Wednesday, 28 September 2011

(9.30 am)

(Proceedings delayed)

(10.03 am)

PROFESSOR RICHARD TEDDER (sworn)

Questions by MS DUNLOP

THE CHAIRMAN: Yes, Ms Dunlop?

MS DUNLOP: Thank you, sir. I'm grateful to you, sir, for allowing us a bit of extra time. It has enabled me to talk to Professor Tedder briefly about some of the more technical aspects of this morning's evidence.

It has also enabled us to dig out a very large white board which Professor Tedder may want to use at some point to explain some of the science.

We don't, I think, have a CV for you, professor. I hope that we might be able to receive one, if you could perhaps send one to us in due course. I see that you are a consultant medical virologist and you actually have sent your letter from Colindale, but could you please just tell us your current position or positions?

A. Resolved by a contract being confirmed for the next three years yesterday.

I'm on the faculty of University College as a professor of medical virology and I retain that position on the faculty.

I am an external consultant virologist, contracted to or paid for -- I have an honorary contract with the National Health Service Blood and Transplant, which is essentially NHSBT, the transfusion organisation in England.

I also am an honorary medical clinical virologist to the Health Protection Agency at Colindale in London, where I head up the blood-borne virus unit, which is one of the small number of units contained within the virus reference department.

Q. Thank you.

We wrote to you posing certain questions in connection with our topic B4, which concerns the screening of donated blood for what was to become known as the HIV virus. You have provided a response. It's my intention to work through the questions and answers this morning, asking some supplementary questions as we go.

We will need to have open both the schedule containing the questions, which is [PEN0170523], and your response, which is [PEN0171831].

It might be helpful if we look at the questions document, just to see the first two of the questions. If we could look at the questions document and if we go to page 3 of that, it consists of a letter and then

a schedule which actually contains the questions.

In fact the first numbered paragraph isn't a question, it's a statement. I don't propose to ask you anything particular about that, Professor Tedder. We are very conscious of controversy in the whole area of credit for the identification of the virus and we had some discussion about that with Professor Weiss yesterday. It's very, very interesting but I suspect, if we took too much time over it, we might not have time left for other things.

In paragraph 2 we noted that American virus -- I think actually an isolate labelled "HTLV-III B" -- was provided by Dr Gallo to Professor Weiss and used by the two of you. We go on to say that:

"When the DHSS asked if the isolate could be used to assist in developing a test for the UK market, indeed for the NHS, permission was refused."

And we asked how much of a set-back this was to you in your work.

Can we go, please, to the answers? Thank you. Just passing over paragraph 1 and moving to numbered paragraph 2, you say:

"In May Dr Gallo made available HTLV-III to Professor Weiss at the Chester Beatty laboratories."

You had already worked on developing an assay,

a test, for HTLV-I, which was an earlier virus that Dr Gallo had isolated. Is that correct?

A. HTLV-I was the first of the genre of retroviruses known to infect humans.

Q. Yes.

A. Originally described by -- actually Japanese groups, where it causes disease in that country. In the previous year the first time I met Professor Weiss -- Robin Weiss, if I may call him that, as he is a personal friend of mine now -- was going down myself as a medical virologist going to him as an expert in retroviruses, saying, "I want to know more about this virus, HTLV," because I had heard Bob Gallo talking at, I think it was, the Institute of Child Health in 1983 about this virus and this set up a collaboration with Robin to develop serology, which was already well underway when the HTLV-III B isolate was produced.

Q. Without moving back into the territory covered by paragraph 1 too much, is it correct to understand that for a while Dr Gallo was trying to prove that HTLV-I was the cause of AIDS?

A. Yes. There was a meeting in, it may have been, 1982 or early 1983 in Washington, which was the first -- we didn't call it "AIDS" in those days but it was the first retrovirus meeting and he was putting forward the idea

that HTLV-I was more commonly found in people with the various diseases, the pneumocystis pneumonia and the Kaposi's sarcoma, and that was probably because of the risk groups actually harbouring the drug abusers in North America. The recreational drug users would have harboured a sister virus of HTLV-I -- I don't want to go into too much virology -- HTLV-II. The gay men who had the pneumocystis pneumonia would have had HTLV-I and at the time the Americans were unable to differentiate serologically between that. So this was HTLV reactivity.

I already had a brush with Gallo in that meeting in 1983 because I said the data that we have in the UK does not support this at all because we found the prevalence of 1 or 2 per cent in amongst people who have various illnesses, and certainly not enough to be aetiological, not enough to be causative of the disease.

Q. Right.

A. Does that answer your question, sorry?

Q. Yes, thank you.

You do explain that you had been involved in developing an assay for HTLV-I, which then, I suppose, led naturally into a similar sort of work with the Gallo isolate.

A. I think you should ask Robin about our first meeting.

I think he felt that I was a keen clinical virologist and was going to be a nuisance. He gave me a big advantage in that he gave me a serum, and it was quite amusing going back about six or eight weeks later saying, "I have got a prototype test, let's do some epidemiology," and that was in 1983 and that carried through into 1984. We refined the tests. And of course, having shown him that we were capable of developing assays, once HTLV-III B -- access to that was granted -- it was really not difficult to rework the system but using HTLV-III B and sera from people with AIDS and making a test.

Q. We are going to go on and look at some of the technicalities shortly, but just staying with your numbered paragraph 2, you do say that Luc Montagnier had offered CBL access to the French virus, IDAV, and arranged for a courier to bring the material to London in the autumn of 1983, but that didn't work. I think we have established from Professor Weiss that he did get some LAV also from Montagnier in February 1984.

A. That was four, five, six months after where we could have been if we had -- there were two viruses, LAV1 and IDAV. They are both AIDS viruses, both HIV-1.

It was just rather galling that the flask had been brought over. It was actually left in an overnight

security locker on, I think, Waterloo Station and picked up on Monday morning. Of course, by that time I am afraid the concentrate had died and it couldn't be resuscitated.

Q. Right. Professor Tedder, I'm already off piste here and I shouldn't be because it's dangerous.

A. That's a dangerous place to go.

Q. Yes. You are talking about there being two French viruses. I think we are more familiar with the description of LAV as the French virus but you said the second virus, IDAV, was also --

A. Immunodeficiency Associated Virus. It was the name given to the first isolate.

Q. But it's not the same as LAV?

A. Well, I would need to see the molecular sequences to say it's not the same. I mean, LAV1 and HTLV-III B were very, very similar.

Q. Yes.

A. They were epidemic HIV-1.

Q. Right. You say in your letter that you can't comment on the refusal of the National Cancer Institute -- that's where Dr Gallo worked -- to grant commercial access to HTLV-III. In fact, the letter that was sent was sent to the Department of Health and Human Services, so part of the American Government, I suppose, because by that

point it was the American Government which was licensing commercial companies to prepare test kits from the virus. We know that the request for your kit to be used within the NHS was ultimately denied.

I wanted just to look at a contemporaneous resume of the position, which is contained in a Department of Health document. There are twin documents. The first one gives us the date. So could we look, first, please, at [DHF0020430]?

This is an AIDS position paper from the end of 1984. I think it's probably written by Dr Alison Smithies. It sets out the current position with regard to AIDS, as requested by the chief medical officer. The actual paper is [DHF0020431]. We can see that there is a resume of the current position, and then in section 3, "Development of Tests", the author reports that the study reported by the team, led by -- and I think this is, obviously -- Robin Weiss and yourself, using a competitive radioimmunoassay, is of major interest. We know that this is a study which was reported in the Lancet in September 1984.

Can we go on to the next page, please?

This is really the little piece of narrative about what had happened in relation to the contacts with the United States. In order to obtain sufficient test

reagents for the National Blood Transfusion Service, someone, possibly Dr Walford, wrote in August to the assistant secretary for health at the Department of Health and Human Services in Washington, asking for his help in allowing the use of this isolate to develop tests for the NBTS. We have that letter but we don't have annex 3 for some reason, or if we do, I can't find it:

"An unhelpful reply to this request was finally received on 14 November 1984. By the time the response from ..."

That should be understood as "the United States":

"... was received ..."

Presumably the next blank will be "Dr Weiss":

"... had succeeded in isolating the virus from a British patient. A holding reply had been sent."

Then narrating that there had already been negotiations with Wellcome to use the British isolate to develop a UK test.

I think what we were interested in was whether this delayed your research, and in the first place is it correct to understand that a lot of virus is necessary in order to make test kits? The test kits have to be made from virus as one of the raw materials?

A. Correct.

Q. Yes.

A. But the manufacturer of the American style of assay uses large vessels to grow virus in cells and then merely takes the soup in which the cells are growing and purifies the virus from that, and that is quite a lot of hard work because the amount of virus which is extruded into what we call the supernatant fluid, the fluid around the cell, in tissue culture is usually not a terribly high yield.

You then have to purify the virus, remove all the proteins from the tissue culture fluid that were around the cells, pellet the viruses and then probably clean them up physically by putting them through a density gradient so that they band in a tube as a purified virus, take that and use that.

So that's quite a lot of hard work. We didn't go down that pathway. Pragmatically, from previous experience with the HTLV-I, which actually is a virus which is very, very unlikely to be passed into the supernatant, so we didn't know how well HIV, as we would call it now -- and if I can use that -- translate HTLV-III B which is a mouthful -- we didn't know how well HIV at that stage was going to grow in the supernatant. So we used a different approach, the same as we had used with the HTLV assay, which is to take the

virus from within the cell, and because of the format of the test that we were using, it didn't matter if there was a lot of other cellular material there.

This was not an option open to the American protocol because the American protocol has to have pure virus, "pure" in inverted commas. Our protocol was smash and grab cells, take the antigen from the cells and use that in an assay, and we could do that with our format, which the Americans couldn't do. I might have to use the white board in a minute.

Q. Yes. As part of the development of the test, which became the Wellcozyme test, the process of generating large amounts of virus was carried out at Porton Down. Is that correct?

A. Yes and no. The -- our work in -- really from probably May -- probably June/July onwards, we were using five litre stirrer vessels and growing our own antigen. We continued doing that for the whole of that year, initially using the HTLV-III B isolate, which we had adapted to grow in the cells, which I suspect Robin Weiss would have told you about yesterday, the CEM cells.

Q. Yes.

A. Which produced both better virus in the supernatant, which we used for passing the infection, but also a very

high level of viral antigens trapped in the cells; and that was ideal for our purposes.

So we were using the cells, passing them into more stirrer cultures. And we did that, as I say, really up until spring 1985, because although Wellcome had contracted with CAMR, the first few months of CAMR's antigen really did not work -- were not fit for purpose in our assay, and we had to ensure that they used our protocol for expanding the cell cultures rather than their approach.

Q. Right. You actually deal with this further on in your response.

A. Indeed.

Q. So to come back to whether the unhelpful response from the United States delayed you, would your answer to that be, not really?

A. Yes.

Q. Because you were already working with the British isolate?

A. Well, we were working -- from an experimental purpose, we were working with HTLV-III B and then, as the British isolate became available at the end of autumn/beginning of winter 1984, it was very easy, because that had already been adapted into CEM cells, to just change the cultures that we were doing.

Q. Right.
A. And there was little to choose between HTLV-III B and CBL1.
Q. At one level this is a fatuous question because I'm asking you to get inside the mind of the letter writer in August 1984.
A. Which letter writer?
Q. The British letter writer from the Department of Health and Social Security, who may have been Dr Diana Walford. It doesn't really matter. If there wasn't really a problem in not using the American isolate, then why did the DHSS think it was important to try to get permission to do so?
A. I think because at the time -- I mean, the difficulty that not having at the stage in the end of autumn 1984 -- not having an isolate which you could take to a commercial manufacturer in the UK posed a problem that they had -- Wellcome would have had -- or whoever we went to -- Northumbria Biologicals we talked to, Wellcome we talked to -- we eventually went with Wellcome. The same would have been true for BPL.

The assay substrate, the important antigen component was not available at the time that the negotiations were being conducted in autumn 1984 -- end of 1984. It was only once the Chester Beatty isolate number 1 became

available that that could be put on the side and it no longer mattered whether we had an American isolate or a UK isolate.

As a research worker at the bench, it made no difference to us because we were growing antigen and we had a lot of antigen and we had plenty to work with. So we were never deflected. It was only the second order, trying to say, "Where are we going to go with this? Are we going to go with the Blood Products Laboratory? Are we going to go with Northumbria Biologicals? Anybody else we could work with, including Wellcome Diagnostics? We can't talk to those people because we don't have free access to an antigen for NHS use."

And whoever wrote that letter I think would have been pretty irritated by the terms of reference which would have been used from NCI and the US Government.

Q. Yes. So I think we understand that when the time came for the handover to Wellcome or to CAMR of an isolate with which to work, there was one available?

A. That is my recollection. And I think that's borne out by what the time-course that's laid out in the various letters.

Q. Right. Thank you.

Can we move back to Professor Tedder's letter, please, and go on to the next page? Our question 3,

I'll just paraphrase: we were asking about this very topic, the development of the British isolate, and access to French virus and so on. I think you have really dealt with the basics of that. But you go on to talk about having a prototype test in the summer of 1984 and you tell us that actually the assay was considered to be working by the end of the first week in July. I think perhaps somewhat ironically in the context of this discussion, you told me earlier it was 4 July.

A. Yes, it was.

Q. Yes. What breakthrough did you recognise as having been made on 4 July?

A. Well, I can provide for the Inquiry an actual photograph of the first entry in my colleague's book, which shows titrations of people with serum from people with AIDS, titrating to 1,000 and 1 in 10,000 reactivity in a test and blood donors being unreactive.

It wasn't really a breakthrough, and I'm not trying to be falsely modest in any sense at all. It was so easy and we were so lucky. We had plenty of antigen, we had people with easily identifiable disease, who have, as we now know, massively high levels of antibody in their plasma. It's a really driven immuno-response in the HIV-infected person. An ideal reagent, now we know -- because then we had to select -- to make

components of a competitive assay. And having done that with HTLV-I, the four weeks it actually took us was to select the best samples that we could find from individuals. We honed down from 100 seropositive samples -- we honed down on two, who gave us the best samples in terms of their performance as reagents in the competitive assay.

That's what took the time. And the 4 July, when we said, "Okay, we have done it," we knew that we had agreement from individuals to give us plasma, through the transfusion service, they would bleed these people. We knew we had enough plasma for perhaps two or three years' supply of reagents. We had a months' worth of antigen and we had an assay which worked. It wasn't a sort of eureka moment. It was, "Thank heavens we are where we are. Look, it works. Here are the titrations. We have banked the plasma. We have banked the antigens. We can now start doing some seroepidemiology." That was 4 July.

In fact it was within a week of getting the antigen we had an assay that differentiated between positives and negatives, but not good enough. A threefold difference between your negative and positive was pretty impressive first time round but we wanted to stretch that full-scale.

Q. I have already mentioned about the paper in the Lancet in September 1984; there is a description of the radioimmunoassay in that paper. I think we should ask some more technical questions about the different kinds of assay. You have told me that you are going to help us to understand what those are, at least to gain the understanding that we might need, which perhaps is quite basic.

Can we look at the papers. [LIT0010417].

A. God, that takes one back in time, doesn't it?

Q. Yes. Quite a lot of contributors. But certainly Professor Weiss there and yourself as well. This paper, I suppose, achieved a number of different objects. Well, at least three, and please correct me if this is wrong, but it assisted in an understanding of the prevalence of the AIDS virus, if we can put it like that. It also provided an explanation of the test which had been devised in London, and actually along the way it showed that LAV and HTLV-III B were, for practical purposes, the same thing.

Is that correct about this paper?

A. Correct. I had forgotten we had made that statement, yes.

Q. That's a controversial area as well. We are not going to go off down that track. But if we look at page 2, we

see there the description of the competitive radioimmunoassay for antibodies to HTLV-III. Some of our questioning has concerned the difference between radioimmunoassay and ELISA, and we will come on to that but I think we have been persuaded already by Professor Weiss that that is a less important difference when one is talking about the effectiveness of a test than the difference between the different kind of formats, particularly a competitive format and, I suppose, a non-competitive format, although you tell me there are basically four different kinds of assays.

I think it would be helpful if you could explain to us what type of assay the five American companies were all using, before we go on to look at the difference to be found in a competitive format. You call it a type 1 assay. Is that right?

A. Yes, I suppose the human mind likes to categorise things. Four types of assays. I think, with the agreement of the company this morning, I would probably just talk about one and two.

Q. I think that's fine by us.

A. Bear in mind we also used 3 and 4 in -- a horrible phrase -- an algorithm, which means if you test a sample by type 1, type 2, type 3 and type 4 assay, if it's a genuine positive, it will come up in all four assays.

And one of the big arguments we had, which rattled on with the WHO for about five years -- or beyond that -- was that it's much better to have an algorithm of two or three different ELISAs than it is to have one ELISA plus a Western Blot, because a Western Blot was so incredibly expensive.

The whole world was spending fortunes of money on confirming HIV with Western Blots, in spite of the Scots amongst us telling them to cut the Western blot into strips, longitudinally, of course, not across, and that would save money but that was not popular.

Can I come back to type 1 and type 2 assays?

Q. Confirmatory testing is interesting too, and I think again at a general level and a logical level, we understand that confirmatory testing is very important because when the test was rolled out in the blood donor population, there were false positives and obviously you have to have some kind of mechanism for deciding whether a screen positive is a true positive?

A. Yes, I mean, a sort of ballpark figure, 99 out of 100 antiglobulin positives in blood donors would be false. 50 per cent of the -- 25 to 50 per cent of the competitive EIA samples would be false. That's a very great difference in the amount of testing and confirmatory work that you need to do, depending on your

screening test.

Q. Yes.

A. That's why I felt, for whatever purpose, a competitive test is preferred over an antiglobulin test; a type 2 competitive test is preferred over a type 1 antiglobulin test.

Q. In fact in this paper, in the group of people who were unselected blood donors, there were actually no positives at all.

A. Correct. It was something like one in 178,000 repeat reactives by competitive ELISA, of which half would be -- or one third would be genuine. So that would be one in 10 to 20,000 blood donors might be seropositive.

Q. Right.

A. Something of that sort of order.

Q. All right. So it was just this particular thousand. If you had kept going --

A. If one had kept going -- and that was indeed the question, that we wanted to keep going but we were constrained by other -- which I shall come back to -- constrained by other anxieties of not keeping going through the whole of the transfusion service. So if we had been doing it in one centre and word had got round, it might have had a very detrimental effect on the donor make-up in the centres who did not have a test. That

was a real anxiety.

Q. I think another basic insight, which we need to have -- and we will need it when we come to look at the story of Hepatitis C screening as well -- is ways of talking about the number of false positives, because I think I have seen this expressed in different ways. Professor Weiss yesterday explained to us that a false positive rate of 300 per cent would mean that for every true positive, there were three false positives. Do you agree with that?

A. Yes, it's not the way one would normally put it.

Q. That's what I'm seeking. What is the way in which one would normally give the statistic for false positives?

A. Well, a false positive -- okay, you test a sample. It reacts. That's IR, initially reactive. The first way of getting rid of false reactions is to repeat that, and generally you repeat it in duplicate. Because if you do one positive and one negative, you would never know which god you pray to, and which is real. So you do it in duplicate the second time round. So you test first.

Q. So it's the best of three?

A. The best of three, yes. If it is negative, repeatedly negative second time round, that was the false reaction, initially reactive, false reaction, forget about it. You might want the manufacturer of a kit to address the

initial reactive rate. So what we normally do, in a kit, in any situation, you say, "What's the initial reactivity? What is the repeat reactivity?" And a good test -- no, that's a value judgment -- a robust test, which is reproducible, your repeat reactive rate should be very similar to your initial reactive rate.

Q. Yes.

A. Your repeat reactive rate is another parameter of the test. So you have got your initial reactive rate, your repeat reactive rate and then the proportion of the repeat reactive rate which are confirmed.

Q. Right.

A. In a low prevalence -- that's a population that you are testing where there is only a small number of people infected and an awfully large number of people not infected, and I would say the best model of that is probably a UK donor panel, blood donor panel -- most of your repeat reactives are going to be not confirmed, false reactivity. And the false reactivity rate is going to be much higher in the antiglobulin test than in the competitive test.

In the competitive test, in a low prevalence situation, it depends how reactive but at least half of those are going to be real. In an antiglobulin test, it's a fraction of those. It's about 1 per cent or less

will be real, confirmed. Confirmed positive.

Shall I just put that on the board at the top?

Q. Yes, absolutely.

A. So that we remember.

Q. Yes.

A. I'll put it in black. Your initial reactive, you retest and that gives you a repeat reactive, and those can be positive confirmed, negative, not confirmed. And it's the ratio of the IR to the RR to this outcome -- do you want me to -- it's the difference between initial reactive, repeat reactive, which are really parameters of the test from the operator, and then the readout of the test of the repeat reactives is confirmed and unconfirmed.

The more specific the test is, the higher the proportion of the confirmed than the not confirmed. And, in my experience, the competitive test is much more likely to go that way and the antiglobulin test is much more likely to go that way. Just proportionally.

Q. Right. So among the testing community, as it were, when people are speaking in shorthand about how good a particular test is -- I have seen a number of different percentages used -- what would be the most likely language they would use? I have a test kit and the --

A. Repeat reactive rate in a low prevalence situation should be 0.05 per cent.

Q. Right.

THE CHAIRMAN: Ms Dunlop, can I remind you that if one has to go back and look at this later, the professor's indication that a certain proportion goes "that way" and a certain proportion goes "that way", it will not communicate very much.

A. Should I rephrase that?

THE CHAIRMAN: Yes, simply to ensure that we have got all the words in, rather than gestures. Gestures don't come through terribly well in a transcript.

A. One of the best ways of defining the performance of a kit, it doesn't matter what it is, a kit for testing for something, is to ascribe it first the initial reactive rate. That's putting samples through and something signals.

Repeat testing of the IR, the initial reactive, will then give you the second parameter you measure, which is the repeat reactive rate, and for a test to be acceptable nowadays in transfusion screening or donor screening, the repeat reactive rate should be no more than 0.05 per cent. That's one every 1,000 or one every couple of thousand is going to be repeat reactives.

Q. Right.

A. You then have to say that the next parameter of the test is to define what is the outcome of confirmatory testing on the repeat reactive, and that's in a low prevalence situation.

Q. Yes. I'm sorry, I'm interrupting but just to be sure that we understand, that means that people are living with a difference between the first position, which you have drawn, which is initially reactive, and repeatedly reactive, which is quite significant but which can be explained by operator error or some sort of basic glitch, which doesn't manifest itself the second time the test is done.

A. Yes, it may be operator error, it may be something inherent in the fragility of the test, it may be the washing of the test, it may even be the signalling of the test, all of which you can say, I don't like this sample, go away and repeat it. Oh, it hasn't repeated, that was initial reactive. Or it has repeated, now we have to go into confirmatory testing.

Q. Right.

THE CHAIRMAN: The very low repeat reactive rate refers to this scope for operator error and other matters of that kind being more significant than the test itself and its sensitivity or what? Why is it 0.05 per cent?

A. The 0.05 per cent is actually going to be a parameter of

the test itself and the reactivity of human plasma -- or whatever you are testing, Lord Penrose, in the assay. The IR, the initial reactive, is going to be the parameter of the individual who is setting the test up and the equipment that's used. That's the parameter which is most susceptible to human inexactitude. By the time you have got to the repeat reactive, it's a parameter of the test.

THE CHAIRMAN: How is it that the human dimension, as it were, has been removed at the repeat reactive stage? Just because greater care is taken? Or a different approach is adopted, or what?

A. In this day and age, mechanisation, robotic sample processing -- use of the appropriate sample, robotic sample processing and designing assays where washing is again instrument, robotic-controlled, rather than human hand-controlled, that has reduced the reactivity rates induced by human activity to a bare minimum.

THE CHAIRMAN: Right.

A. Of course, we are talking back 25 years, when robotic sample processing wasn't there.

THE CHAIRMAN: Well, indeed.

A. I think, I mean --

THE CHAIRMAN: But greater care must have been taken then at the second stage.

A. We trained people. I don't think we do nowadays but that's a different question.

MS DUNLOP: Just to go back, let's imagine a convention of testing kit manufacturers and the person who is going round looking at the different stalls and looking at which one he is going to buy, is looking, I think you said, for a kit that has a repeat reactive rate of about 1 per 1,000 of those tested. Is that right?

A. Yes, that is today.

Q. Right.

A. Yesterday or yesteryear one was probably more worried about what's the sensitivity of this test on the first hand, because we didn't know where the virus was and secondly, what is the outcome of confirmatory testing and how much confirmatory testing do you need, which is not dissimilar from saying: we want as low repeat reactive as possible but not so low that we don't detect the real positives.

Q. Yes. Everything so far has been about the journey from the left-hand side of your drawing to the mid point and then, as the chairman says, we have to be sure that when we read this again we can understand it and we are going, I think, to have a photograph, but we need then to move from the mid point of the diagram to the right, and we can see we have a choice of directions to take.

We can go north, east, or southeast.

A. Well, we also can go in the middle, which is a horrible phrase, which -- I mean, as we are going back a long time. Philip Mortimer and I would not let anybody use the word "equivocal". He said it was a disease that was as important -- an infection that was as important as HIV. "You are not allowed to use the word 'equivocal'. You have to make a value judgment."

The reason for that was it's too easy to say, "I don't know what it means," equivocal, and that doesn't help the patient or the donor. So we tried to force people -- I certainly would not ever in my unit allow anybody to put "equivocal". I don't let people put "equivocal" on anything. You have to make a judgment.

THE CHAIRMAN: I know the problem.

MS DUNLOP: Yes. Please don't draw any equivocal because we are content to accept your explanation for why that's unacceptable. But if you could take us to confirmed or non-confirmed and tell us what it is the purchaser of the test kit is looking for.

A. Well, in an ideal world, which we don't live in, but were we to postulate an ideal world, if a kit gives you a positive result, you would want that to be confirmed in by way and far the majority of the repeat reactive

samples.

Q. Yes.

A. And you would want it to be confirmed by an assay which is objective, if possible, not a subjective assay, something where you can say, "Okay, I have measured it here, I have measured it here, that gives me confirmation," or, "I have done something different." Nowadays we use molecular tests -- to try and sort out serology, we use a molecular test. That helps; it's not perfect. That would give you confirmation that a person is infected by or carries this marker, whatever this marker is, that this marker is specific, and if it's not confirmed, then you have the false positive camp -- the southeast camp, which is the false positive, unconfirmed, and the northeast, which is the confirmed.

Q. Yes.

A. And that is essential to do no harm when you introduce a new test. The last thing you want to do is tell somebody, "Oh, well, you have got a reaction for this marker. It might mean you are going to be dead in five years' time, it might be nothing and we don't really know. We can't help, you, sorry, it's an equivocal result."

That's the one thing you do not want. People don't like uncertainty. It's better to have bad news than

live with massive uncertainty; it's even better to have good news. And whichever the test is working, whether it's a test for good news, a test for bad news -- uncertainty is a bad principle and you don't want to have too much uncertainty. Back in 1984 everything was uncertain.

Q. Yes.

A. But we wanted to remove as much uncertainty as possible.

Q. Yes. So, ideally, if, after a period of carrying out tests, one has N, which is the number of repeat reactive tests, the absolute number, then you would want the number in the northeast corner to be as close to N as possible?

A. Correct.

Q. Yes.

A. Taking the words that you said and turning them round a bit, you said after a certain amount of time the testing -- of course, back in 1984/1985 one of the best ways of knowing what you were dealing was retesting the patient because if the patient was in the not quite negative zone and you retested them two or three weeks later, if it was a real marker of an infection, they would have moved into the reactive zone, and that was an absolutely crucial feature. It's one of the benchmarks that we have in serology, seroconversion, going from

being negative to being positive. That is a hallmark of seroconversion and it is, if you like, a benchmark standard, saying, "This person is now seropositive. They were seronegative." And these repeat reactives at the time -- and this was the substance of wanting to be able to retest, if you like, as a reference laboratory, to have access to bring people back, retest them and see how many of these repeat reactives become seropositive.

Q. Yes.

A. So time gives you an answer as well as clever testing at the first bite, the first time you have the sample.

Q. Right.

THE CHAIRMAN: That strikes me as being quite difficult because it's a different kind of variable coming into the question of the effectiveness of the initial test. It doesn't relate to the efficiency of the test itself so much as to the state of development of the condition of the patient.

A. Well, Lord Penrose, I think you are right there but I would plead my case in the following way: the only way that you are going to put a value judgment on the repeat reactive is either be extremely clever and sophisticated, which we certainly weren't in those days -- we didn't have the tools -- or allowing a retest, what we did in the transfusion service in the

mid-1980s. We couldn't afford to lose many people on these initial reactives. There were too many of them with those people who were using the DuPont test. It was a nightmare.

We actually engineered the way that the donor could come back after six months and testing them in an alternative assay, and if they were seronegative in the alternative assay, (a) we knew that the first repeat reactive was incorrect, and that fed back and told us a lot about the repeat reactives, and also that the donor was recoverable and could be readmitted to the donor panel, which was desperately important for us but under a different testing --

MS DUNLOP: Right. Suppose you have a test kit. Let's say it's a type 1 test kit and there is a confirmatory test applied, which is something like Western Blot --

A. Yes, I am listening, I can do two things at once. I know I'm a boy.

Q. To go back to what it is the purchaser of a three months' supply of test kits is looking for, say, and the concept of N -- using the not particularly efficient test kit, there is a big difference between N for the number of tests and the number that, on Western Blot checking, turn out to be confirmed. How would that be expressed? How would the dissatisfied

purchaser go back to the manufacturer? He would say, "I am finding ..."

A. " ... that most of your samples are -- you want the real answer?

Q. Preferably.

A. I tell you what actually happened: they all went on to Western Blot and what answer do you think we got then?

Q. I think you had better tell me. I don't want to speculate.

A. "Equivocal."

Q. All right.

A. P24, P55 lines on Western Blot, two lines on Western Blot, WHO recommendation, perhaps equivocal, don't know. That's what happened and that caused immense problems. Half of the DuPont repeat reactives -- two thirds of the DuPont repeat reactives threw up a P25, P55 and sometimes a P59, a duplex of core high molecular weight and core low molecular weight lines, and of course -- in fact in Western Blot there are only two types of Western Blot that were any use: multiple lines, all blue or completely white. It's a lovely test but it's not a good confirmatory test.

Q. Right.

A. So if you bought a test from a manufacturer of the antiglobulin format and even using Wellcozyme, any of

the manufacturers would have said, "You need a confirmatory test, go and buy Western Blot."

In fact ourselves and Philip Mortimer and the PHLS as a whole managed to get the UK out of the Western blot mindset because we said, "The Western blot is nothing other than an antiglobulin test." I will have to explain that in a minute.

Q. Western Blot is expensive as well.

A. That's why we told people to cut them longitudinally, as long as you validated that. You can get three Western Blot strips out of a commercial one. If you are Scottish, you might get four. I'm a Celt myself. So we were cutting Western Blots, if only just to know what was going on. We didn't use them in anger; we used an algorithm of different assays.

Q. The reason, Professor Tedder, that I'm asking about the language is that around the turn of the year 1984 to 1985 there are quite a lot of papers which rather blithely talk about such and such a test having a false positive rate of -- and I'm not sure whether all these people who made these statements (a) were using consistent language and (b) understood what they were saying.

A. I think probably not. You actually need to go back into the paper and you need to think about initial reactive,

repeat reactive and the confirmatory outcome. One of the things which an epidemiologist will say is, "What is the positive predictive value? Okay? We haven't (inaudible) about this, the positive predictive value of this test, and that is: the positive predictive value is, you take a population, you test it, you get the repeat reactives. What proportion of those repeat reactive signals are actually predicting that this person is infective? So that's a positive predictive value, and I don't think people were using necessarily -- you would have to go through the literature and retranslate it into IR, RR, confirmed, and then work out the positive predictive value to get everything right, because the positive predictive value of the anti-globulin test was low, the positive predictive value of a competitive test was high.

THE CHAIRMAN: We have got the terrible problem, of course, that not all the authors had the same professional background. We have got people writing from different points of view at about the same time and not necessarily understanding each other's disciplines.

A. Serology is a dark art even now and people don't use the same terminology. In our paper I don't think we use the term "positive predictive value". It is certainly nowadays what an epidemiologist would talk about,

a marker. What is the predictive value of that actually, telling you that it is real? Depending how you are using the test, what's the negative predictive value of it, you know, telling you that something actually isn't there, and what's the sensitivity. The sensitivity is if you take a group of people who have the disease, you put the test on to it, our sensitivity was 97 per cent, 32 out of 33.

Q. Yes.

A. Something like that. It would be about 97 per cent. Then, of course, you have got the question, was that actually an AIDS patient who genuinely had AIDS or was it some other condition in the risk group who was seronegative? I don't know. I suspect it was probably that.

Q. To go back to the concepts of N, being the number in the middle, and then the number in the northeast corner, if the number in the northeast corner is the same as N, which is the number in the middle, then your positive predictive value is 100 per cent, is it?

A. Correct, and the best is N equals C equals 100 per cent.

Q. Yes.

A. Life is never like that but that would be nice, wouldn't it?

Q. Yes. With that digression into terminology, you were

going to tell us at a pretty basic level, if you would, please, how --

THE CHAIRMAN: By "basic", you mean "simple", rather than "basic".

MS DUNLOP: Thank you. It seems I can't even get the adjective right.

At a pretty simple level how the test kits developed in the United States worked, what the technology was, and then we will go on and look at the difference between that technology and your technology, the competitive technology.

A. Okay. We have in any of these assays a solid phase, and the solid phase is usually plastic, a polystyrene well, a polystyrene bead, polystyrene microparticles, a plastic solid phase which has been extruded, which will absorb protein on to it.

Q. Right. So it's a piece of kit, it's in the serologist's tool kit and it's generally a piece of plastic or a lot of small beads of plastic, something in that form?

A. Or a 6-millimetre bead, if it's the Abbott test.

Q. And that's what we should understand by "solid phase"?

A. Yes.

Q. Good.

A. In the American-style assay you absorb on to the solid phase viral antigen.

Q. Yes.
A. You have a solid phase coated with viral antigen. You make an assumption. The first assumption that's made is that this is pure and that the only stuff that sticks on the solid phase is virus antigen. Okay?
Q. Yes.
A. You then have a first incubation and you put over that test serum. Okay? In the antiglobulin test it's test serum probably diluted 1 in 10 to 1 in 100. If you put it on too strong, you get too much non-specific sticking because the serum proteins will stick on other sites in the plastic. If you make it too weak, the signal will be too small. So you are on a little bit of an edge with getting enough on there to detect the positives but not so much that you get --
Q. Right. And for our little worked example test serum is a sample from patient X in San Francisco, let's say?
A. Yes, can we have "a patient X from San Francisco and a blood donor from North London," because that gives you your two extremes. That gives you somebody you suspect to be positive and somebody you suspect to be negative.
Q. Let's start with patient X in San Francisco then.
A. Okay, your test serum is incubated and then washed, so you now have the solid phase with the virus antigen. We are now talking about the San Francisco patient. The

San Francisco situation is this: solid phase, virus antigen, and we have lots of antibody stuck on there. Okay? You don't know it because you haven't asked the bead or the solid phase what has happened to it, but I can tell you that the virus antigen is now coated with antibody.

Q. And that's because the sample has been poured in the laboratory over the solid phase?

A. Incubated over the solid phase at a dilution. Given time for the antibody to stick, the antibody has stuck to the virus antigen. We then have a second incubation, which interrogates this mixture and says, is there antibody on there? And the second incubation is now with a marker called "antiglobulin", which in this case is probably a rabbit or a guinea-pig that has been immunised with human immunoglobulin, human antibody protein, made a very high titre reactive sample and if the antiglobulin then binds -- I'm going to use the antiglobulin and I'm going to mark it in red because that is the signal -- it will stick on there and carry with it the marker.

So when you wash everything on the second incubation, you are left now with a complex in the well of the plastic surface with the virus, on top of the virus is the patient's serum from San Francisco, on top

of the patient's serum antibody, which is bound, is the rabbit antihuman, which is either glowing in the dark, if it's chemofluorescence, producing colour if it's an ELISA, or producing radioactivity if it's a radioimmunoassay.

The difference between the radioimmunoassay, the chemiluminescence assay or conventional ELISA is trivial in one sense. All it is at that revealing agent which tells you that the antiglobulin has bound on the solid phase. That is the American assay that the five companies ran with, purified virus antigen -- "purified" in invert commas -- on the solid phase, first incubation of a diluted serum for testing, second incubation of the solid phase now with an antiglobulin, and if there is antibody bound, the antibody binds and gives you a signal.

Q. I think it's that last bit that certainly I could do with a little bit more explanation of. Why does the serum from the rabbit in this example stick to the combo of the patient's serum and the virus?

A. Because the rabbit has been injected repeatedly with human immunoglobulin.

Q. Right.

A. That is the immunoglobulin fraction. This is the antibodies against anything fraction from you, from me,

from anybody in this room, put into a rabbit, repeatedly. The rabbit produces its own antibody, which will recognise human immunoglobulin.

Q. Okay.

A. So where the human immunoglobulin binds to the virus on the solid phase, that will pull down the rabbit antibody and that will signal.

Q. Yes, okay. So the rabbit immunoglobulin is sending out a signal that it has found the human antibody bound to the virus?

A. Correct.

Q. Right. That signal can be a radioactive signal?

A. Correct.

Q. In which case you have an RIA, a radioimmunoassay test?

A. Correct.

Q. Or it can be a dye, which is what's used in the ELISA?

A. No, it's an enzyme.

Q. Sorry, an enzyme.

A. It's actually horseradish. Horseradish produces a very high level of enzyme, horseradish peroxidase, and that will generate colour.

Q. I have seen the references to horseradish, and of course that's the attraction of the familiar in an otherwise unfamiliar world. But I suspect that it's false comfort. It is not what I have with my roast beef.

A. It is but it's highly purified, it won't taste very good.

PROFESSOR JAMES: Abbott lab's genius was to introduce a touch of garlic into the horseradish.

MS DUNLOP: In an ELISA, the signal is coming from the use of an enzyme which might be from horseradish.

A. It is usually from horseradish, it can be alkaline phosphatase as well.

Q. How does the enzyme send its signal?

A. If the enzyme is captured on to the solid phase, because it's linked to the rabbit, the enzyme will then do one of two things, depending on how -- if you say to the enzyme, are you there, the enzyme will say, yes, and you are asking if it is there by giving it something to chew, which goes coloured. That's the most conventional.

The slightly less conventional is if you give it something to chew, like the back end of a firefly, you use luciferase or something like that. You use a light-emitting assay, and it glows. So it either glows or it makes something go brown or something go blue or something go yellow, depending which way you ask.

Q. Before we have our morning break, I think you should explain to us now the same process but using the London

blood donor. We could perhaps have an Edinburgh blood donor, since that's where we are.

A. I don't mind, a British blood donor. Let's be politically correct.

Q. A British blood donor, fine.

A. Can I, just before I do that, I'm just going to put down here what doesn't happen if you put the British blood donor in. The antibody doesn't stick and when you put the antiglobulin in -- sorry -- that doesn't stick either. So the difference here is, if it's positive, your well goes dark. If it's negative, your well goes colourless. Antiglobulin gives you a signal, you get a dark well, no binding of the antiglobulin, no binding of the rabbit on the human on the virus, it's colourless.

THE CHAIRMAN: One slight concern I have about that is that in the second of the two situations you say, "Both the antibody doesn't stick", and I think I can follow that. You also said, "And the antiglobulin doesn't stick either". Why should it if there is no antibody there?

A. No, it doesn't. But it does in the first.

THE CHAIRMAN: It cannot stick independently, in other words?

A. Well, if you make a good test, it doesn't stick independently. That's the addition of the garlic, which

is so important.

THE CHAIRMAN: Are we taking the garlic seriously for this purpose? An additional element of some kind, then?

A. It's not garlic but there are a whole series of proprietary materials which are put into these labels, saponin is a plant extract, for example, which is a biological extract, which is extremely difficult to QC but is absolutely essential in some of these assays to get the background, to stop non-specific sticking. Not quite garlic. Sorry, we digress.

MS DUNLOP: I think this is a logical extension of where we have got to. We are not yet looking at competition formats but in this form, if we think of the -- this is just a quote from the Crewdson book, it is not particularly attractive but the staid German matrons, the group of people who had a high rate of positives, any group of people who had a high rate of positives, who were not in fact HIV positive, can you explain to us what had gone wrong in the sequence?

A. Okay, I think the best group that I would use as an example was a publication by Carl Saxinger and Bob Gallo in 1985, which purportedly showed that 85 per cent of young children who had been bled during a malarial epidemiological survey on the west bank of the Nile, Ugandan children who had been bled, were seropositive

for HTLV-III B. Arrant nonsense, and has never been retracted, which is an awful shame because those of us who then went and worked with colleagues in countries in Africa, we were continually being asked, "Why should we trust you, given what has happened and you got it wrong with the Ugandan children?"

I can explain what happened. I'm not going to draw it on here but I will use the illustrations, bearing in mind that we have got to get the sense on to the record.

If we come to the assumption which I said about the solid phase, which is that the only proteins on the solid phase are virus-driven, that was an assumption which was obviously incorrect. The H9 cell is a lymphoblastoid tumour line, which supports HIV replication very efficiently, but it has a lot of signalling proteins in the surface of the cell and when the virus pushes through that cell membrane to get out of the cell, which these retroviruses do -- it is what we call "budding". So the virus buds through the membrane and becomes nipped off. It carries into its membrane, as an integral part of its membrane, a whole series of cellular proteins.

So on a priori evidence, we know that the viral antigen on the solid phase is not only viral antigen, it has lymphoid cell antigens in it as well. It will also

have components of the cell culture, probably absorbed on the envelope. It will probably have a bit of bovine serum albumin in there. It may have lipoidal antigens in there. If you have a bacterium or a microplasma, let's say you had one of these very small microbial elements in your culture, it would get on there as well.

So you have a false assumption that everything on there is real. So that's the first problem.

Q. So the virus is not pure. You are not coating the solid phase with pure virus?

A. You are coating it with pure virus plus a lot of other stuff --

Q. I should have said: only pure virus, yes?

A. We have got gubbins, whatever the gubbins is. You have got a lot of other material on the solid phase.

The second assumption you make is that the interaction between the test serum antibody and the virus is specific. I have already said that you have to do this at a dilution, which prevents too much of the antibody being trapped on the solid phase through a non-specific interaction.

Serum is sticky and some antibodies in some situations, the family of antibodies that you have in your plasma is more non-specifically sticky than others. Post-surgery, post-acute infections, post-malaria,

antibodies become non-specifically, as a phenomenon in the plasma, more sticky. So you have two reasons for materials sticking on to the solid phase. Firstly that the viral antigen isn't pure, there is lots of other material in there, and secondly that the test sample itself may be inherently more sticky than others.

Q. Yes.

A. So when you -- depending on where your test sera come from, if it's an antenatal woman, or a multiparous female, a woman who has had many children, she will have HLA antibodies defined by what her conceptors, the HLA mapping of her conceptors, which is half her husband's HLA genes. So she will have a whole range of antilymphocyte antibodies, which is actually one reason that we don't use female donors to make immunoglobulin production.

Q. Because pregnant women have to manufacture antibodies against the part of the child --

A. They do, yes.

Q. -- which comes from the man in order to sustain the pregnancy.

A. And her HLA epitope profile can damage the recipient of her blood donation. Blood donation -- we take most of the plasma away nowadays, but if you are making a plasma product, you tend not to use female donors because they

have these antibodies.

So if you go into a population of multiparous women in an African country, you will get a lot of false positive signalling, and if you don't do your Western Blots properly -- and in that original paper I don't think they did Western Blots -- you would say, "There is a lot of seropositivity, it must be real".

If you go into a group of children who have had malaria with sticky plasma, you will end up saying that 85 per cent of young children in 1965 in Uganda were HIV infective, which is arrant rubbish.

With the competitive RNIA we did a population of Zairean mothers, taken in the late 1960s, early 1970s, and we got one in 2,000 or 2 in 20,000 seropositive, and everybody else was claiming 50 or 60 per cent seropositive. So we were able to differentiate very, very quickly, the real reactives from the false positives.

Q. Right.

A. Do you want me to move to the competitive and then you have your coffee break? I don't want to lead counsel.

Q. I obviously have to defer to the chairman.

Should we stop now?

THE CHAIRMAN: I think we should probably stop at this point because -- I'm not quite sure now how to express it but

we have a certain amount of cooking to do of the information we have had and we may come back with questions. I think it's quite a good point to break.

MS DUNLOP: I'm conscious it has really been quite arduous for those who are capturing everything that's going on.

THE CHAIRMAN: There are physical problems for the stenographer.

(11.22 am)

(Short break)

(11.50 am)

THE CHAIRMAN: Professor, can I ask you one question? I'm astonished that I come back only with one to ask at the moment, but then I have had the advantage of another tutorial outside.

You said earlier that it would, in your view, be more effective to have four shots at the American-type test to build up a matrix of results, rather than use a confirmatory test of the kind of Western Blot.

If you were repeating the test, would they all be precisely the same or would there be variations among the different components of your matrix?

A. They would be variations.

THE CHAIRMAN: Would that depend on the type of material you introduced at subsequent stages?

A. Indeed, yes.

THE CHAIRMAN: That's fine. I don't think I need to know more. It's just at my very simple, if other than basic, level, I think the important thing is that you have a degree of variation within the testing protocol that gives you the extra assurance that you are not simply doing the same thing over again.

Ms Dunlop, I'll leave it to you to decide whether to follow it.

MS DUNLOP: Thank you.

We were going to move straight to the idea of the competitive assay, if we could, please, professor, and you were going to explain that to us in similar fashion.

A. My microphone will follow me.

All right. If one looks at the September 1st paper, I will actually take you through how we did it according to the recipe on the paper.

Q. I think we have all got that in front of us. Yes, we have.

A. Okay. The method here differed from the American antiglobulin assay in a number of respects. They purified the antigen and let it stick on the solid phase. We actually used a high titre sample from somebody who was infected, to coat the solid phase. So we put their antibody on the solid phase, knowing that their antibody would then pull down virus antigen. So

we used an indirect coat on the solid phase for virus antigen onto the plastic. Do you follow me so far?

Q. Yes.

A. That gave us an advantage in the sense that we didn't have to have highly purified virus, we could just use the material from the cells, where there was an awful lot of antigen which was yet to bud out of the cells. We could take a culture at the time that the virus had grown in the cells, spin the cells down, fracture them, spin out all the cell debris and you get left with an extract, and that is what we used to put over the antibody, to put the antigen on the solid phase, and that's the method that we used.

Q. Right.

A. Now, we then used the same antibody as on the solid phase. We used that as a labelled ligand. So here is anti-HTLV-III, same as on here, and we used that as a label.

Now, I'll explain what I mean. This is where your horseradish peroxidase was put on, and this is the antibody, which in some of the papers is the antiserum which Wellcome were working with. We originally used it as a radio label. So I'll put a different -- instead of putting "horseradish peroxidase" we put "125 iodine" on there.

So that was the radioimmunoassay version but the commercial firms wanted an ELISA because it's safer to manufacture, it's more stable, it doesn't have the shelf life problems of 125 iodine. So the same antibody was conjugated by our colleagues in Wellcome with horseradish peroxidase.

Q. You have just answered a question, professor, which arose from the paper and makes me feel very dense because the "125" is shown in superscript, and of course you look in vain for a footnote with some sort of reference "125", but that's the significance of the "125I"?

A. Yes.

Q. Yes.

A. Radioisotope 125.

Q. So that's radioactive iodine, which you are attaching to the antibody?

A. Correct. So it carries with it its own revealing agent which you measure in the gamma counter.

Q. Right.

A. Okay. This all happens in one and only one incubation. So whereas we have in the antiglobulin a first incubation and a second incubation, in this there is only incubation. And it is a mixture of your labelled ligand and your test serum.

Operationally, that has two advantages: the volume that goes into here is a single addition of undiluted plasma or serum. You don't have to pre-dilute. And the incubation is simultaneous. So after a set period of time -- and I would have to defer to how we did it in 1984 and look at the method -- I can't remember but I should think it was probably a couple of hours at room temperature.

I'm hoping counsel will tell me.

Q. I'm hoping I can find it. (Pause)

You placed your antigen -- you incubated it for two to three days at room temperature.

A. The last paragraph, the mixture was incubated overnight in the wells. So we did a long incubation. We subsequently, in the enzyme immunoassay, we could cut the incubation down to 30 minutes to one hour at an elevated temperature. So it gave you tremendous compaction of the assay.

What happens in the competitive assay? Shall we go to the UK blood donor first?

Q. Yes, before we do -- this is probably a defect in my English rather than my science, but the concept of a ligand; what is a ligand?

A. It is something which interacts with a third party.

Q. Right.

A. Usually one talks about a ligand in an immunoassay as something which has a detector on it which gives you a signal.

Q. Okay, thank you.

A. If we come to --

THE CHAIRMAN: Sorry, is that doing the same job then as the antiglobulin going in?

A. Yes.

THE CHAIRMAN: It is.

A. Yes. That is your -- "revealing ligand" would be the technical term. The revealing ligand here is the horseradish peroxidase or the 125 labelled antivirus/antibody.

If we move first of all to the blood donor, who is the negative, there is no competition between the test serum and the horseradish peroxidase or the radio label. So here a lot of ligand binds on to the antigen and you get colour. So in this case your negative --

Q. Or radioactivity?

A. Or radioactive. Yes, it glows in the dark.

Q. Yes.

A. If on the other hand the San Francisco sample is put in here, if the San Francisco sample is put in here, the high amount of unlabelled antibody binds and your well is coloured. So you have a complete reverse of the

signalling.

In the antiglobulin assay, if the ligand binds, you have colour and you are antibody positive.

Q. Yes.

A. In the competitive assay, if the ligand binds, you are coloured but you are antibody negative because you have no blocking antibodies to prevent the ligand binding.

Q. Right.

A. It's turning the signalling round the other way. To go from negative to positive in the antiglobulin, you go from colourless to coloured. In the competitive, single-step assay, to go from negative, which is coloured, positive is colourless.

Q. Yes.

A. Now, the control which you can bring to the interaction between the ligand and the viral antigen is open to all sorts of manipulations with reagents, which are very difficult to achieve here in the antiglobulin test because each serum has its own characteristics. A competitive test is inherently more specific.

The criticism that was levelled against us in the 1980s was competitive tests are not sensitive, but you get round that by putting neat plasma into here. There is much more plasma or serum goes into a competitive test than goes into an anti-globulin test. So you

trade-off the reputed lower sensitivity by putting more serum in, which doesn't alter the specificity of the signal. If you put more serum into the antiglobulin assay, you have higher backgrounds and a higher rate of false positivity.

Q. Just to see if I'm following this, the perceived problem with sensitivity of the competition format was that for someone who was weakly positive, perhaps, it might not work, and you are saying that the response to that is a quantitative one; you can put more serum in, which increases the chances of a positive result?

A. That is correct.

Q. Yes.

A. And I think this was one of the reasons that none of the American firms were interested in taking the risk.

The video -- their view was, "You won't make it work," and our view was, "Well, we know it works for HTLV. We predict it will work for HIV, HTLV-III B, HIV," whatever we called it in those days. And it did indeed work and it still is, paradoxically, a very good test. The reason it is not used any more is we have a sister virus out there. We have HIV-2. And the specificity that you get with a competitive test is so great that it's not terribly good at recognising HIV-2, which is an awful nuisance, but such is life.

Q. Right.
A. At that time we knew not about HIV-2 and we were just concerned with the pandemic HIV.
Q. Yes. So Professor Weiss yesterday was saying he wasn't completely sure if it was correct to use the verb "dislodge" in relation to the competition assay, but it sounds from your description as though "dislodge" is the correct verb?
A. Well, "dislodge" would imply that it had already bound and was being kicked off.
Q. Right. So it's preferential binding, as it were?
A. It's --
Q. One binds and the other doesn't?
A. It's competition with.
THE CHAIRMAN: Differential binding?
A. Yes, it's because there is a lot of cold antibody in people who are infected and you reduce the amount of labelled antibody. Your stoichiometry is that you have a thousand-fold or ten thousand-fold excess of cold antibody over hot antibody. So the hot antibody does not get a chance to bind. So it's competition with, and that's why we --
THE CHAIRMAN: I think stoichiometric modelling is a bit much for us this morning but I would like to understand it, as I think Ms Dunlop would.

So if we go back to the right-hand column, you have introduced the ligand as part of your general soup, your general mixture, going in and at that point what is adhering to the solid phase is the viral antigen that has adhered to the antibodies originally inserted. You have now introduced a sample from the target patient, or whatever it is, and something added to it, which would either be the radioactive or the chemical factor or whatever one cares to call it, and those two things are confronting the virus antibody?

A. The viral antigen.

THE CHAIRMAN: The viral antigen --

A. They are competing amongst themselves to get onto the viral antigen.

THE CHAIRMAN: To get onto it.

A. That's why I say "competition" rather than "displacement".

PROFESSOR JAMES: Can I draw you an example of a football ground with five entrances. In the negative example, the blood donor, there are five people who have got the label on them, each of whom, in a timely fashion, can get through one of the entrances to get into the ground.

Now, in the positive person it's equivalent to introducing 10,000 people to the five, so the odds of those five getting through the turnstiles, that will

only take one person at a time, become much, much lower, and they are left outside the ground with the other people.

That would be a way of describing it, wouldn't it?

A. Yes, and if you make it even more graphic than that, let's say there are only 100 seats. Your chances of getting one of your signalling individuals, if they have to compete with 1,000 to get onto the 100 seats, is ten to one against.

THE CHAIRMAN: I'm never good with football analogies.

A. Well, a test match, you know, trying to get into Lords. The Olympics, maybe, is an even better one.

MS DUNLOP: I must say, I'm thinking of Total Wipeout and people struggling to get onto inflated wet devices, and one gets on and another one doesn't. That's my image. Perhaps we have all got our different mental pictures.

A. I like the term "competition".

THE CHAIRMAN: Coming back to competition, you have two bodies of competitors, trying to make a connection with what is there already. If you have an infected sample, it's going to make the connection and give you a colourless outcome.

A. Yes.

THE CHAIRMAN: If there is no infection in the sample, your radio, or whatever element, will make the connection and

you get a discoloured result. Is that too simple?
A. That is correct. And that's true for many different antibodies to many different viruses and it's a jolly good way of making assays.
MS DUNLOP: Yes.
THE CHAIRMAN: Except that unfortunately you can't get HIV-1 and 2 on your solid phase at the same time.
A. You can do.
THE CHAIRMAN: Oh, you can do.
A. But it's rather clever. You have to have an enzymatic cascade where you need both components to give you a signal and if you knock off the HIV-1 component or the HIV-2 component, you can make a competitive assay which will detect both moieties but --
THE CHAIRMAN: Have you got a patent specification in for that yet?
A. We discussed it and we felt it was -- is this an open meeting by the way?
THE CHAIRMAN: You mustn't go too far. It is an open meeting but I think we know that there was a certain amount of sensitivity at an earlier stage so far as this was concerned?
A. Yes. Too many things are said can't be done but can be done if you --
THE CHAIRMAN: We don't want any prior publication here of

matters that might disadvantage you.

MS DUNLOP: Right. So we have the explanation that's in the paper of how a competitive assay works and we also now have your explanation in the transcript, and we will have the diagram as well. Perhaps using a combination of all of these, or whichever one appeals to any individual person the most, we will be able to retain the information.

I would like, if I may, to go back to the question and answer papers, and I think we have covered most of your answer 3. So can we go back to [PEN0171831], please? I think in the second paragraph you explain how to make a competition assay, the highly selected plasma from infected individuals.

Lysis is the breaking down of cells. Is that correct?

A. Splitting and opening of cells.

Q. Yes. You have clarified the offer by the French group. I think this was because we were asking about the access to the French virus early in 1984, and Professor Weiss explained to us that there wasn't really any particular reason why in June and very early July 1984, you were using the HTLV-III B rather than LAV, which was also present.

A. It makes -- it makes little difference.

Q. Yes. I think we had wondered at an earlier stage whether use of the French virus would have avoided the problems with the American Department of Health and Human Services, but since you have told us that that didn't result in a delay anyway, the question is probably academic.

Just before moving on, I think I should have picked up your comment on page 1 that things might have been different if you had had access to the French culture in 1983. Are you simply meaning by that that everything would have been more advanced time-wise?

A. I mean two things. Yes, we would have been six months ahead of where we were in September 1984 in terms of the early epidemiology. We might have had a British isolate, a UK isolate, much earlier. We might have been able to work with commerce much earlier.

As a scientist, it grieves me that we lost six to nine months on the field. Had we been publishing the 1984 September paper in January 1984/February 1984, we would have presaged the entire Gallo and Montagnier disclosure in the Science paper of May 4th. We would have not only demonstrated the virus, in reality we would have had the break on epidemiology. And I really -- I look back and some things happen and some things don't. This young man carrying a bottle of LAV1

in his hand, nobody to meet him, leaving it in a lock-up on Waterloo Station, such are things fairy stories are written about, you know? Such is life.

Q. Right.

A. I still weep about it. But, you know, we didn't do badly in the end.

Q. You do explain at the end of your answer 3 that you made contact with the five firms which were licensed in the United States. I think actually licensed by the American Government to develop tests. But none of them was prepared to work with you and that was exasperating because they were discarding large amounts of -- well, antigen, which you could have used.

A. All the cellular components, which is what we worked with, were autoclaved and poured down the drain, and they were dealing with fermenters of 1,000 litres at a time. About six months to a years' worth of antigen for the whole of the UK in the assays that we were using. Again --

Q. Why, if you are able to tell us, were the reactions so negative?

A. I believe that their terms of engagement with NCI through the US Government were such that it was an exclusive arrangement to access and use that material, and to have a third party attached to that agreement

would have been at the very best difficult. And I think there was also, as I have said, the comment, "You can't be serious doing this with a competitive assay, it won't work".

Q. Yes. So scepticism and contractual fetters really?

A. I think the other -- I would say contractual features and scepticism. I would put it the other way round.

Q. Going on to paragraph 4, I think we recognise the information that you are communicating there about timing, and you did allude earlier to some -- perhaps calling it "difficulty" would be putting it too high but there was dialogue between yourselves and Porton Down about how exactly they were going to work. Is that correct?

A. Yes, it was -- I mean, I think to be fair, they were scaling up on a large-scale. We had a protocol of using a mixture -- a large volume of infected cells with a moderate but high density of uninfected cells, incubating that for three or four days, taking the material from the cell pellet. And I think they -- as far as I can recall -- I know that a number of batches came up which were singularly ineffectual in the assay that we used.

I think, looking back on it now, the conditions of culture which they used encouraged the virus to come out

into the supernatant, whereas the protocol of high density pass that we used, got a lot of virus replicating in the cells but before it was passed out, and that was ideal for us and we -- you know, in retrospect now all we knew was we had a protocol that worked, and if you didn't follow our protocol, virus presumably was shed by the cells and wasn't retained in the cell pellet. And there were some early, fairly frank discussions in the beginning of 1985 as to why on earth was another batch of antigen not working.

Q. Right. I think we also understand from other information that there was a change from using radio signalling to the ELISA form of test in your process as well, and perhaps if you could just encapsulate for us -- a number of others have done this -- why at this time people were moving from RIA to ELISA?

A. Radioimmunoassays have a biological risk; there is no safe amount of additional radiation you can give a human. They also have a problem. The half-life -- and that is the amount of radioactivity on your ligand -- drops from 125 to -- I think the half-life is about 31 days/30 days. So every month your efficacy in terms of signal generation by your label drops by 50 per cent.

So a radioactive label, although it's terribly easy

to make and it's very sparing of the protein that you iodinate -- that's putting the iodine on. One can do it in a laboratory, it's very easy -- it's not a good idea for a widespread proselytization of assays into the community.

We were heavily involved -- when I say "we" that's generically, the virus department at the Middlesex Hospital. We supported the Blood Products Laboratory, radioimmunoassay for Hepatitis B antigen, and all the technology that BPL had for making those reagents came from my colleague Dr Cameron, in our department. And it's very easy to do that.

Q. Yes.

A. Because of the concerns and the global move to enzyme immunoassay which was occurring at the same time, it seemed to be -- once we had elected to work with the British diagnostic industry, or indeed the global diagnostic industry, it would have been very difficult to run against the global move away from radioimmunoassays.

There were already questions at this time of what was going to be the long-term future for the BPL RIA. And as I think I say somewhere, I discussed this at some length with John Patterson -- Sir John, who was then my dean at the medical school, and trying to work out what

was the best way of moving things forward quickly. It seemed to be to espouse collaboration with industry and also to move away from radioimmunoassay.

Frankly, I was quite glad to get away from radioimmunoassay because at the time I was having to make all the radio ligands.

Q. You do mention this at a couple of points in your response and I think we have picked up from our references that there was, within the National Blood Transfusion Service, certainly in the second half of 1984, a wish to have an RIA. I suppose because that was what they were familiar with, and indeed also, in some minds, a hope that BPL could make the test kits. And of course, neither of these things came to pass. Do you remember that being people's hope or expectation?

A. Well, I do. I mean, they had a radioimmunoassay. Having said that, it was a much more robust radioimmunoassay than our radioimmunoassay, and the only way we could make the radioimmunoassay signal well, as we said in the September paper, was an overnight incubation and that was a constraint which wouldn't have fitted terribly well with rapid donor screening.

Q. Yes.

A. And the advantage of the EIA, there is no biological hazard in bumping up your ligand concentration to get

your signal quickly. And in fact if you drive the reaction in an EIA, you do not have the hazard of everybody glowing in the dark because there is too much radioactivity around.

So we preferred to move from radioimmunoassay to the EIA, to the ELISA, because we had already seen, towards the end of that year, working with -- the end of the year and the beginning of 1985, working with Julian Duncan and Charles Corker's laboratory at Wellcome.

He was preternaturally able to stick enzymes on to any protein and he was brilliant at making these enzyme ligands, and when we started experimenting with that, we took a rather frail radioimmunoassay -- although, a good immunoassay as you saw from the paper -- and made it into something which worked very quickly in a simultaneous incubation and gave us very tight, clean results. And just technically, it was easier to make the test into a good performer by EIA rather than radioimmunoassay.

And if we were going to go down an EIA pathway, the only way we could do that, with the best will in the world -- neither we at the Middlesex, nor BPL had the technology to make excellent horseradish peroxidase ligands. There is a lot of infrastructure you need to

get the coupling between those two proteins.

Q. There has been reference to a meeting -- I suppose termed by some a "secret meeting". Let's just call it a "confidential meeting" -- around the turn of the year, I think it must have been, 1984/1985, involving the Department of Health and Social Security, yourself, Professor Weiss and representatives of Wellcome. Do you have any recollection of a particular meeting and was it to address these very issues?

A. No, I don't. I would have been slightly surprised. I have no recollection of that. I do recall having two or three meetings with Richard Lane and CBLA and BPL, talking about the radioimmunoassay and then eventually having to let them down and say, "We don't want to do a radioimmunoassay, we are going to run with Wellcome".

Unless there are papers to the contrary -- and they may well correct me -- I don't remember even a tripartite meeting like that. It would have been a little bit strange to have a manufacturer who is going to take an assay from a research department, sitting with the DHSS.

Q. Yes.

A. There certainly was no conspiracy.

Q. No. Thank you.

A. I am afraid I have thought and unfortunately I don't

have the papers. There would have been many discussions involving various combinations of those parties, but essentially my relationship with DHSS was not exactly good, for reasons that can be explored some time, and my cri de coeur in December was one of the extreme frustration of having a small team at the Middlesex Hospital doing good things, where everybody was working until 7/8/9 o'clock in the evening -- in fact Rachanee Cheingsong-Popov, who was one of the authors, one of the top three authors on that paper -- I think she was principal author -- actually came out of the labour ward, when she was in early labour, to finish washing a radioimmunoassay, to get results, two hours before she produced her first son.

That was the sort of pressure that we were under at the time and I deeply resented being told MRC is funding all this. Not a penny of MRC money went into that at the time and we had no funding from the DHSS, and that really rankled. You are getting me on a pedestal and I will climb off it humbly and say at the end of the day it all worked out right but it was jolly uncomfortable -- incredibly uncomfortable.

Q. It may be that some of the documents we are going to look at will trigger these memories further and I'm sorry about that.

Can we move, please, on to the next page of your response? You said a moment ago that you had to let Richard Lane and others at BPL down. I think that's what you are meaning when you say that you realised in retrospect that there was a disappointment for colleagues in BPL.

Then question 5. We asked about the development of the radioimmunoassay and the proposals to extend it. I think in the summer of 1984 there were plans to try out the RIA in various different transfusion centres, different demographic groups being represented in the centres chosen. So I suppose what was involved here was some sort of notion of evaluation of your test?

A. I think there were two reasons behind that. I'm not sure that I'm correct in my response where I say a total of 2,000 blood donors; I think it was less than that. But that's a terribly small number in relation to the 1 million to 2 million donations taken every year.

Q. I think it was 1,042?

A. Oh, well.

Q. That's the number that appears in the table.

A. A twofold error. I apologise for that. My response was without going back to the September paper.

Whichever way you look at it, it was a tiny snapshot of the blood donor population in this country.

Q. Right.

A. In the UK.

There wasn't so much a field trial of the assay, it was more a desperation to know what the prevalence was in blood donors. Suspecting it to be low, therefore the denominator has to be much larger than the 1042 or 2,000.

Q. I see. Just moving on through your numbered answer 5, you say:

"At the end of 1984 there was an understandable reluctance in the National Blood Transfusion Service to institute screening in part of the service, even if only for a zero prevalence survey and for a limited time, since this could be anticipated to draw into donation individuals who were curious to know their own status."

And I think we can understand that point. We have seen suggestions in other documents and from other witnesses that some sort of limited screening of blood donors could have been introduced, for example selecting men between the ages of 18 and 30 or something like that.

But the point you are making is that that could then have been a magnet for people who were anxious?

A. Even if one had done a targeted subset of the donors, the concept, I think, was entirely understandable, that

the word would get out. You can't contain doing something like that in any covert sense. Somebody would say something. It would be picked up by either the press or a lobby group. "Oh, we are doing AIDS testing in the transfusion service," and then the amount of damage you could do -- because, remember, at that particular time we did not have the strict deferral of men who have sex with men, which is the current politically correct terminology. We didn't have the MSM deferral at that particular time in anything like the strict sense that we lived with later on in the 1980s, 1990s and through until now.

Q. Yes.

A. So the potential for recruitment -- and you have to be terribly careful. I mean, there are examples of where we have tried to enrich donor panels for HLA or rare blood group purposes, only, suddenly, to rue the day because we are bringing in populations who carry other viruses. I think I was disappointed that we couldn't do a bigger survey, but knowing, even then, as much as then I knew about donors, I could concede that it was just not a risk worth taking. I mean, even you go one step beyond that, even if you had had HIV testing in the whole of the transfusion service, the one thing you didn't want was people who had recently been exposed

coming in because -- and I gather you have been inculcated into the window phenomenon.

Q. Yes.

A. So I needn't go over that. But the real risk would be bringing a lot of window donors in, who are exquisitely infectious, and for the blood component issue that's bad news but for blood product that could be devastating.

Q. Yes. I think we understand that, really from quite an early point in the story of the introduction of screening, there was an appreciation of the need to provide alternative testing facilities and to make these as user-friendly as possible.

A. In very real quick time, to enable those people who felt under epidemiological pressure to be investigated to go to the appropriate health service providers, have testing, have it freely available, and with appropriate confirmatory testing.

Q. Yes. We asked you about a statement in a DHSS memo from the summer of 1984 to the effect that if these surveys went ahead in North London Transfusion Centre and another two regional centres, it would enable decision-makers to be in a strong position to decide about the need to buy from one of the five American pharmaceutical companies. I think we were probing what was meant by that because it does seem to have a whiff

of a policy goal, to try to avoid buying the American kits. But you say you are not in a position to explain this statement? Reasonably enough, since you didn't make it, I'm sure.

A. I don't really know that I can understand it, other than take the words at face value.

Q. Yes. You say that your recollection is that any test considered fit for purpose would be subjected to scrutiny in the UK and that all tests suitable and available would undergo investigation. You go on to comment that there was no intention to delay in order to favour the Wellcome assay kit. You were particularly concerned, as an independent scientist, that no favours should be given to your assay in view of the very real potential conflict of interest:

" ... since both my institution and myself stood to benefit from inventor's rights."

If we just read on to the end of that paragraph, you suggest that we look at a letter in the New Scientist, which we do have. Just to let everyone see that, it's [DHF0017755]. This is actually a letter that appeared in the New Scientist in the summer of 1985. We do deal with this whole episode in the preliminary report but there was a suggestion that Abbott were saying that the whole process was being delayed to benefit Wellcome and

then Abbott themselves denied that they had ever said that.

All of that was in the New Scientist. Just for reference, it's paragraph 8.135 of the preliminary report. I think the story started on 8 August with the report in the New Scientist that Abbott were accusing the government of delaying approval until a British test was available and Abbott then wrote to the New Scientist to say that they hadn't said that.

Anyway, you have drawn our attention to the letter, which is now on the screen, from Dr Barbara and Dr Hewitt refuting any such suggestion. Perhaps we can just read it for ourselves. (Pause)

So you agree with the views in the letter plainly. Is that right?

A. Yes. Over the years one has had experience of assays being introduced into the transfusion setting, in fact into diagnostic use, which have not been tried on the population of humans from which the sera are derived which are going to be tested. You must do some degree of field trial testing, to know how your country's sera and your target populations behave in an assay because, without that, you are running the risk of finding devastatingly high levels of false positivity, not so much in European situations, but it's a principle that

should be adhered to.

You conduct a field trial to make sure that assays are giving you useful and as accurate as possible results and, of course, without having your repeat reactive panel from your donors, you do not know what form of confirmatory testing you need. So, until you have got the substrate for your confirmatory testing, which is your repeat reactive donors, you can't define what's going to be the best algorithm or the best protocol for confirmation. You really don't want to be screening donors and developing a large panel of repeat reactors without knowing how to deal with them. That would be very damaging to transfusion practice.

Q. So that is another essential prerequisite for the introduction of the screening programme, that you have to have your confirmatory testing in place. So that goes along with alternative testing facilities in this instance as something which has to have been organised in advance of a screening programme starting.

I suppose it's not then ever going to be good enough for the manufacturer of a test kit to say, "Well, I have tested this on 5,000 citizens in Orange County," because that, being a different demographic group, will not be results that can necessarily be extrapolated to the British population?

A. Not necessarily to the British and certainly not to other global populations.

Q. Yes. Can we move to question 6? We asked actually about the meeting on 27 November 1984. That's the meeting of the working group of the advisory committee on the National Blood Transfusion Service. You said you don't remember the meeting. At the time an awful lot of work was ongoing. You were actually on the working group. I think you were there.

A. I'm sure I was but I have -- I recall meetings after meetings. I don't recall that particular one.

Q. No. I think we know from other blocks of hearings that in the second half of 1984 you were doing a lot of clinical testing, I think in particular for various haemophilia centre directors around Britain. Is that correct?

A. Going back to the September paper, the data in there were available to relevant healthcare professionals in each area, whether it was GUM physicians, haematologists who were looking after haemophiliacs, or people providing care for intravenous drug users, each of which had a higher prevalence in the risk group, and each of those risk groups was knocking on our door and on Philip Mortimer's door saying, "Can you help us? Can you delineate the size of the problem in our community?"

It was an incredibly difficult and busy time.

Q. Yes.

A. And as I have already said, I got strung out, myself and my colleagues -- my colleagues bore the brunt of this. We were strung out almost to breaking point and that's why my letter was fairly forthright in December to our colleagues in DHSS.

Q. Yes. So in that part of 1984 I imagine you had more work than you could handle in the form of testing for these different constituencies. Is that right?

A. Yes, it was very difficult because we had a shrewd idea we knew what we were doing. I think in retrospect we didn't do anything wrong, but certainly nowadays you wouldn't be able to do that again. We would be constrained by governance, we would be constrained by legality, we would be constrained by everything under the sun. It was hard work, really hard work.

Q. You have mentioned your interactions with DHSS. We actually have a little string of letters that I would like to show you. Can we go first to [DHF0018856], please? This is you writing to Dr Alison Smithies at DHSS on 18 December 1984 and you are pointing to the need to scale up the RIA and your related need for more staff.

Can we look at the next page, please?

A. It seems an awfully small sum of money in comparison to today, doesn't it?

Q. Yes. Professor Pattison, is that your dean?

A. That's my dean. That's Sir John.

Q. Yes.

A. Yes, a pretentious phrase, isn't it:

"Necessary UK commitment in this problem increasing over the next few years."

It reads oddly, doesn't it?

Q. I suppose you didn't have a lot of time for your correspondence. Can we look next at [DHF0019040], please? This is again Dr Alison Smithies. She has done a draft paper to go to, I think, the Research Liaison Group? It may be the correct translation of "RLG":

"I also attach a copy of Dr Tedder's letter of application. I hope the proposal will meet with approval."

Can we go to [DHF0019036]? This is, I think, the first of several minutes from around this time. So your letter is going forward as an application for funding, and this is, we think, possibly the final version of Dr Smithies' draft, which was sent in its final form on 4 January. If we scroll down through the narrative, we see again the mention of the development of the RIA and

the wish that it be suitable for routine use in blood transfusion centres.

A little bit further, please. Go right down:

"The Middlesex Hospital-Chester Beatty RIA is thus a product of the cooperation of British science and British industry ... general agreement that it is the most sensitive RIA for HTLV-III presently available."

A. Can I just make a comment on there?

Q. Yes.

A. Because if this is January 1985, Alison is already referring to antiserum being produced by Wellcome Reagents Limited. That's interesting because they never got -- they were specifically unwilling to work with radioactivity. So the implication of that is that we were -- and I'm sorry, unfortunately all the records got chucked out by UCL some months ago and the Windeyer Building no longer exists, so we can't go back on this, but I think we would probably have been doing enzyme immunoassay from October or November.

There is a slight disparity, that we are talking about a radioimmunoassay and the implications of this, we were already working with materials from Wellcome Diagnostics, which would have been EIA not RIA. So we were clearly already beginning to move to a different ligand, although the assay in format would

have been entirely compatible with the 96-well format that the Blood Transfusion Service used.

Q. Yes.

A. I suppose I'm going to be accused of slightly egging the case because I was saying, "Give us the reagents to the RIA because we have got that running," and I suspect that I already knew that we were going to be moving into an EIA format because that's what the writing on the wall said: radioimmunoassays are not going to continue much longer.

This wasn't the first time that I had been trying to get funding from the DHSS.

Q. So in as much as there are comments around this time about the benefits of the Wellcome test, if we can call it that for shorthand, including the fact that it's an RIA, which British Blood Transfusion Services know and understand, that possibly was inaccurate because those who were saying those sort of things had failed to appreciate that you were either about to move or had already moved moved to the EIA format.

A. I think so, and of course I didn't really make that terribly clear in my letter of December.

Q. Right. Can we just scroll through this, please?

A. It is actually the only RIA for the HTLV-III antibody.

Q. Can we go on to the next page?

We can see the further discussion. Yes, this is the proposal, and there has been some discussion with you to clarify aspects. Then we can see what was being sought. I think the sums of money have gone up slightly.

Can we just finish this document, please, by looking at the final aspect, which I think is on the next page. Yes:

"Finally there is an opportunity to assess commercial products, which will be inevitably be introduced to capitalise on an established need."

So at this point there does seem to have been a perception that you would also be doing the work to look at the test kits which would be coming from commercial manufacturers and decide how efficient and effective they were, but I think we will see that that actually didn't happen. Perhaps we can just trace the audit trail forward.

Can we look next at [DHF0027106]? This is actually Wellcome writing because they have received their letter about the evaluation exercise, and they say they are very happy to submit their product for the evaluation but their main priority is to make available a test for use in the BTS as quickly as possible.

It did strike us that it looked as though Wellcome were under the impression that evaluation might trundle

along but testing might be introduced before the evaluation had concluded. So they are saying they want to get on with making available the test for the BTS as soon as possible.

A. I take a different interpretation of that. You can read it the way it's written. I don't think it was. As I have said in my reply, I think manufacturers normally like to have a detailed portfolio of performance of the assays on positive samples, negative samples, to give you predictive value, positive predictive value for a reaction and so on, and I think all they are saying here -- and I suspect this would have been -- judging by the smallness of the signature, I should think it might have been Kit Madden but I'm not certain -- saying, "We are running with this test. When it comes to an evaluation, fine, but we won't have the normal portfolio of manufacturers' claims that you would have expected with something as important as this." That's my interpretation of this. And knowing how hard they were working at that, my interpretation is saying, "Okay, fine. Evaluation, fine. We are not going to have all the data that you would want before it goes into an evaluation because there just isn't time."

Q. Yes.

A. Not that we don't think it's going to be evaluated.

Q. Right. I suspect you are right about the identity of the letter writer because the reference at the top is "CJFM".

A. I didn't see that.

Q. What was the first name?

A. Kit.

Q. Short for "Catherine"?

A. It's a he. I don't know why he was called "Kit". It was always Kit Madden.

Q. Short for "Christopher", probably. And in fact you have recorded your interpretation of the letter in your numbered paragraph 13 in your answer.

Can we look next at [DHF0019175], please?

This letter makes a point about the commercialisation of the BTS test being quite separate from the evaluation programme, and actually I think, looking to erect something of a Chinese wall within DHSS. Or is that not an appropriate analogy? It looks as though there are to be two different streams of communication.

A. Yes. You know, I tore my hair out with our colleagues in DHSS over these early years. I think it's actually correct to have some form of Chinese walls because otherwise there is a conflict of interest, and I can't see how you can have a commercialisation of a test being

carried out under the same umbrella as the evaluation programme. I think you do need to separate them because they are different issues.

I mean, they are intertwined in the sense that if the commercialisation doesn't work and there isn't a kit to evaluate, the evaluation doesn't go ahead, but the terms of engagement have to be different. And I don't know if there were terms of engagement in commercialisation. That was not in my remit.

My collaboration with Robin through Chester Beatty Laboratories was directly through Wellcome Diagnostics.

Q. Can we look next at [DHF0019212]? This is 13 February 1985 from within the DHSS, concerning what actually your project is to comprise. In the third paragraph this minute narrates that:

"The proposal included evaluation of all the kits on the market by the Middlesex Hospital. This is no longer part of the proposal since it would not be proper for Dr Tedder to be evaluating commercial kits when he is in the process of developing and commercialising one of his own."

Which I think is what you have just said.

A. I think that, for me, would have been inappropriate because you can't be collaborating with one sector in the -- one independent component of the diagnostic

sector and then be expected to be judging other components of the sector for the performance of the kit. So it would have been inappropriate.

I mean, I think what we would have wanted to do, we would have wanted to look at the performance of tests in order to define the best algorithm. And that would have been a different purpose for wanting to have extensive access to assays.

Q. I think Professor Weiss had a recollection of how it was that that part of the proposal was tacked on in the first place. Do you have any memory of how that came to be included in your application?

A. No, I don't actually, other than it was a low-hanging fruit to try and get some resources.

Q. Right.

A. I haven't talked -- Robin and I have not talked around this. We have both been talking to you so perhaps I can find out what his recollection was. I don't remember.

Q. Yes. Just on the topic of the notion of the evaluation exercise, could we go, please, to [DHF0019097]?

This is a memo about going back to 16 January, about the evaluation programme and attaching a draft letter about it, and that's [DHF0019098].

Just so that we know that that's the evaluation programme being considered in the middle of January 1985

and the letter that was to go out to the companies about it. Can we just look at the second page, please?

I think looking for some initial preliminary information. We did ask you about what you knew about this period, I think in our question 10. You say you understand the reason to have a properly funded investigation of both sensitivity and specificity, and I don't want to go back over that.

And you say:

"It was entirely natural that the Central Public Health Laboratory of the PHLS should undertake this work."

And obviously that's the answer to what would have been a conflict of interest.

A. We were already working with Philip Mortimer at the time. He was a close collaborator and had been for many years.

Q. Perhaps we could go back to our questions document, please, could we? It's [PEN0170523]. I don't know that we need to look at the particular documents concerned because we have quoted the key passages in our question 11. So can we go on, please, to page 530? Particularly the second one:

"It would be wise to establish X as an evaluation centre."

You think "X" might have been you?

A. I'm not sure. Either myself or -- it's difficult. This is 21 January.

Q. Yes.

A. It's funny because it's sort of slightly counter to what we have really heard as reservations about trying to do two things -- trying to do both.

Q. Yes.

A. I mean, I think probably by then Phil and I were working, Philip and I had been involved in thinking about -- when HIV -- well, it wasn't HIV -- when AIDS fist came round in the risk groups, those of us who had worked in Hepatitis B, it was pretty obvious following on from the MMWR paper, whenever that was, 1981, beginning of 1982, the first description of the cases, it felt so much like Hepatitis B under another cause. So Philip and I were continually talking about this and thinking about that and once the isolates were around, he gained access very quickly and we talked about algorithms for confirmatory testing.

So even if I tried to blag some money to fill the shortfall of resources, it would have been so much more sensible to have CPHL and Philip doing that because there would have been no conflict.

Q. Yes.

A. I suspect, because of the context in which these letters are written, that I am actually "X". But it is difficult to know.

Q. If you bear with me more a moment, I think we actually have the answer.

Yes, we have had an unredacted copy back from the Department of Health, and it is you.

A. Oh, well, there we are.

Q. But I take your point that it's slightly at odds with some of the other developments around this time.

I think certainly Mr Rogers, a civil servant who wrote the memo that we just looked at in February, he seemed to have been uncomfortable about the conflict of interest, but maybe other people thought this was something that would work --

A. I think that's entirely understandable and I think, as long as it didn't take away from the very slender resources we were being promised, I would have had no qualms about saying to Philip, "Over to you."

Q. Right.

We also asked you about another memo, Dr Smithies' memo of 21 January, where she said it had been discussed:

"... whether or not any reference should be made to tests not being accepted in the UK unless they had FDA

approval, and decided that such a stipulation might not act in Wellcome's best interests in the short-term."

You thought that was slightly strange.

A. I think the concept of using validation, to me there is little -- some people will carp about what I'm about to say. There is little difference in having an American manufacturer or the FDA pontificating on the performance of a test and then accepting matters as gospel in this country. That would run completely counter to everything that we had ever done in the transfusion service in the UK and anything that we do nowadays. And indeed, if we had been tied to FDA as I said earlier over coffee, we would have been in a position in this country to have an HIV test which has a P24 component, because it's only in the last six to 12 months that the FDA have now agreed to license what we call the "fourth generation assay". So we would have been locked into an antediluvian regulatory system.

Q. I suppose we are coming back to the point you made earlier about the need for "local" evaluation or validation of a test performance.

Perhaps I should put to you what I think is a related point, that it would have been difficult to know what to do with a test kit which had actually been denied FDA approval.

A. Or not been proposed to have FDA approval and indeed, it always amused me that Wellcome did not go for FDA approval for Wellcozyme or any of the competitive assays, because frankly it would have been refused almost certainly, either from a political grounds, because American industry has a strong lobby in the FDA, or because FDA couldn't perceive how you could make a reliable reagent having human components.

It was always a source of amusement and some disappointment that we could never take the battle to our colleagues in America with an assay that was infinity better than anything they had access to.

Q. So we are not really in a position to say exactly what was in Dr Smithies' mind when she made that comment. I think the only point we were trying to make in our question was -- and you say this -- that it is perhaps not so much that the memos are at odds with each other, it's just that they are setting up the conflict of interest we have been discussing. You know, that if one is proposing that someone be both a candidate in an assessment exercise and the assessor, then there is going to be a difficulty.

Going on through the questions, we have covered 12 and we have also looked at the letter that's mentioned in number 13, and you have given us your interpretation

of that letter. And then question 14, we have also looked, in fact, at that letter. Question 15, you have spoken about your collaboration with Dr Mortimer. 16, I think we have covered and that's the reference to the secret meeting, then 17 also. Then we asked you some questions about your role in relation to the Department of Health and the National Blood Transfusion Service in 1984/85, which you have answered.

Just to go back briefly to the whole concept of the evaluation exercise, could we look, please, at [SNB0010170]?

This is a note of a meeting of the screening test subgroup of EAGA, the expert advisory group on AIDS, that meeting having taken place on 15 February 1985. You were on the screening test subgroup of EAGA and Dr Smithies was the chairman.

By my reckoning there were at least three groups who were monitoring or in some other way connected with the evaluation exercise and this is one of them. The regional transfusion directors also had a working party, which was looking at the evaluation of the tests and the introduction of screening, and if we look at item 4 in this minute, we can see the reference to what I would call the third group:

"The DHSS had invited companies developing test kits

to take part in a departmental evaluation; an ad hoc panel of experts with DHSS officers would agree a protocol and arrange for a PHLS virologist to carry out the evaluation."

Were you a member of the ad hoc panel?

A. Sorry, which ad hoc panel?

Q. That ad hoc panel mentioned in paragraph 4, an ad hoc panel of experts who, with DHSS officers, were going to agree a protocol.

A. I frankly can't remember. I know that I would have had -- I know the PHLS virologist would have been Philip Mortimer, supported by John Parry, both of whom I have known for a very long time.

I mean, there was a multiplicity of groups. The EAGA group -- the expert advisory group was involved with Tony Pinching. This was for GUM and diagnostic practices, which was a slightly different portfolio of people and expertise and drivers than was the BTS, and you needed people to deal with the confirmatory testing.

I should think I probably would have been -- or I might have said, "I have got too much on but keep me in touch with Philip". There was a lot of discussion about how to confirm and then -- a fairly resolute unwillingness to go down the Western Blot pathway.

There was a need to have secure confirmatory

testing, obviously, for patient welfare. Certainly Tony Pinching was inherently of the view that the test should not be widely available and we had a lot of disagreement at about the time I knew Don Francis, who had been at CDC and moved to San Francisco, and was talking with him about what he would do in San Francisco if he had a good reliable test. And he said, "I would use it tomorrow, every day of the week." And Tony was saying, "You can't do it, it is very special. Put it on a pedestal." And I was very uneasy with that, very uneasy.

Q. Professor Tedder, there is actually only one more thing I need to ask you about, but it's ten past one and I need to find a particular document so I can ask you about it.

I think, sir, if possible, can we stop at that?

THE CHAIRMAN: Yes, after lunch.

(1.13 pm)

(The short adjournment)

(2.00 pm)

MS DUNLOP: Thank you, sir.

Professor Tedder, there was really just one other thing. I think we had finished looking at the questions and answers document and I just wanted to ask you a little bit about personnel.

Can we look at a document, [SGH0070734], please?

It's the third meeting of the CBLA, Central Committee for Research and Development in Blood Transfusion, BPL, on 28 February, 1984.

It has been clear to us from the documentation that an awful lot of the events surrounding the introduction of screening were managed in -- at least in the Department of Health and Social Security -- by Dr Alison Smithies and Dr Smithies hasn't been able to assist us but just looking at the personnel, we can see from this that Dr Smithies, by February 1984, had taken over Dr Walford's duties. That then made her a senior medical officer in DHSS, I think.

You knew both Dr Smithies and Dr Walford. Is that right?

A. Yes, I mean, obviously, I was more in contact with Alison because of her position, once we were actually hands-on involved with HIV testing. But I had met Dr Walford on one or two occasions prior to that.

Q. Had you met her in connection with the whole AIDS problem?

A. Yes, I had. I had been -- I think I mentioned the NIH meeting in Washington, where there was discussion of the aetiology of the infection and the disease which was presented in the MMWR first paper. After that and after the meeting, the NIH meeting, discussing this, it must

have been early 1983, Philip and I went to DHSS to ask what the plans were for -- what was ready -- what was going to be the plans for readiness to deal with what, I think I alluded to earlier this morning, was a disease or infection which sounded awfully like Hepatitis B in terms of affecting the same group, having the same sort of transmissions. And the moment we heard, in early 1983, end of 1982, about haemophiliacs also being involved, that gave one -- there were two reasons people put forward for the involvement of the haemophiliacs: either David Parillo(?), the American physician, immunologist, was saying it was antigen overload which was damaging the immune system, or there was the virology camp, in which Philip and I were deeply embedded, saying, "This sounds awfully like a transmissible virus infection. It's going in blood products, it's going in gay men, it's going in people who we know get Hepatitis B."

So we felt empowered to go and ask the DHSS what could we do to explore this, and it was as cold a meeting inside the room as it was outside. It was a sort of cold spring morning up in one of the DHSS towers and we were told this was really not any of our business and it was not going to be a problem and go away and stop rocking the boat.

Both Philip and I -- well, I can't speak for Philip. You would need to ask him. But I was somewhat taken aback and pretty irritated.

Q. Right. Thank you, Professor Tedder. I don't want to ask you any more questions about the whole screening topic?

THE CHAIRMAN: Mr Di Rollo?

MR DI ROLLO: Sir, I don't have any questions to ask about this topic.

MR ANDERSON: Neither do I.

MR JOHNSTON: Neither do I.

THE CHAIRMAN: There is no scope for you to ask anything more in these circumstances.

MS DUNLOP: No.

THE CHAIRMAN: Professor Tedder, thank you very much.

A. Obviously, you know where I am.

THE CHAIRMAN: Knowing where you are makes you more vulnerable.

Thank you very much.

MS DUNLOP: Sir, we have, as our next witness, Dr Graham Scott.

THE CHAIRMAN: It did occur to me there were some questions that might have been asked of Dr Tedder not on the immediate project. Is there going to be an opportunity at some other time to find out about them, about his

relationship with Edinburgh testing and so on?

MS DUNLOP: Sir, we did send questions and he did send a response in June, which we looked at at the time. It was pretty brief but I think he said he had difficulty in recalling much of the detail, and I think a lot of his correspondence has gone.

THE CHAIRMAN: Yes, he told me how it had gone.

DR GRAHAM SCOTT (continued)

Questions by MS DUNLOP (continued)

MS DUNLOP: Good afternoon, Dr Scott.

A. Good afternoon.

Q. I think we should just remind ourselves, because it is some time since you were last here, that you were deputy chief medical officer in Scotland from 1975, I think it was, onwards.

A. Yes.

Q. Yes. And you actually were going to retire in 1987 but Kenneth Calman became the chief medical officer and he asked that you stay on for a couple of years.

A. Yes, that's correct.

Q. So you in fact retired in 1989.

A. Yes, I did.

Q. And I think we certainly appreciate that we are asking you questions about events that are now a very long time ago.

A. A very long time.
Q. We certainly take that on board. You have provided us with a statement, which we should have in front of us. It's [PEN0170513].
A. Yes.
Q. I think that will come up on the screen. I should also mention, in case we need to look at the questions, that there is a questions document, [PEN0170481], which perhaps we could open but we don't need to look at it at the moment.

Dr Scott, you make an introductory point along the lines of what I have just been saying, that it is all a long time ago and we appreciate that, and you have been retired for some time and you have been doing a lot of other things that are not connected with medicine.

We asked you about a statement that had been puzzling us in a DHSS memo. The statement is from the summer of 1984 and it records that Dr Smithies thought that it would be good to pilot or evaluate the British RIA test in different blood transfusion centres, and that the material obtained from such an exercise would assist with decision-making, particularly because -- and this is the quote:

"We would therefore be in a strong position to make decisions about the need to buy from one of the five US

pharmaceutical companies."

And you said you don't really know what she meant and you do not think that it was necessarily intended that commercial tests from the USA would only be brought into the UK in the event that the Middlesex/Wellcome test proved unsatisfactory.

We then asked you about the meeting on 27 November 1984 and whether that had been the first forum in which the introduction of donor screening was discussed. I think we actually understand from other material that we have seen since then that it really probably wasn't, and you drew our attention in fact to a document we have just looked at, [SGH0070734], which is a CBLA meeting at which surrogate testing for HTLV-III was discussed and indeed an earlier, similar meeting on 9 November 1983, and that was [SGH0070761].

We do understand that there was some mention of the possibility of surrogate testing in connection with AIDS, I think particularly using the Hepatitis B core antigen, but it's not a topic which we have decided that we need to investigate specifically in our hearings.

You then dealt with our paragraph 8 in which we asked about various discussions. These were some of the discussions, I think, between Dr Smithies and Dr Tedder, and you say perfectly reasonably that you do not recall

having been involved.

You talk about the assessment, which would have been intended to test the efficacy of the tests being developed, and then can we go on to the next page, please? You say:

"An evaluation process such as this is completely standard in circumstances where a new testing process is being introduced. There is no point in using tests which have high rates of false positives or false negatives. To use such a test would distort the true picture and would, in any event, simply be dangerous."

We have certainly heard it said that it's necessary to evaluate a possible new screening test in the particular local population concerned because a test may perform very differently in one population, perhaps a group of people in America, from how it would perform in the United Kingdom. Is that right?

A. I believe so.

Q. Right. Then we asked you about the details of the assessment, and again that's not something in which you personally were involved.

Paragraph 10. We asked a little bit about the dissemination of information on the evaluation programme and we asked about a meeting, and I think this is actually a meeting that was going to be happening in

Scotland, and you are not actually sure at this juncture if it took place.

Could we look, please, at [SGH0027302]. That's the correspondence referring to the proposed meeting. I'm going to show you some documents which all go together.

A. I see, right.

Q. This one, a handwritten letter to Mr Murray at SHHD from Alun Williams at DHSS dated 17 January 1985. Can we just glance at the bottom so we can see the signature there? Thank you.

Do you remember Sandy Murray?

A. Yes.

Q. Right. He was a non-medical member of staff. Is that right?

A. Yes.

Q. Yes. Within SHHD. And what Mr Williams is doing is sending to Mr Murray a copy of a submission which Dr Alison Smithies has prepared. The submission deals with the need to introduce into the NBTS an HTLV-III antibody screening test for all blood donations, and Mr Williams is telling Mr Murray that, "It has been endorsed by the CMO and put to our ministers but I have not yet had their decision," and obviously it's promoting liaison between the two departments to this general issue, which I think you would have seen at the

time as entirely appropriate, would you?

A. Yes.

Q. Right. Mr Williams is saying:

"Perhaps we could discuss with you [that is Mr Murray] and Dr Bell when Dr Smithies and I come up to Edinburgh shortly."

That's the meeting you say you do not know if it happened and you do not remember being there.

Can we look at [SGH0027302], please? This is the enclosure that came with the handwritten letter. It's the minute, Dr Smithies' minute that goes with her submission, and it gives a little bit of information for the CMO.

This is a submission which has been prepared by Dr Smithies with administrative colleagues and it's looking for approval in principle for the introduction of a screening test for AIDS antibodies into the National Blood Transfusion Service, so England and Wales:

"The UK test is currently being used at the Middlesex Hospital and at the Central Public Health Laboratory in Colindale to detect antibody carriers."

Then:

"Scale-up of production of the reagent is necessary before the test can be applied more widely."

Then the actual submission, which I think we have seen before too, but [SGH0027304]. Can we look firstly at the bottom of the first page? That is about current action. So there has been a working group, the NBTS AIDS working group. There is going to be an expert advisory group, meeting at the end of the month, that's January 1985:

"The advisory committee on dangerous pathogens."

Whose remit, as I understand it, was more to do with health and safety at work, and it had prepared guidelines for hospital staff and then there is a revised leaflet coming.

If we look at page 2. The need for a screening test. Dr Smithies is saying that there has been a campaign to dissuade higher risk groups from donating blood but it's not enough, and she is pointing to some of the reasons why a screening test is thought to be necessary.

Then going on to talk a little more about the screening test. She does say in this section on the screening test, which is section 5, only about 10 per cent of those infected with the virus apparently develop the disease, which I think we now know to have been incorrect, but certainly understand that around that time there was a lot of confused information.

She says:

"Certain blood products made from large pools of plasma can be heat-treated but heat treatment cannot be applied to blood itself."

Then if we just look down that page, she goes on to talk about the financial implications. We have seen a range of different estimates, Dr Scott. This one is saying that the likely cost will be between 75p and £2 for each donation. Then details of the tests are in an annex. Can we look at page 3, please?

The decision which the ministers are going to be required to make is whether or not to agree in principle to the introduction of a screening test for AIDS antibody for all blood donations, and indeed to make an announcement to this effect indicating that the development of a test was being backed by the DHSS.

Then if we just perhaps look briefly at the remaining pages, which represent the annex, this is the explanation of the testing. Some results already obtained, the significance of the test, and the development of the test.

Then on to the next page, please. Blood transfusion and AIDS. A reference to the infection in Scotland of the group of people who came to be known as the "Edinburgh cohort". That's at the end of that section,

section 4.

Then section 5, the introduction of a screening test. Then on to the final page, if we can, please. The directors will probably introduce tests initially from the USA, then later from Wellcome.

I suppose it must have been very helpful that officials in the DHSS were willing to send their submissions of this type to you in SHHD?

A. Oh, yes, to see whether that would be approved or not was another matter. But, yes, it was interesting to see their submission.

Q. Yes. We look, I think, in a little more detail at what then happened as far as the decision-making process in Scotland is concerned.

A. Yes.

Q. [SGH0027295], please. This is a minute to you from Mr John Davies. Do you remember him?

A. Yes.

Q. He is another non-medical member of the department. Is that right?

A. Yes, more senior than Murray.

Q. I see. He is corresponding with you and copying to Mr Macpherson, Dr McIntyre and Mr Robertson. We can see the information he is imparting, that:

"DHSS ministers have now agreed, apparently with

great reluctance, that all donations of blood in England should be tested for the presence of antibodies to HTLV-III. We now have to decide whether we have any alternative to advising our ministers that it is necessary to follow suit in Scotland."

Mr Davies is saying:

"Only one donation to date has contained antibodies to HTLV-III."

He thinks. Pointing out at the end of the second paragraph:

"Haemophiliacs in Scotland are now not at risk as all Factor VIII is heat-treated. The situation in England is different. In any case, only a proportion of those with antibodies develop AIDS. I have seen figures ranging from 10 per cent down to one in several hundred."

Then pointing out:

"It will be necessary to arrange follow-up for all individuals whose blood gives a positive result. It's not clear whose responsibility that would be or what the cost implications are."

He talks about false positives and false negatives. And then he says:

"As you yourself have said, there is a considerable danger that people considering themselves at risk may

attend blood donor sessions specifically for the purpose of having their blood tested."

Then talking about financial implications. I think the tone of this minute, as far as the possibility of introducing screening is concerned, is quite negative, isn't it?

A. Yes, it was generally recognised it wasn't very good tests.

Q. The tests that were then available, you think, weren't very good?

A. Weren't very good.

Q. Right.

A. Nevertheless, they would have to be used.

Q. Yes. Can we then look at [SGH0027294]?

A. Yes.

Q. Because this is from you.

A. Yes.

Q. I'm sure you do not particularly recognise it, do you, other than from having seen it recently?

A. No, I don't recognise it but I accept that it was by me and what I said. I stand by that, yes.

Q. Yes. So you are responding to Mr Davies and you are copying to Drs McIntyre and Bell and Mr Macpherson and Mr Robertson? Is Mr Robertson a financial person?

A. Yes.

Q. And Mr Macpherson, what's his role, if you can remember?
A. He would be an assistant secretary involved in these issues.
Q. Right. And you are drawing a distinction between a test which looks for antibodies and a test which identifies the virus itself, and you thought that the case for introduction of the test was not clearcut but obviously the fact that the DHSS ministers had agreed was a factor that bore some weight in the decision-making process in Scotland. Is that right?
A. We would take it into account.
Q. Yes. You are actually hoping to have an office meeting and wondering if Dr Cash could be there. By this time Dr Cash is the consultant adviser on transfusion matters to SHHD. Is that right?
A. Yes.
Q. I think you are recognising that there will have to be a submission to ministers in Scotland as well.
A. Yes. Correct.
Q. Then can we look at the next document in this series?
THE CHAIRMAN: Before we leave it, in the paragraph that's second from the top of the page, as we see it at the moment, you express the view that testing for HTLV-III antibodies is technically different from testing for HBV. You say:

"In addition, the test is much more expensive, as well as being seriously unreliable."

Was that your own view, Dr Scott? Can you hear me?

A. It wouldn't be my view but it would be a view depending on what I had seen and been told elsewhere.

THE CHAIRMAN: Where would you get the advice that led you to express that view?

A. From Dr McIntyre and Dr Bell and Dr Cash. I don't know whether all together but these were the kind of people that would have told me.

THE CHAIRMAN: Substantially the people you are writing to, I suppose. So were you meeting these people and discussing this issue with them?

A. I would see them from time to time. We wouldn't have -- there would be no need for formal meetings. We would be seeing each other on a day-to-day basis as required.

THE CHAIRMAN: Yes, thank you.

MS DUNLOP: I suppose you might have read things in the general media or specialist medical journals, other journals.

A. Perhaps, I can't remember.

Q. Well, in general terms, did you try to keep in touch with what was in the BMJ and the Lancet?

A. If I didn't, other people would have drawn my attention to it.

Q. Yes. Can we look at [SGH0027293], please?
A. Yes.
Q. This is another reply to Mr Davies' minute of 7 February but this time from Mr Macpherson, who I think was an assistant secretary. I'm sure I have that information somewhere.
A. Yes.
Q. Perhaps he is taking more of a policy line because he is saying that it may be that everything said is valid but it would be very difficult for Scotland not to introduce screening when England was going to introduce screening, which I suppose at a common sense level must have been right.
A. Yes.
Q. Yes. But Mr Macpherson is also thinking that a talk about it would be a good idea. Can we go a little further forward, please, and look at [SGH0027226]?

You refer to this in your statement, Dr Scott. I think this is 21 March now. Can we just check the date of this so that we are -- I think the date's at the end. Yes, 21 March, from Mr Macpherson, sorry. Can we go back to the beginning?

This, I think, is the submission or the briefing paper that was going to -- it has the ministers in Scotland. We can see it is going via their private

secretaries to Mr MacKay, he will have been the health minister, is that right?

A. Yes.

Q. And the Secretary of State, who I think at that point will have been George Younger?

A. I can't recall.

Q. In fact it's going to quite a range of people. It's going to Mr Ancram and the Under Secretary of State as well. Perhaps if we just have a look at the minute, please. It really deals with two issues, this document. It deals firstly with the question of whether or not AIDS should be made a notifiable disease, which we don't really need to spend any time on, and with the topic of screening.

So could we go on to the next page, please? There we are, "Blood Transfusion", section 6.

We can see that this minute actually carried with it a copy of a letter in the Lancet. I think we know that letter because we looked at it yesterday, more than once. A very recent publication in the Lancet. As the minute says:

"Strongly supporting the screening of all blood donors but advising that such a screening programme should be delayed until the available test systems have been evaluated and until alternative testing facilities

are made available to individuals who may be at high risk of transmitting AIDS."

So this minute is recognising the same point about the need to prevent people who simply want an AIDS test from coming to give blood, and I think we understand that that was a perceived risk.

Then on to the next page, if we could, please.

Some unanimity between individuals in the department and the transfusion directors. Is this an example of a document, Dr Scott, in which a percentage figure is given for a rate of false positive results?

I don't think I'm going to ask you anything about it, Dr Scott, because we understand from our discussions with Professor Tedder this morning that assessing, as it were, the success rate of a test -- or discussing the success rate of a test in picking out true positives requires its own special language and I'm not sure -- I mean, the 4 per cent figure that has been given here seems just to be probably 4 per cent of 280,000 donations, I think, with a small discount.

Anyway, the real point, I think, is that if false positive results are obtained from test kits, then that will give rise to a group of people who will be understandably very anxious and who will require additional healthcare and support, and I expect that's

just common sense, is it?

A. Yes, no doubt Professor Tedder commented on this high rate in America, which I don't think -- he probably didn't agree with.

Q. Well, yes, he has explained to us in some detail about the different ways in which American tests and the Wellcome test worked?

A. Yes.

Q. And that there were various features actually inherent in the whole structure of the American tests which gave rise to a risk of false positives, that were not present in the Wellcome test.

Then can we just go down through the minute? Thank you.

There is a mention of cost, which we would perhaps expect, then this difficulty of people coming really just for a test, and then the recommendation at the end, a phased policy. You see that? That's paragraph 12.

So currently available tests have limitations, a high rate of false positives is going to cause significant difficulty, there is a practical need to provide alternative screening facilities and asking what ministers think.

Can we look then at [SGH0027225]? Dr Scott, I think this is a telex?

A. I didn't know we were as advanced as that by then. Maybe it was.

Q. I think probably only dinosaurs can recognise telexes -- and I can. But it looks like a telex to me and it's coming from the private secretary to Mr Mackay. It's going to the private secretary -- to the Secretary of State. Why would telex have been used? I mean, is somebody in London and somebody in Edinburgh?

A. Yes, from this MacKay must have been down in Edinburgh -- DH -- that's probably where he was at the time, in the Scottish office, and the Secretary of State was perhaps in St Andrew's House, just as things worked out.

Q. I don't think we have given this a date but actually it's 22 March 1985 because we can see that in the line.

A. Yes.

Q. Do you think "DH" is Dover House?

A. Probably, yes.

Q. Right, thank you.

So Dover House in London and then New St Andrew's House for NSAH?

A. Yes.

Q. It's all falling into place. It refers to Mr Macpherson's minute of 21 March. Mr MacKay has commented:

"I fully appreciate the logic of this advice, especially the danger that at-risk men may use the transfusion service as a screen, and as the test is not absolutely reliable some blood may enter the system, which is infected. Whatever we do on the BTS, recommendation 12(c) is essential."

That was the one that we saw in the minute, related to the provision of alternative testing facilities:

"Also we do have to keep in line, or ahead of, England, otherwise we would be subject to very severe criticism."

That's Mr Mackay. Then can we look at [SGH0027224]? This is Dover House and this is 26 March 1985. This is coming from the Secretary of State, and we can see that the Secretary of State has seen the minute of 21 March and has agreed the recommendation.

So whatever risks there might have been about the introduction of screening and the need for it, perhaps, as anticipated, a decision at least in principle to go ahead has been reached by this point in March 1985. Is that right?

A. Yes.

Q. Right.

Can we go on, please, and look at another document, [PEN0170565]? This is just to pick up the reference to

the need for alternative testing facilities. The Inquiry team has been doing some investigation on what steps were taken in Scotland to ensure that such facilities were available and I thought it would be helpful if we just looked at a letter of response that we have had from the Scottish Government in August, then we will look at the actual documents referred to.

Can we go down a little bit? Thank you.

We can see that what has been found is a letter from you to chief administrative medical officers dated 6 July 1985, in which they were asked to tell SHHD what arrangements they had made for alternative testing facilities. The chief administrative medical officers, were they found in each health board?

A. Yes.

Q. Is that right? Right.

This is, in fact, the letter, sir, which gives a little bit of information about Dr Covell. Dr Covell -- am I pronouncing that correctly or should it be "Covell"?

A. Covell.

Q. Do you remember Dr Covell?

A. Yes.

Q. I suppose he has had some involvement in this area because of his particular areas of expertise in

communicable and sexually transmitted diseases?

A. Yes.

Q. Yes, because we are dealing with both issues of blood transfusion, but also issues, obviously, of sexually transmitted infections, and otherwise communicable infections.

Then can we just look at the end of the letter, please? Actually Dr Covell has been contacted but was unable to respond to any of the questions.

It's pointed out that there perhaps was no written guidance on alternative facilities to Scottish regional transfusion directors, but perhaps also relevant to bear in mind that this will have been the responsibility of the health boards to provide anyway. And we know too that Dr Cash wrote to the Common Services Agency on this topic in February 1985 and actually sent a draft letter, which he thought ought to be sent, suggesting liaison in connection with this issue.

So can we move then, please, to look at [PEN0170567]?

This is the first of those letters referred to. Dated 8 July 1985 and it's, I think, from you, is it? Yes, there we are.

Dr Scott, you seem to have been responsible for a lot of this correspondence, rather than the chief

medical officer.

A. He was probably away at the time.

Q. Yes, I think he was away a lot, was he?

A. He was away -- I shouldn't refer to him, but he was an absentee landlord. He spent most of his time on WHO business elsewhere and I had to act on his behalf.

Q. This is a warning that routine screening of blood donors -- it's probably going to begin before the end of the year. The provision of alternative screening facilities is described in your letter as "essential" and people have to get back to the department to explain how they propose to provide the facility.

THE CHAIRMAN: Who was the CMO at this time?

A. Dr John Reid, deceased.

THE CHAIRMAN: Yes.

MS DUNLOP: Then the next letter is actually [SGH00026982]. This is on a slightly different topic but I think also from you, is it? Yes. 6 August 1985. You are writing to chief administrative and medical officers again, and you are also writing to, I suppose, the director of Scottish Blood Transfusion Services, Dr Cash, is it?

A. Yes.

Q. And then regional directors at SNBTS?

A. Yes.

Q. I think to inform them about the results of the first

phase of the evaluation exercise. So saying that the first phase of the evaluation exercise has been completed and also pointing out that confirmatory testing is going to be available at the department of bacteriology in Edinburgh and at the Regional Virus Laboratory at Ruchill in Glasgow.

Convenient for us just to look at the attached report. Can we look at [SGH0026968]? If we keep that open for a moment and also look at the document immediately before, [SGH0026967]. This is just to orientate ourselves, because I think this is the covering memo, at least for England, 1 August 1985. And we can see that this again refers to the completion of the first stage of the evaluation. It says a summary of the recommendations is attached. A more detailed account of the PHLS evaluation is to be available later that month.

Can we then go back to 6968, please? We can just see that this is the resume of the results. It looks as though you have just sent it out with your own covering memo and we can see that the memo lists the different kits which have been evaluated. There has been an evaluation protocol and the kits most suitable for use in diagnostic laboratories are thought to be those of Organon, Ortho Diagnostic Systems Limited and Wellcome.

Sir, I think this may be the document Professor Cash had in mind. I may be wrong but in the light of what he had said yesterday, I did notice in this paragraph under the heading "Kits most suitable for use in diagnostic laboratories", that Abbott had emphasised that heat treatment of sera before testing was not part of the company's standard operating procedure.

So possibly one of the documents that he had in mind when he said that heat treatment, which was employed in phase 1 of the evaluation exercise, was something that may have complicated the picture.

Anyway, that's really just something to note in passing.

Then there is to be this second stage evaluation in blood transfusion centres. We can see that the list of three has shrunk to two, if we go on to the next page. So we are really talking about the kits from Organon and Wellcome. So you must have felt, Dr Scott, that you want to disseminate this information more widely, the information about the evaluation exercise that had been conducted under the auspices of the DHSS. Would that be right?

A. Yes.

Q. Right.

THE CHAIRMAN: And you would have done that at this stage

without reference to Dr Reid?

A. I don't know whether he was there at the time. He probably wasn't. If I signed the stuff, he probably wasn't there.

THE CHAIRMAN: So really at that stage are you effectively acting --

A. Yes.

THE CHAIRMAN: -- in his place?

A. Effectively.

THE CHAIRMAN: Right.

MS DUNLOP: Then can we look at [SGH0026995]?

This is the letter of August, a Dear Doctor letter, going to the chief administrative medical officers again, and dealing once more with the topic of alternative testing facilities. By now it's anticipated that the screening will commence in mid-October.

Can we read a little bit further down the letter, please? We see, Dr Scott, that there is a mention of genitourinary or sexually transmitted disease clinics, who will be in a position to offer alternative testing to patients, but it seems that there was also a perceived need to offer facilities to those who didn't want to go to a clinic of that nature. Is that right?

A. Yes.

Q. Yes. And making, I suppose, some essentially simple

points about the need to publicise the facilities, to tell GPs, and then there has to be appropriate counselling as well. And we can see that you are able to take advantage of courses at St Mary's Hospital in London. Actually this letter also contains information about infection control, infection control guidelines, which I don't think we need to look at.

So that deals with the question of the introduction of alternative testing facilities, which we know were perceived as necessary from quite early on in the story. Can we just go back to the statement then, please? [PEN0170513]. Actually I have asked you all these questions and put to you all these documents stemming from the minutes that we looked at from the early part of 1985. So we were really just at about paragraphs 10 or 11 but we then asked you a series of questions which you really weren't able to answer. I think because you weren't involved. Some of these are English minutes and memoranda.

If we look on to the next page, please.

Although you didn't have any direct involvement, again the decision to have an evaluation process seems to you to have been something that was inevitable. It was always going to have to be evaluation of tests and, you say that in 17.

A. Yes.
Q. And then you point out also, in 19, about the difference between commercialisation of the indigenous test, as it were, versus evaluation of the commercial tests, and it seems to you right that they should have been kept apart. The secret meeting didn't ring any bells for you?
A. No.
Q. And then you again reiterate the point in paragraph 22 about it not being correct to introduce a test which has not been evaluated.

Can we go on to the next page, please? The only DHSS person whose name you actually recall is Dr Smithies. Did you have some contact yourself with Dr Smithies?
A. No.
Q. No?
A. I recognise the name but ...
Q. Right.
A. I don't think I ever met her.
Q. And you weren't involved in any discussions which resulted in SNBTS abandoning its own evaluation?
A. No.
Q. No. Then you cover in your answer 31 all the pieces of advice that you issued, and I have added in the one

from July 1985 as well.

I think we should just look, Dr Scott, at a final tranche of minutes and memoranda, showing the ministers being kept up-to-date in the autumn of 1985. Can we look at [SGF0010831], please?

This is going to Mr Mackay and it's updating him since the Macpherson minute of 21 March and then another minute, which we haven't actually looked at, from Mr Davies in June. We can see that firstly there is information about the incidence of AIDS. Statutory powers. Education. And then various other publications have been distributed. A paper entailed "AIDS: General Information for Doctors". Then can we go over to the next page, please? Thank you.

Then blood tests, arrangements have been made to screen all blood donations as from mid-October.

I don't think anything in paragraph 6 is news to us. Paragraph 8, a need for adequate publicity in connection with the facilities available outside the Blood Transfusion Service.

This is coming from SM Liddle. Do you remember him or her?

A. Him.

Q. Him?

A. Yes.

Q. Yes. So another non-medical member of staff in SHHD. Is that right?
A. Yes, I think he was a principal or something like that.
Q. Right.
A. Or an SEO. One or the other.
Q. And offering to the minister the opportunity to discuss the matter with officials if he wishes. Then into October, [SGH0027079]. This actually is from Dr Reid. And he is sending to chief administrative medical officers, on 1 October 1985, a letter to go to all doctors within the individual health board areas. And there is also going to be a paper enclosed entitled "Information for Doctors Concerning the Introduction of HTLV-III Antibody Test. AIDS Booklet 2". Again, Dr Covell is the contact for this.

Then the next document is [SGH0027080]. That's the enclosure, the dear doctor letter, that the CAMOs are to send out, then another enclosure is the booklet, which we shall just look at briefly too. It's [SGH0027081] "AIDS Booklet 2". Then if we perhaps just have a look at what it deals with. It covers quite a wide range of different issues.

(Pause)

Procedure. We can see that there is to be repeat testing of those donors who have an initially positive

screen test and then if they become repeat positive donors, then the reference laboratory will get involved and a protocol has been devised for the communication that's to take place with the donor.

There is to be counselling about the significance of test results. Then on to the next page, please. Arrangements made for any donors in this position to receive further medical help.

A mention is made in paragraph 4 of a potential problem with false negative results. And a bit of information in paragraph 5 as to what to expect in patients who come to doctors by this route. Clinical assessment is to determine whether or not a patient should be referred for any further investigation and treatment and how frequently follow-up is required.

Then alternative testing facilities. Advice for GPs.

Then on to the next page, if we could, please.

So it was thought necessary, Dr Scott, to provide with some care for how any individual having to cope with a positive test result should be dealt with. Is that right?

A. Yes.

Q. And we see considerations like their need for further clinical examination, their need for information, and

then we can see a specific section dealing with seropositive women of child-bearing age. There is actually a passage underlined, in fact, at the end of 8:

"All HTLV-III positive individuals, whether or not asymptomatic, must be regarded as capable of transmitting infection through sexual contact or through transfusion or inoculation of blood. Their counselling should include the guidance given in appendix 2."

Appendix 2 is actually a set of guidelines for individual patients. Then there is a reference to employment matters. We can perhaps just read on through this booklet "Lab Investigations", and precautions to be taken then, and I think if we look on to appendix 2, we will find the details for individuals. Here we are, "Guidance to Individuals on Measures to Control the Spread of HTLV-III."

So some quite detailed information for individuals whose infection comes to light by this particular route.

Perhaps we can just read to the end. (Pause)

Can we just go on and look at the last page as well? Thanks.

This is actually mentioning some possible contacts for people with haemophilia, so whoever has put these guidelines together has had in mind that some of those who may be needing advice may have been infected by that

particular route. Right, thank you.

Dr Scott, that's an examination of the decision-making process in Scotland, concerning the introduction of screening and some of the practical steps that had to be taken so that the screening could be introduced and would operate as efficiently and effectively as possible, and we have looked at your own part in those decisions and the preparations.

I did just want to ask you one final question, however. There was a lot of liaison between Scotland and England over this period.

A. Yes.

Q. Particularly between SHHD and DHSS.

A. Yes.

Q. And from time to time we have seen that sort of contact described in different ways. I suppose one could say that the Scots delegated the decision-making to the English and would just have done whatever was decided in England, or the Scots were watching what was happening in England or a decision was being reached jointly or something of that sort. I just wondered how, as you look back on it now, you describe the decision-making process?

A. Well, we had liaison with the DHSS at all kinds of levels. I would go down and attend the policy meetings

of the chief medical officer of the DHSS and I would take -- listen to the discussions and then come back. But there would also be contacts at all levels, going backwards and forwards, talking to each other, what we were doing, et cetera. That doesn't mean to say if DHSS decided to do something, we would necessarily do it.

If they hadn't decided to do it, then we might well have done it. In this case DHSS were very equivocal about introducing tests and we decided that we would go ahead whatever happened. As it happened, it worked out and we went together at the same time. So there is no simple answer to it.

Q. Right. What do you think would have happened if, say, during 1985 it had become clear that Scotland was ready to introduce screening whereas there had been a problem in England and England wasn't ready?

A. It might have delayed it by a little but not by much.

Q. Right. So would it have been possible that Scotland would have introduced screening ahead of England?

A. Yes.

Q. If circumstances had been different?

A. With the agreement of ministers.

Q. Scottish ministers?

A. Scottish ministers.

Q. Right. Okay. Thank you very much, Dr Scott.

Questions by MR DI ROLLO

MR DI ROLLO: I would just like to follow up on one or two points, sir, if I may.

Dr Scott, can we have a look, please, at [SGH0027295], which is the memo from Mr Davies, I think, to you. Is that right?

A. Yes.

Q. It's fair to say that he is not terribly sympathetic to the idea at this stage of introducing screening?

A. I beg your pardon?

Q. The author of this is not terribly sympathetic to the idea of introducing screening at this stage.

A. No, he really wasn't very keen on it but if it had to go ahead, finance was not going to be a problem. That had been cleared with Mr Robertson. It was quite a considerable cost but it wasn't a determining cost.

Q. If we look at the second paragraph there, there is one statement in there which I would like to ask you about. It says:

"Haemophiliacs in Scotland are now not at risk, as all Factor VIII is heat-treated."

Do you know if that's accurate or not?

A. Well, I doubt we would have said it if it wasn't true.

Q. You see, I think our information is that haemophiliacs, at least haemophiliac B patients, would be at risk still

at this time because Factor IX was not heat-treated. Factor VIII was heat-treated but haemophiliacs in Scotland -- or certain haemophiliacs in Scotland would be at risk at this time. Were you aware at this time that for instance Factor IX was not heat-treated?

A. I can't remember. I don't think so.

Q. If we go to the advice to ministers, [SGH0027226]. There is an earlier version of this draft but just looking at this one, in the first paragraph there is a sentence I want to ask you about. It says:

"The public health hazard does not therefore warrant alarm on the scale manifested in the popular press."

Then it goes on to say:

"However, such alarm undoubtedly exists and it is desirable to take visible steps to reduce it."

There is a possible ambiguity there. Is the desirability to take visible steps to reduce the alarm or to reduce the health hazard?

A. Reduce the alarm.

Q. Right. So the motivation may be about reducing alarm, as opposed to reducing the perceived risk to health in relation to this whole issue. Is that right?

A. No, I don't think so. I think everything would have been done that could be done.

Q. We have heard from Professor Cash, who has told the

Inquiry, I think, that he wanted to go ahead and evaluate in Scotland screening tests, and he was told by SHHD that that wouldn't be possible, that he wasn't to do that and that we were to wait for evaluations to take place in England. Do you know anything about that?

A. No, I don't know why Dr Cash says what he says.

Q. Is he wrong to say that?

A. I would not presume to comment on Dr Cash's views.

Q. Right. So you are not in a position to say he is wrong to say that?

A. I would say that Dr Cash is a first-class scientist of the highest order. His views on SHHD, as you can see from his evidence there, are not entirely always favourable, shall we say?

Q. I think that is probably fair to say that. I think the impression one gets is that there is a feeling that SHHD in some way were holding him back in doing what he wanted or would have liked to have done in terms of progressing matters.

A. He may well have felt that way. As I say, I can't get inside the mind of Dr Cash.

Q. Is he right to think that though, is what I'm asking you?

A. I don't care to comment on any of Dr Cash's statements about relations with SHHD and what they prevented him

from doing and that kind of area.

THE CHAIRMAN: I think it may be quite important in some circumstances that I know what the relationships are, Dr Scott. So can I prevail on you to apply your mind to it please? If Mr Di Rollo asks you a question like that, I think you should take it that there is some significance in it.

A. Yes, I think there is significance to the effect that Dr Cash was highly critical of SHHD in many aspects. Whether he was justified in that, I don't know. But he usually tended towards being critical of SHHD.

MR DI ROLLO: I think it probably would be helpful -- this is an opportunity for you to give your side of it, I suppose, or SHHD's side of it, if you are in a position to do so, and that's what I'm really inviting you to do.

A. Other than to say, if Dr Cash would find an opportunity to criticise SHHD, then he would do so.

Q. The specific issue that I have asked you about is the question of the delay in being in a position to evaluate screening tests in Scotland. He has made a specific criticism in relation to that. Is that criticism, in your view, justified?

A. I think he decided that -- I think, as I recall, he withdrew the idea of doing the evaluation tests under

his own free will.

Q. He was told, as he puts it, I think, in no uncertain terms, that he wouldn't get the support of SHHD in relation to this and that he had no option but to withdraw it.

A. I can only comment that Dr Cash, where possible, would be critical of SHHD, no matter what they did.

Q. Is it the case that SHHD did not support the idea that Scotland should go it alone in relation to this particular issue?

A. On what issue?

Q. In relation to the evaluation of screening tests?

A. I can't recall the exact words Dr Cash said over evaluation. I thought he had first of all suggested it and then withdrew it. The suggestion -- without any pressure from SHHD to do so.

Q. My understanding of his evidence, both in his statement and to us yesterday, was that as a result of conversations he had with Dr McIntyre, he was told that an evaluation in Scotland would not take place. It wouldn't be permitted to take place because the evaluation was to take place in England, and that's what SHHD had decided to do. Now, is he right about that?

A. If Dr McIntyre says so, that would be right. He would remember better than I do.

Q. I know the minister says in his response that he doesn't want to be behind England, and perhaps suggests that being in front of England would be quite a good thing from his point of view, politically, but the civil servants at least don't appear to be terribly keen to go down the road of introducing screening tests, at least initially, and even in the advice to ministers, the concern seems to be more about alarm rather than health issues. Do you see my point?

A. I think it was on both issues.

THE CHAIRMAN: Mr Di Rollo, we are going to have to have a break for the benefit of the stenographer. We will try and make it as brief as we can.

MR DI ROLLO: Very good.

(3.35 pm)

(Short break)

(3.54 pm)

THE CHAIRMAN: Yes, Mr Di Rollo?

MR DI ROLLO: Dr Scott, I was really just exploring this issue about the decision-making in relation to the introduction of screening tests and in particular the question of carrying out an evaluation in Scotland. I think we all know that Professor Cash can be critical of SHHD.

A. Thank you for recognising that.

Q. I'm not sure that's necessarily the point that I want to make. The question I want to look at really is the merits of this particular criticism and whether it's justified or not. In other words, leaving aside other criticisms he may have made of SHHD over the years -- and no doubt there were one or two criticisms -- perhaps more than one or two -- the question I want to get to is your side of it in relation to whether this particular criticism is justified.

Dr Cash, as I understand it, has told us that essentially he was in a position to get an evaluation of screening tests in place in January 1985, get that up and running, and if that had happened, I think he has also indicated that we might have got a screening test in place earlier than we did. The question I'm asking is whether you are aware that he was prevented from doing that by SHHD. In other words, did SHHD or did anyone from SHHD say to him, "You are going to have to wait for the English test evaluation to take place"?

A. I can't recall the exact events but as I understood it, he withdrew it on his own volition. Whether he was advised to by someone in SHHD I do not know.

Q. Right.

THE CHAIRMAN: You see, the implications of the answer, Dr Scott, include that he had such a proposal.

A. There was a proposal.

THE CHAIRMAN: That he had such a proposal for testing.

A. Yes.

THE CHAIRMAN: He said it was in Glasgow, using a really well developed team there and that at some stage that proposal was departed from.

If SHHD were involved in the process that led him to depart from it, there could be all sorts of great reasons why they did: economic, lack of confidence that it was necessary to have a separate test, confidence in the English test that the PHL service could produce, all sorts of reasons, but if SHHD didn't take part in it, the reasons are totally irrelevant. So really it is quite important to follow Mr Di Rollo's line and see whether you can help us.

Dr Cash may be unqualifiedly critical of SHHD for their role. That's not necessarily where we would end up, but it's important to know whether they had a part to play.

Is that a reasonable way to put it, Mr Di Rollo?

MR DI ROLLO: Yes, indeed.

A. I think Dr McIntyre might well remember the circumstances. I don't. I can't remember the circumstances in which the evaluation was not carried out. Dr McIntyre may have spoken to him, I don't know.

Q. We have a statement from Dr McIntyre, and I don't really think it helps us very much to resolve this particular question, because I think his recollection doesn't assist on this particular issue.

It does seem surprising from my standpoint that there is no documentation about this at all, of any kind. This discussion, if it takes place, there is nothing in writing, no memorandum or any information which suggests what the SHHD position was about that.

A. I can't help you there, I'm sorry.

Q. Such material as does exist tends to support the view that, leaving aside the issue of evaluation, SHHD weren't terribly sympathetic to the idea of introducing screening tests at all at this stage. That's what that memorandum -- the original one that we saw this afternoon and the one that we have on the screen just now -- tends to suggest, that we are just simply going to follow what the English are doing on this one. Isn't that what the SHHD position seems to have been?

A. I think we were aware it wasn't really a very satisfactory test. But if it had to go ahead for other reasons, then it had to go ahead.

Q. Dr Scott, you say, "We were aware that it wasn't a very satisfactory test," can you just explain how that awareness came about?

A. Well, I think Professor Tedder would have been able to answer that question better.

Q. No, it's not why it's unsatisfactory, it's not that. You said, "We were aware that it wasn't satisfactory," what I want to know is: how were you aware that it was unsatisfactory?

A. From all the information that was going around.

Q. Who gave you that information?

A. I beg your pardon?

Q. Who gave you that information, how did you get that information?

A. I can't remember who gave that information, but we would know what Tedder was thinking. We would know what the general tenor of events were.

Q. Paragraph 12 of this memorandum, [SGH0027226], on the third page, it says:

"No doubt there will be public pressure for routine screening of blood donations once it is known that commercial tests are readily available. However having regard to:

"(a) The limitations of currently available tests;

"(b) The disproportionate effects of a high rate of false positive findings; and

"(c) The need to provide alternative screening facilities to divert 'at-risk' individuals from the

Blood Transfusion Service,

"We recommend the adoption of a phased policy leading to the routine screening of blood donors, which would take into account a comparative evaluation of the tests available ..."

Et cetera. It does appear from that that the urgency that one might have anticipated in relation to this particular matter perhaps isn't there; in other words, that we are dealing with a situation where we know that there is HIV in the blood supply, we know that haemophiliacs have already been infected as a result of that. We know that anyone receiving a donation of blood by transfusion could potentially be at risk. One would have thought that the need to introduce screening tests was very urgent at this stage, rather than this notion of a phased introduction.

In other words, what I'm suggesting to you is that the ministers are not being told the seriousness of the situation and the need to press on with this at a much greater speed. That's what I'm suggesting to you.

Do you have anything to say or do you have any comment about that?

A. I thought ministers had reacted to that saying that -- 12(c).

Q. I'm sorry, Dr Scott?

THE CHAIRMAN: Dr Scott is looking for the document on which the minister's comment is sent back, generally accepting the advice and drawing particular attention to paragraph 12(c). I can't remember precisely the number.

A. Recommendation 12(c) is essential, the minister says, and the Secretary of State agrees with it.

MS DUNLOP: It's the same as 7224.

MR DI ROLLO: We will maybe put that up on the screen.

MS DUNLOP: Sorry, 7225 is the one that has that comment in it, 7225.

MR DI ROLLO: That's to do with introducing alternative donor testing. That's what 12(c) is to do with, but I don't think that detracts from a general point, it's really a suggestion that there was a lack of urgency at this time on the part of SHHD in respect of --

A. I don't accept that.

Q. I have no further questions, sir.

MR ANDERSON: I have no questions.

THE CHAIRMAN: Mr Johnston?

Questions by MR JOHNSTON

MR JOHNSTON: I just have one question, Dr Scott.

You have just been asked about technical issues such as the reliability of tests and all I wanted to ask you is, if you needed some guidance about a technical point such as that, who would you ask?

THE CHAIRMAN: Dr Cash perhaps?
A. About the reliability of tests in general or ...? Or all kinds of tests?
MR JOHNSTON: You gave some evidence a few moments ago about how you absorbed the state of scientific knowledge or that sort of thing, and you told us sometimes other people looked at medical publications. I'm simply trying to get a feel for where you gathered the information that you felt was necessary to make decisions, or advise on making decisions.
A. From around the department, from the medical press, from whoever I was talking to at the time.
THE CHAIRMAN: I wasn't being facetious. Wasn't Dr Cash, in relation to blood transfusion matters, your scientific adviser?
A. Yes.
THE CHAIRMAN: Yes. Wouldn't you have gone to him?
A. About matters of both false positive in relation to -- blood transfusion matters, yes, but in general false positives in a lot of other areas.
THE CHAIRMAN: We are talking at the moment, Dr Scott, about a scientific factor that is central to the operation of the Blood Transfusion Service, are we not?
A. Yes.
THE CHAIRMAN: Mr Johnston?

MR JOHNSTON: Thank you, sir.

Could I follow up perhaps by asking you to look at one document that you have seen already, this is your memo of 8 February 1985. [SGH0027294].

A. Yes.

Q. We see there in the first half of the memo, you are talking about the scientific situation and then you make reference to public interest and so forth and then you suggest the office meeting. Can we see there in the last two main paragraphs, you say:

"For consideration whether Dr Cash, as our consultant, might also be invited to the office meeting. He strongly advocated introducing the test despite its limitations, as the minister would be open to criticism if he did not agree."

Then the following paragraph, just at the end:

"If Dr Cash were to advise unequivocally against the introduction of the test, that might be another matter."

Do you see those points?

A. Yes, I see them.

Q. Can you tell us, is that the sort of consideration that cropped up only on this one occasion or is that something you would routinely want to consider, the involvement and the views of Dr Cash?

A. If it in any way affected SNBTS, yes, we would have

consulted him.

Q. All right, thank you very much.

THE CHAIRMAN: I'm still worried a little bit about the reality of this.

We know that Dr Cash wanted a test, isn't that so? There is a difference of emphasis perhaps, whether the test should be evaluated in England or evaluated in Scotland or evaluated in both, but that a test was needed seems to be a matter of common opinion right throughout.

A. Correct, yes.

THE CHAIRMAN: The issue that I think Mr Di Rollo was raising was how Dr Cash came to be diverted, as it were, from an initial view that the resources of the Blood Transfusion Service in Glasgow, highly experienced in evaluating tests, shouldn't be used on this occasion but that the matter be left to be pursued by the Department of Health in England, with the Public Health Laboratory Service. I think that's what the real issue is, Dr Scott. Can you not help us with that at all?

A. No, I don't know why they gave up the idea. They did give it up.

THE CHAIRMAN: I think the sequence of documents shows that he adopted a different line after a certain point. Whether that can properly be called "giving it up" may

be an issue.

A. Well, they changed their mind, they weren't going to do it. And I have no recollection of whether advice or pressure was put on from SHHD. I cannot recall that.

THE CHAIRMAN: Of course, if Dr McIntyre can't help us and you can't help us, and Dr Cash is the only source of evidence I have got, then it might be that a certain consequence follows. You understand that?

A. I don't know what Cash would say about why he gave up doing the evaluation.

THE CHAIRMAN: I think we do know what Cash would say as to why he gave up. Anyway, that's as far as I think it's proper for me to take it.

Ms Dunlop, have you any further questions on this?

MS DUNLOP: No, I have no further questions, thank you, sir.

THE CHAIRMAN: Thank you very much Dr Scott.

Right, where do we go now?

MS DUNLOP: Dr McClelland is coming tomorrow morning and we will, I think, be finishing around lunchtime.

THE CHAIRMAN: I certainly hope we are since I have to be at Heriot-Watt University.

MS DUNLOP: Yes.

THE CHAIRMAN: Very well, thank you very much.

(4.10 pm)

(The Inquiry adjourned until 9.30 am the following day)

I N D E X