records Department to be re-bound, they would hang on to them for a couple of months. And these patients are presenting fairly

regularly. You didn't want their notes out of circulation for that long. And at one point I actually employed somebody to try to organise the notes and re-bind them. But we gave up after a little while because it was all happening so slowly. And he actually did that in the department.

So with some of these patients I actually went through the notes with them to help them to find what they were looking for. I can remember spending three-quarters of an hour one time, in clinic, with a patient who had been through his notes, had been unable to find them, then -- we shuffled through them all. It took me quite a long time. I showed him what he wanted to find. I explained to him what it signified. And then he came back to have another look at his notes, and he couldn't find it again, and accused us of taking this bit out. And -- you know, as if we would have any motive to do that. You know, why should we edit his notes when he's not even trying to sue us?

Anyway, there was a lot of that, and it was generated by an attempt at a class action.

Q. One final document -- sorry, two final documents. The penultimate one, HSOC0020017, please, Soumik.

There is was a letter you wrote to the

Department of Health in November 2005, and you've addressed it, I know, in your statement, and the context was the issue of funding for recombinant.

If we go further down, please. Can we go to the next page. Yes.

So you say that:

"... any attempt to roll back the policy of recombinant ... would result in a considerable increase in such activity, with multiple judicial reviews, other legal activity and considerable patient protest. I suspect that it would cause complete chaos both for the [Department of Health] and for Haemophilia Centres."

Then you say this:

"Many centre directors are already fighting a low grade guerrilla war with patient activists who want a hepatitis C public enquiry and who are reporting their centre directors to the GMC and manipulating both newspapers and television."

I've already asked you about the GMC, I don't need to ask you about that again.

But why did you characterise attempts by campaigners to achieve a public inquiry as the fighting of a low grade guerilla war by directors against activists?

A. Because of the way that they were conducting their campaign. Reporting your Centre Director to the General Medical Council on the grounds of -- well, for reasons that are entirely fictitious is a hostile act. And how they ever imagined that that would influence the Department of Health into giving a public Inquiry is entirely a mystery to me.

What happens when you report somebody to the General Medical Council is that that individual gets no support whatsoever from their trust. Nobody wants to interfere with the action, and the doctor in question is isolated. If it's a serious complaint, they may be suspended from work. That certainly didn't happen to me. But, you know, it's a serious matter and it causes a lot of work and a lot of aggravation.

And so I think to describe this, plus a degree of mischievous litigation, as "low grade guerilla warfare" is, if anything, a little bit of an understatement, and it goes back to what I said before about the medical profession feeling that they were caught in the crossfire. Because we had very little influence over whether there would be a public inquiry or not, and I think it's probably an uncontroversial thing to say that this inquiry might have been better

held 20 or 30 years ago, rather than now. You know, if there was going to be an inquiry, the earlier the better. So that's the background to that.

Q. You -- I'm not going to put on screen, but you've dealt with it in your witness statement, but you also sent two emails to the Archer Inquiry which you've said in your witness statement the tone and wording of which you accept was intemperate and which you regret.

A. Yes.

Q. Do you understand why patients or some patients at least might want a public inquiry?

A. Of course I do.

Q. Do you --

A. And, you know, the patients and their relatives have suffered greatly. And I perfectly understand on an emotional level how many of them have been very embittered by their experiences. I perfectly understand that.

Q. And do you accept that patients have a right to, if they believe things have been done in a way that was wrong, or misguided, or incompetent, have a right to raise that through a range of different appropriate forums, in principle?

A. In principle, I have no problem with that whatsoever. Similarly, if someone has behaved in a negligent way,

it's entirely reasonable that they should take legal action.

Q. One final document, HSOC0001265. It's the next page. Well, actually, we'll look at -- we'll go to the next page, first of all.

This is a letter sent to the chief executive of the Haemophilia Society in September 2006. If we just go down to the bottom of the page. It's sent by you in your capacity as Chair of UKHCDO. And then if we just go up again, it says in the third paragraph:

"The Committee asked me to emphasise to you [this is the Advisory Committee of UKHCDO] their collective view that a public enquiry [sic] into this matter is not in the patient's best interests and is likely to harm rather than enhance patient care."

Why did you think that?

A. Well, I was reporting back the discussion from the Advisory Committee.

Q. Well, it's --

A. And I think they felt -- patients were saying that there was some sort of conspiracy of silence which I don't think we recognised. I certainly, on a personal basis, have always tried to be as open and transparent as possible. So we did not feel that there was a conspiracy of silence, and when the

patients said, "We want to know the truth," we weren't quite sure what truth they were after because, you know, we felt that we had been quite open.

And when it comes to the suggestion that this might harm them, well, I have to say to you that I have seen many patients after the onset of this inquiry who have been quite distressed by it. It has not been universally welcomed by the body of patients. I think it would be true to say that there is a lot of ambivalence out there. Many patients who have come to terms with what they've been through in the height of the HIV era were upset that this raked it all up again.

Now, I appreciate that that won't be the universal view, and I'm sure that your witnesses very much welcome the inquiry, but other patients don't. You will find a wide range of opinions from the patient body, but I've had to have many long conversations with some of my patients, some of them in tears because this has brought it all bubbling back up to the surface. And they have clearly suffered greatly during the HIV era, losing their children, for example, or their husbands, you know, and I can think of nothing worse than to lose one's child from an iatrogenic illness.

number of years you have been a Centre Director?

A. Yes, absolutely. And in the early years, there would be odd batches rather than a whole product re-call. It would be unusual to re-call a whole product, but there may be a problem with an individual batch. You might suddenly get a lot of reports of patients getting reactions with a specific batch.

They would all be pyrogen tested to minimise the risk of reactions, but sometimes, nevertheless, they would give reactions. Reactions are much, much commoner with plasma and cryoprecipitate and could be quite severe.

SIR BRIAN LANGSTAFF: Thank you.

A. And as the product purity improves, there were fewer and fewer of those reactions. Then there were occasional product re-calls because of things like the advent of heat treatment. Some unheated products were re-called, and so on.

SIR BRIAN LANGSTAFF: Thank you. And how often did that happen? The unheated product being re-called? Do you remember?

A. Well, that only happened when they were being introduced back in 1985. BPL re-called some of -- well, what was left of their unheated product, and then they were going to heat it and re-issue it.

You know, I don't dispute for one moment the degree of suffering that the patient body went through as a result of all of this. But many patients accept that the treatment was given in good faith, and it couldn't have been avoided. And so, you know, opinion in the patient group is variable. And, you know ...

MS RICHARDS: Sir, those are my questions. I understand you may have some for Professor Hay.

Questions by SIR BRIAN LANGSTAFF

SIR BRIAN LANGSTAFF: Yes. It's a bit of a ragbag arising out of some of the things that counsel has been through with you.

The first is this: you mentioned early on in your evidence the issue of product re-calls.

A. Yes.

SIR BRIAN LANGSTAFF: And I just wonder if you can give me some sense of how often products supplied to you by a commercial supplier or, for that matter, by Elstree, were re-called.

A. Not very frequently.

SIR BRIAN LANGSTAFF: So in terms of -- in any year, if you could average it, how often might it happen?

A. Oh, much less frequently than that.

SIR BRIAN LANGSTAFF: I see. So the number of times that you've had a product re-call would be less than the

SIR BRIAN LANGSTAFF: And that was the material that you found unusable because it didn't dissolve very easily?

A. That's right.

SIR BRIAN LANGSTAFF: Thank you.

The second thing I wanted to ask you about was this: when you were talking about relationships with the pharmaceutical companies, you mentioned that sometimes a pharmaceutical company would ask you, or the haemophilia doctors, to conduct an analysis, and you would charge them for it.

A. Yes.

SIR BRIAN LANGSTAFF: May I ask the basis upon which the charge was worked out. Was it the cost to you, with perhaps a small profit element, or was it the amount that you thought the pharmaceutical company might be willing to pay?

A. It's a compromise between those two, I would say. We do not make a huge profit on it, but we need to cover our costs. And that cost is currently calculated by a manager.

SIR BRIAN LANGSTAFF: Did you ever have any, or much push-back from the company to say, "Oh, we won't pay that"?

A. Sometimes. Yes.

SIR BRIAN LANGSTAFF: But not usually?

A. Well, we tried to avoid getting into that position by not charging an outrageous amount.

SIR BRIAN LANGSTAFF: I see. Right.

The next question, when you were speaking about talking to patients about the results of their HIV test, you observed that you thought that Professor Preston's approach in Sheffield was a good one. You said the different clinicians had different practices, some good, some not. Can you give me more detail about the some that were good and the some that were not?

A. Well, I didn't feel that the practice in Liverpool was very good, because as far as I could make out from my conversations with my patients, they'd been informed by post and offered very little support. So when I arrived, I inherited a group of patients who were understandably very angry, felt very let down. And I agreed with them, frankly. And they needed a great deal of psychological support, and many of them were, quite understandably, very embittered about the way in which they had originally been informed.

And, you know, I couldn't support that. Although it was a long time ago, I don't think that that practice was acceptable, even in 1985.

You know, we didn't know a great deal about HIV

at that time, but we did know that it was potentially fatal, because there'd been some cases of AIDS. We didn't know how many of the patients would develop AIDS, because in those early days, bearing in mind that it was only an antibody test, what that test told us was that the patient had been exposed to the AIDS virus, and there was an expectation, soon to be dashed, that some of those patients would actually be immune, in the way that somebody who'd had hepatitis B but recovered from acute attack would be immune. And, you know, with hepatitis B, 95% of people turn out to be immune without chronic viraemia.

Now we expected something similar to emerge with HIV, and sadly it didn't. But, you know, that was the level of knowledge in '85. But I think there was a lot of uncertainty about it and patients should have been told, apart from the fact that having a positive test didn't mean they had AIDS, that they would be monitored and supported.

SIR BRIAN LANGSTAFF: Thank you.

Were there --

A. And --

SIR BRIAN LANGSTAFF: Sorry.

So -- sorry.

A. And that we were looking for treatment and there was

a degree of uncertainty about the outlook.

SIR BRIAN LANGSTAFF: Were there any other practices elsewhere that you became aware of and thought were poor? Or, for that matter, good?

A. Well, I heard that in some places patients were told in groups. And I find that amazing, because there's a confidentiality issue there, apart from anything else. And I think it's always more sensitive to tell people one at a time. I thought that the system that I heard about at the Royal Free was particularly good, where they were taken into a soundproof counselling room, with a counsellor, and with someone else, and they were -- they informed them. And I think there is some video evidence of that, that I understand the Royal Free have shared with ...

SIR BRIAN LANGSTAFF: Thank you.

The next question was this: it was in relation to hepatitis-reduced products. Now, plainly, hepatitis-reduced didn't mean to say that it had no hepatitis virus in it.

A. Yes.

SIR BRIAN LANGSTAFF: But were those products, so far as you were aware from your own experience at the time, were they at all successful in producing a lower incidence of the disease?

A. My understanding is that they were probably better than we initially thought, because -- to take Alpha Profilate as an example, as I told you yesterday, 24 of the 27 patients in that study did not develop non-A, non-B hepatitis, and three did. But once we used it, commercially, I don't think any of the patients developed hepatitis C from that particular product. Other products were less successful. They were all pretty good at eliminating hepatitis -- eliminating HIV, because fortunately it turned out that HIV was more heat labile than the hepatitis viruses.

And also -- they were generally a bit better. But we continued to monitor the patient group, both for HIV and hepatitis, for several years after that, because there remained some residual doubt. And as time went by, further viral steps were introduced and further purification steps were introduced to progressively increase the level of viral safety.

SIR BRIAN LANGSTAFF: So, in summing that up, I think what you're saying is that some products, anyway, which claimed to be virus-reduced, actually did work to some extent?

A. Well, most of them worked very well.

The exception, about which I'm sure you're

going to come back, is to that early Armour product that transmitted HIV to a few patients, sadly. And that product is a good example of a product recall, where they recalled the whole of the product, because clearly the process as a whole was inadequate.

SIR BRIAN LANGSTAFF: Yes. The last thing I want to ask you about is simply to get some information about how the national contract for a product works.

Because of your policy, and your general policy that we've heard from others, of not all the eggs being in one basket, presumably whatever the national contract is, it's for a range of products.

A. Yes.

SIR BRIAN LANGSTAFF: Nationally negotiated.

A. Yes.

SIR BRIAN LANGSTAFF: And that shows cost advantage, does it, over negotiating per centre?

A. Well, actually, the way to get the best price would be to go for a single product, but we don't want to do that for a variety of strategic reasons, which the Department of Health accept. And the Department of Health accept that there will be a financial price to pay for that strategy.

And that sort of strategic approach is apparently accepted by the Department of Health in

relation to a wide range of products and is not peculiar to our particular area.

And the strategic reasons are: you don't want to be dependent on a single manufacturer, because if you become too dependent, apart from anything else, what's to stop them turning round and putting their price up at a later stage? You know, when the next contract comes round --

SIR BRIAN LANGSTAFF: They're a monopoly supplier, and you might imagine they might do that. So I can understand that.

A. Well --

SIR BRIAN LANGSTAFF: Can I --

A. They also --

SIR BRIAN LANGSTAFF: Can I ask you just to -- if you know anything about, you may well not, because it's before you were centrally involved in much of this world, but in the 1970s, ending in about '79, I think it was, there was central contracting for commercial product. Then it ceased. And plainly, at some stage, national contracting, as you've described it, started up again. Roughly when was that? Do you remember?

A. When did it really start or when --

SIR BRIAN LANGSTAFF: When did national contracting start to replace the system of buying by centre.

A. The first time we had a proper national contract was with recombinant for all.

SIR BRIAN LANGSTAFF: I see.

A. And we established a national contract, and that led to surprising discounts which had practical implications because it enabled us to start some patients earlier than we would otherwise have been able to. Obviously, we would have preferred to have started them all at once.

But then there was this threat to the continued funding and one of the responses with the Department of Health to this funding threat was to introduce a system of central contracting for all products, for all the patients. So that was the first truly national contract for everybody. And so the Commercial Directorate became involved. Deloitte offered a device with the very first round, and our objective was to reduce the cost and, therefore, make the continued supply of recombinant Factor VIII for our patients more secure, and to maintain freedom of prescription to have as many suppliers as we could so that the market would not be vulnerable to interruptions of supply. Bearing in mind that, as recently as 2002, we'd had a major interruption in the supply of recombinant when Bayer stopped supplying.

You know, so it's a very recent memory, a very real problem. And the Department of Health accepted that even though Deloitte said, well, you'll get the biggest saving if you just go for two suppliers, as group of clinicians, and with the department's support, we said no, we don't want to go down that route. And we organised it in such a way as to make the suppliers behave in a commercial, competitive way. And we told them that if they didn't offer us a good price, we wouldn't buy their product. Whether that was a real threat or not, it had the desired effect, and with each round, the price has reduced to an extent that, frankly, exceeded our expectations.

Right at the outset of this, Deloitte told us that 90% of the cost of a drug is usually profit. I was staggered by that. But when we did a survey, we discovered that the unit price for a given Factor VIII product varied by over 50% from one Haemophilia Centre to another. So even if we just paid the average price, we would have saved something like £15 million. So clearly, there was enormous scope. I mean, the manufacturers always said, "Oh this is an expensive product to manufacture. We're not making much money on it," and so on. And we had no way of knowing what profit they were making. But it has been very useful

because during the period during which we've had this, we have wanted to improve the intensity of treatment and the quality of treatment for the patients.

And when we started that contract, the average amount that patients with severe haemophilia were using was 120,000 units of Factor VIII a year. And it has increased now to an average of about 300,000. But the total cost of that has actually been reduced. We're now paying the -- unit prices that are similar to those that pertained in the 1970s.

SIR BRIAN LANGSTAFF: I see.

Now, just to give me a sense of how it is organised as between yourself and the purchasing unit, is this a question of the price being negotiated and you then ask for supplies from the supplier, or is there a central warehouse, as it were, either a notional warehouse or an actual one, which has a store of the product which you are, between you, obliged to take? Do you ask the --

A. There's still some degree of prescribing freedom, and different centres prescribe different products. The price is set nationally by the national contract. Each round is organised between UKHCDO and what was, past, the Purchasing and Supplies Agency, but which is now CMU, the Central Medicines Unit. It's actually

the same bunch of people. Coincidentally, they're just down the road from me.

And they organise the contract. We help them with data, to facilitate that process. Their actual tenders are assessed in a multi-disciplinary way by a group. Very often the products are scored, partly by price, partly by safety, ease of use, things like that.

We have even involved patients and haemophilia nurses in some of those assessments.

SIR BRIAN LANGSTAFF: And when it comes to the question of safety, what are the sort of considerations that would make one product, nowadays, safer than another?

A. Well, the difficulty with safety -- and we haven't always used it in every evaluation recently, because we found that it didn't discriminate between the products. In the past it most certainly would have done, but it's difficult to demonstrate an increment in safety between the various products, and some of it comes down to opinion.

For example, some of the extended half life products are pegylated, that is to say, a molecule of polyethylene glycol is attached, and that's the method that they used to extend its half life. Others have bits of immunoglobulin attached, which is considered

more normal, and has less effect in the way in which the product is dealt with.

Now people are a little bit suspicious about pegylated products because the polyethylene glycol is excreted from the body more slowly, and although there is no positive evidence, we would prefer it to disappear more quickly. We don't know what the long-term consequences of having polyethylene glycol in your body might be.

There are many other pegylated drugs available, but perhaps none given for an entire lifetime. And it's that sort of consideration. So some clinicians have said, "Well, I know there's not much evidence but I would prefer not to take that risk", and they choose to use other products. In my own centre, we have four consultants with an interest in haemophilia and we reach these decisions by consensus.

SIR BRIAN LANGSTAFF: Well, thank you very much. Those are all the questions I have to ask.

Ms Richards?

MS RICHARDS: Professor Hay, do you have anything further that you wish to say?

THE WITNESS: No, I don't.

SIR BRIAN LANGSTAFF: Well, it remains for me to say, professor, that we're very grateful to you for giving

up your time to be here virtually. I know that you would have preferred, as we would have preferred, you to be here in person, but it's rather a long way for you to come, I think. It would have been, anyway, a long way for you to come. Those listening should know that you were prepared to do that and, of course, you have further evidence to give us in due course. We'll have to decide whether we actually ask you to give that orally or not at a later time.

But your willingness to engage is noted, and we thank you very much for that. It's given us, this evidence, at any rate, an insight into what we hadn't had much evidence, as yet, orally given to us: the period in which vCJD was a real threat and how it was handled. It may still be a real threat, but at least we know how it was handled in the 1990s, and what it was like from your evidence to become a Haemophilia Centre Director of a large centre at the end of the 1980s, coming into the 1990s, with all the challenges and the testing for hepatitis C that took place.

That's very valuable evidence for us to have. Thank you very much indeed for coming, or being here, rather, I should say, virtually to give it.

THE WITNESS: Thank you. I hope that it's been helpful.

SIR BRIAN LANGSTAFF: Well, I'm sure in many ways, it will

have been.

MS RICHARDS: Sir, that completes the evidence, obviously, for today and for this week. We're not sitting next week, and we resume remotely, so far as witnesses and core participants are concerned, the following week on the Tuesday, which I think is 17 November.

SIR BRIAN LANGSTAFF: Yes, it is.

MS RICHARDS: Yes, it is.

SIR BRIAN LANGSTAFF: So those listening around the country should know that we will start on the 17th. We are then hearing evidence from?

MS RICHARDS: We have evidence from three witnesses that week, Dr Al-Ismail, Dr Mitchell, and Dr Giangrande.

SIR BRIAN LANGSTAFF: Thank you. So we start at ten o'clock on Tuesday, 17th November. Thank you very much.

(5.05 pm)

(The hearing adjourned until Tuesday, 17th November at 10.00 am)

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