Tuesday, 15 November 2011

(9.30 am)

DR BRIAN McCLELLAND (continued)

Questions by MR MACKENZIE

THE CHAIRMAN: Good morning. Yes, Mr Mackenzie?

MR MACKENZIE: Good morning, sir. We move on to a new topic today, topic C2, which is the non-introduction in Scotland of surrogate testing for non-A non-B Hepatitis, and our witness today is Dr Brian McClelland.

THE CHAIRMAN: Yes.

MR MACKENZIE: Good morning, Dr McClelland.

A. Good morning.

Q. We don't have to look at your CV again but we know that, I think, between 1979 and 2001 you were director of the Edinburgh and Southeast Scotland Blood Transfusion Service. Is that correct?

A. That's correct.

Q. And I think you retired from the SNBTS in 2009.

A. That's correct.

Q. Could we, please, look at your statement you provided on this topic. It's [PEN0170754] and what I would like to do, doctor, is go through your statement and from time to time ask you various questions and also look at some of the documents you have referred to, plus one or two others as well.

You say in your statement -- your first heading is "Opinions of the importance of non-A non-B post transfusion hepatitis in the UK between 1980-1989".

You say that before considering the particular question we asked you, you thought it may be useful to the Inquiry to provide a personal view on the apparent persistence of the belief over the years 1980 to 1989 that non-A non-B post transfusion hepatitis was not an important problem in the UK. And one of the themes underlying this history is the view that was taken of NANBH in the UK from around 1980 to the discovery of Hepatitis C in 1989:

"Many of the decisions taken or not taken can only be understood in the context of a widely held view that despite an increasing body of evidence to the contrary, this condition was rarely transmitted by blood and was usually not particularly serious."

You say:

"I have tried to assemble some evidence that illustrates how this view may have originated."

We will go on to look at the various papers.

Am I right in thinking, doctor, that the papers you list are largely looking at the prevalence of post-transfusion hepatitis in the UK rather than focusing on the seriousness of the disease?

A. Yes, absolutely.

Q. Looking at these papers in turn, please, the first one you refer to is the Medical Research Council Blood Transfusion Research Committee in 1974. This is the year of publication of a report of a study carried out for the UK MRC of hepatitis in recipients of blood components.

You explain that:

"This study is described in some detail since it is one of only four substantial prospective studies of PTH in the UK."

Can you explain, please, doctor, what does "prospective study" mean and how does that differ perhaps with a predictive study?

A. Well, in broad terms, actually the term is quite widely -- it is used in a variety of senses, but in broad terms it implies a study where you, as it were, define the questions that you are asking and then carry out work in advance, according to a planned schedule, to test the answers to those questions.

The -- the sort of gold standard -- and we will come back to this I'm sure -- of a prospective study is what's called a prospective randomised clinical trial, which is designed in such a way -- it is designed, if it is well designed, to -- to compare at least two groups

of patients, one group who receives a particular form of treatment or intervention, which could be a diagnostic test or anything in principle, and the other group who either is a control group that receives -- does not receive that intervention or treatment or that receives another one, in which case it could be comparing two treatments. Those studies, if properly designed, should see that the groups of patients who are enrolled to the treatment group and the control group, if you like, are randomly selected, and one of the tests that you apply in analysing a study like that is to see that actually the make-up of gender, age, social class, co-morbidities and so on, is very similar between the two groups. There are, you know, a number of very well evolved criteria for -- to determine the quantity of design and execution of the prospective randomised control trial.

At a sort of lower -- below the gold standard, if you like, there are studies which set out to look at what happens in the future when you initiate an action in the present, and those are broadly called "prospective studies", but they don't all by any means tick the -- all the boxes required for a very high quality study.

Q. Yes, and predictive study, what is that?

A. It is not a term I have ever used. I don't really know

what it means.

Q. I see. We might give it some context if we see it in some of the literature we look at over the course of today. That may help.

A. I'm happy to try and do that. I would make the distinction more between a prospective study, which is the sort of characteristics that I have sketched out, and an observational study, which would be essentially looking at what has happened, something that you are already doing and you collect the information about what has been done for a number of years in the past and you then try to draw some inferences about the relationships between one event, for example, the use of a treatment or a test, and another event, which is the development or non-development of an illness in the patient.

But those studies are always very difficult to interpret because of the risk of confounding factors, such as associations between a particular type of patient and the probability of getting a particular treatment, and it's extremely difficult, even with the use of quite complicated statistical techniques -- in fact I would say it's impossible -- to draw conclusions about the cause and effect from these retrospective type of studies.

Q. Yes.

A. But they are very useful for generating hypotheses, for saying it looks as though something is happening because of something else, then you go on to do a properly designed prospective study to test that hypothesis.

Q. Yes. I understand.

Returning, please, to your statement and the MRC study, you explain that:

"From mid 1969 to the end of December 1971, patients at the Central Middlesex Hospital ..."

Participated in giving a pre-transfusion blood sample for ALT and viral studies.

We see that of the 2,184 patients who were transfused during the study period, follow-up was completed on 768 who received an average of 3.7 units of blood per patient.

Over the page of your statement, we see:

"Routine testing of donor blood for Hepatitis B only began during the last five months of the study period:

"Raised ALT values were found after transfusion in 158 patients."

Six of whom underwent liver biopsy:

"None showed histological features typical of acute viral hepatitis."

Then you quote:

"The authors stated that these 158 patients were

investigated for conditions other than viral hepatitis, eg drug induced liver injury. It was arbitrarily decided that where such other potential causes existed, the patient would not be regarded as suffering from viral hepatitis. On this basis, eight patients (1 per cent) were judged to have had post-transfusion hepatitis. Sustained elevation of ALT without other clinical features of hepatitis was present in 35 patients."

You then again quote:

"The authors concluded that 'the overall incidence of icteric and anicteric hepatitis in the present survey (1 per cent) is low compared with the incidence found in prospective studies in Japan (65 per cent) ... USA (18 per cent) ... and Germany (14 per cent).' However if PTH had been defined to include all the patients with ..."

That's the end of quote and you go on to say:

"However, if PTH had been defined to include all the patients with persistently elevated ALT, the PTH rate would have been 35/768 or 4.5 per cent. If PTH had been defined to include patients with any elevation of ALT following transfusion, 158 of the 768 patients (21 per cent) would have been defined as having PTH."

That paragraph perhaps just illustrates the

difficulties at the time, doctor, in trying to accurately conclude the true rate of post-transfusion hepatitis based on elevated ALT levels.

A. Absolutely.

Q. We will come back to the problem of surrogate tests shortly.

You say:

"Although this study preceded the description of NANB hepatitis, it was later cited as making it unnecessary to conduct a further prospective controlled investigation of the impact of surrogate testing for NANBH."

We should perhaps briefly look at the paper. It's [LIT0010116].

If we can go over the page, please, at page 174, about two-thirds of the way down we can see, the objects of the survey were:

"1. To obtain information about the incidence of icteric and anicteric post-transfusion hepatitis:

"2. To establish the frequency of Hepatitis B antigen and the corresponding antibody in blood donors and patients and to try to correlate their presence with blood transfusion and its implications:

"3. To determine the frequency of Epstein-Barr virus and cytomegalovirus by blood transfusion and their

role in causing post-transfusion liver damage."

We can see no reference there and I think indeed in this paper to non-A non-B Hepatitis. Is that correct?

A. Yes.

Q. And that's perhaps not entirely surprising, given, I think, the Prince paper, which mentioned non-A non-B was published in 1974, I think?

A. Yes, and this study was obviously conceived considerably before the publication date of 1974. I think it was the first enrollments were 1969 so as an early study.

Q. And indeed for much of the period, at least for the initial period of the study, there wasn't even testing for Hepatitis B in place.

A. Correct.

Q. So that was perhaps another confounding factor. I think it's also of interest to look at page 180, please.

Before I do that, I should go back two pages to page 178. We can see under "hepatitis patients" the results of this study, and essentially it's as per the quote in your statement, the 158 patients developed raised serum ALT values after transfusion, and it was arbitrarily decided that where such other potential causes existed, the patient would not be regarded as suffering from viral hepatitis and hepatitis either icteric or anicteric was judged to be present in eight

patients, 1 per cent.

If we go to page 180, please, I think we can see some of the difficulties here in trying to rely on elevated ALT as a marker for post-transfusion hepatitis, and that in this passage headed "Other patients showing ALT rises", the authors state:

"The residual 115 patients who showed ALT rises after transfusion were thought not to have viral hepatitis, although liver biopsies showed features akin to hepatitis in five of these. Halothane was accepted as the cause in these five cases."

What's Halothane?

A. Halothane was a very widely used general anaesthetic at that time, which was known to be quite toxic to the liver. And I certainly recall slightly later -- well, no, around about this period in fact, because I was then working in the field of gastoentorology, not blood transfusion, and we barely recall, you know, seeing a significant number of patients who had elevations of liver enzymes following surgery, and one of the -- one of the interpretations, and it was a thing that was discussed widely actually at that time, the early 1970s, was what proportion of these were due to Halothane.

Q. Then returning to the paper, the next paragraph "Drugs or alcohol were accepted as the cause of ALT rises in

nine patients."

Again, presumably drugs or alcohol can cause elevated ALT. It was known at the time, obviously.

A. Yes, essentially the ALT, that is protein released from liver cells, when they are damaged, by anything.

Q. Returning to the paper, the authors state:

"Acceptable reasons for ALT rises were present in 27 patients ..."

Et cetera.

Then:

"50 patients showed ALT rises two weeks after transfusion. In many, the value had returned to normal a week later ..."

Et cetera.

Then:

"All but five of these patients had been recently operated upon and the ALT rises may have been the non-specific effect of the surgical procedure."

So is that another possible cause for elevated ALT?

A. It's well -- there are numerous observations that just coming into hospital increases an individual's risk of having ALT elevations. Having surgery, which always involves having multiple drug, anaesthetic agents, et cetera, also increases the risk of having elevated ALT. It's a very non-specific marker.

Q. In the final paragraph there:

"The remaining 21 ALT rises occurred at longer intervals after transfusion; these too had returned to normal again within one week."

The point in short, doctor, looking at that, is it perhaps illustrates the difficulties of using ALT as an indicator for post-transfusion hepatitis and also perhaps illustrates the difficulties in relying on this paper as an accurate estimate of the prevalence of PTH in the UK at that time. Does that seem reasonable?

A. It was the latter point really was the one that -- was why I chose to cite it, because it was the only study for a long time and it was used -- and I think possibly slightly misused -- the interpretation of the data was used to say the incidence of non-A non-B Hepatitis is very low, and I think that went -- that's not actually consistent with possible interpretations of the results in this paper.

Q. Yes. You, of course, in paragraph 1.4 of your statement refer to the different ways in which the data can be interpreted.

A. Yes.

Q. Moving on, please, to the next paragraph in your statement, paragraph 1.6, you refer to another study by Collins and others reported in 1983, and we will come to

the paper shortly, but you explain:

"In 1983 a UK study of 248 transfused cardiac surgery patients reported that 38 of the 248 patients (15.3 per cent) had some elevation of ALT during the five to 30 days following the operation.

"The increase in transaminase levels was unexplained and reached over 100 international units per millilitre in six patients, all of whom had normal liver function tests when retested at six months. One patient had evidence of chronic persistent hepatitis six months after surgery and transfusion."

And the authors stated, and you quote:

"We conclude that non-A non-B Hepatitis after blood transfusion from a largely British blood donor group probably leads to clinically significant chronic liver disease very rarely indeed."

If can we go to the paper, please, it's [LIT0010212]. We can see from the abstract, I think, picking up in the third sentence:

"During five to 30 days after operation 38 of the patients showed an increase in serum transaminase activities. There was no serological evidence for fresh infection by Hepatitis A or B virus cytomegalovirus, Epstein-Barr virus or herpes virus in any of these patients. The increase in transaminase activities was

unexplained and reached over 100 IU against a normal of less than 40 IU in six patients. The incidence of acute short incubation post transfusion non-A non-B Hepatitis was therefore thought to be 2.4 per cent. These six patients had normal liver function six months after transfusion but a further two of the surviving 228 patients had raised serum transaminase activities at six months. In one of these, liver biopsy disclosed chronic persistent hepatitis; in the other, alcoholic liver disease was suspected. The incidence of significant chronic liver disease after blood transfusion possibly attributable to a non-A non-B Hepatitis agent was therefore only 0.4 per cent."

I think that percentage is one from 248, which presumably is the patient in which liver biopsy disclosed chronic persistent hepatitis.

So that's that paper and returning to your statement, please.

THE CHAIRMAN: You might think that at least one of the contributors to the paper may have changed his mind over time, doctor?

A. All I would say is that the interpretation of the observations in that study was entirely consistent, I think, with the understanding of this condition at the time. In the preliminary report there are very useful

excerpts from Professor Sheila Sherlock's book, Dame Sheila Sherlock's book, which was the sort of British bible of hepatology, and I haven't actually checked them up but I'm sure that the interpretation placed on the Newcastle study findings, which you have just gone through, would have been entirely consistent with the received knowledge and beliefs about non-A non-B Hepatitis, if it had been invented by then, about the significance of ALT liver enzyme elevations after surgery and so on. I think the interpretation is not open really to challenge.

THE CHAIRMAN: Yes.

A. It was the forward projection of these interpretations that I was concerned about.

MR MACKENZIE: And what do you mean by that?

A. Well, the fact there were -- and the others, we will come back to this, but these are studies which were interpreted at the time very reasonably, the findings were interpreted very reasonably as saying non-A non-B Hepatitis following transfusion isn't a problem, and that belief tended to persist despite the fact that more evidence was emerging that it probably was a problem. That's all I'm trying to say.

Q. I suppose when you say it's not a problem, there may be two elements to that, firstly, prevalence and, secondly,

seriousness of the disease?

A. Yes.

Q. Yes. Returning to your statement, please, the top of page 3, paragraph 1.7, you refer to a report by Vandervelde and Mortimer, I think of the Public Health Laboratory Service in England, and you say that:

"At the meeting of the BTS Directors Working Party on Transfusion Associated Hepatitis on 24 November 1986 a report was presented by two workers from the PHLS on an epidemiological study of non-A non-B Hepatitis in the UK. This extract gives a rather vivid view of the confusion surrounding non-A non-B Hepatitis and its relationship to blood. As late as the end of 1986 a doctor ..."

In paragraph 1.8 you give a quote from that paper but I wonder whether we have to be a little cautious with this paper, because if we can go to it, please, it's [PEN0171531]. We can see, top right-hand corner "Not to be published", and we see the handwriting:

"Presented to UK Working Party on Transfusion Associated Hepatitis on 24 November 1986".

Is that your writing doctor?

A. Yes.

Q. Would you have written that at the time or more recently?

A. It's probably at the time, because when I have annotated anything since the beginning preparations for the Inquiry, I have dated the annotations just to make a clear distinction.

Q. Do you have any recollection of that paper being presented to or discussed at this working party meeting?

A. I don't remember. I have a vague recollection of discussing the study with, it was Dr Janet Mortimer, not Philip Mortimer. When it was being done. I don't recall the meeting when it was presented but my habit was to, you know, if it wasn't indicated, to write on a paper that was discussed at a meeting. So I think it must have been discussed and I must have been there. I don't remember.

Q. I can quite understand the paper was presented at that meeting, but I wonder whether it was drafted much earlier than that.

If we look at paragraph 2, we see:

"The study ran from September 1978 to December 1980."

So one would have thought the authors would write the paper shortly after the study had ended.

A. I would think so, yeah.

Q. If we go to the second last page, please, and look at the references, if we have a quick look through the

references, I think we will see the latest reference is 1981, which I wonder, is that another perhaps clue or indicator that the paper is likely to have been drafted perhaps in late 1981 or early 1982, possibly?

A. That's entirely possible. I have no knowledge now of that. I included it because it was obviously felt we were presenting this information to that working party in 1986. It was another -- it's an example of the fact that there was still a lot of diverging thoughts and opinions about the main origin of non-A non-B Hepatitis. That was the only reason for including it.

Q. It's also perhaps -- well, am I right in thinking that we should at least be cautious as to when it was drafted, in that it appears as though it was drafted about 1981?

A. That's a perfectly reasonable deduction.

Q. Yes, albeit it was presented to the November 1986 meeting. And I think as well, it's not a paper restricted to post-transfusion hepatitis; rather it's hepatitis in the community more generally, I think. Is that right?

A. Absolutely. Oh yes, absolutely.

Q. So put that paper to one side, please, and return to your statement.

Paragraph 1.9 you then refer to -- this is the

fourth of the four papers, you mentioned a paper by Contreras and others published in 1991. The full title is "Low incidence of non-A non-B PTH in London confirmed by Hepatitis C serology."

So this papers, I think, comes out after the Hepatitis C test is available and in use. Just for completeness the reference is [LIT0010318].

I won't go to it, doctor, but I think you say you set out in your statement the relevant parts of the paper.

You say:

"A prospective study was carried out by the North London Blood Transfusion Service, enrolling patients over the period July 1986 to July 1989. The authors noted that 'London has the highest incidence of infectious markers in the donor population in the UK: the results of this study would therefore represent the worst case'."

The report covered 387 surgical patients:

"... who received 1,176 blood components from a mean of three donors. Regular blood samples were obtained from the blood recipients over a period of six months with a final sample at 12 months. Three patients had increased ALT levels 'consistent with post-transfusion NANBH'. One patient had clear evidence of transmission

of Hepatitis C. One of the eight blood donations received by this patient was also Hepatitis C-positive. The ALT level in this donation was normal but anti-HBc was present. The report presents no data on routine surrogate tests on the donations but it would appear from the evidence presented that the single episode of Hepatitis C transmission would not have been avoided as a result of ALT screening but would have been avoided by screening for anti-HBc."

You then quote from the authors in relation to Hepatitis C.

That paper is perhaps a little after our period, doctor, which I think is more really the 1980s up until roughly 1989 perhaps. Whereas this paper isn't, I think, published until at least 1991 and has the added benefit of being able to use Hepatitis C tests at that stage.

A. Yes, I included it because the enrollment was within the sort of period which I think is relevant, and it is one of the very few studies that had -- could have had the potential to give us some of the information that we needed, but it was a prospective study.

Q. And, of course, an important point to note, I think, in these papers is that recipients of blood donations were followed up in the studies, whereas when we come in due

course to look at the UK multi-centre study on surrogate testing, that was restricted to donors.

A. Exactly, yes.

Q. We will come on to all of that.

Then we are now at page 4 of your statement, please. In paragraph 1.10 you refer to an abstract you submitted for the 18th Congress of the International Society of Blood Transfusion in 1984, which indicates that you also were of the view that:

"'Clinically apparent NANB post-transfusion hepatitis was also a small problem', that the importance of elevated liver enzymes as an indicator of NANB PTH was uncertain and that for the recipient of blood or single donor components the benefits of improved donor testing were not quantifiable."

Could we perhaps briefly look at that? It's [SNB0086696].

Over the page, please. It's a little hard to read. It's very small writing. I'm sure we can blow it up.

In the first paragraph I think we can see you stated:

"In a non-remunerated donor system which employs third generation Hepatitis B tests, Hepatitis B following transfusion of fresh single donor blood and blood components is extremely rare. Clinically apparent

non-A non-B post-transfusion hepatitis is also a small problem. Although a few transfused patients develop asymptomatic elevations of liver enzymes the importance of this remains undefined. Thus for the recipient of blood or single donor components, the benefits of improved donor testing are not quantifiable."

When you stated, doctor, that "clinically apparent non-A non-B post-transfusion hepatitis is also a small problem," did you mean "problem" in the sense of low prevalence, not serious, or both?

A. I'm sure what -- I mean, I honestly can't remember, and unfortunately I haven't -- I didn't retain either the slides or any speaking notes of this talk, so I don't know what I actually said. But what I undoubtedly meant then was that there were very few reported cases and -- of jaundice, you know, the disease hepatitis presenting clinically as a result of non-A non-B hepatitis presented clinically following transfusion, and that was precisely the experience, of course, of Dr -- in Dr Dow's study that we found, I think; 20 cases of something over eight years that were actually reported as clinical non-A non-B Hepatitis.

So I think the statement remains correct. At the time, the statement about the significance of asymptomatic elevations of liver enzymes was still at

that time, I think, probably fairly accurate in saying it was still uncertain, undefined.

Q. Thank you. Now, returning to your statement, please, in paragraph 1.11 you summarise that:

"The authors of clinical studies mentioned above seem generally to have considered that the 0.4 per cent to 1.0 per cent incidence of post-transfusion hepatitis that they reported in the UK was very low in comparison to rates reported from other countries. It is also likely that because there are many causes of elevated liver enzymes (ALT), some cases that were in fact due to infectious hepatitis could be explained by evidence of another cause such as alcohol intake. The PHLS study..."

Which is the 1986 paper which I cautioned about:

"... illustrates how at least in some circles there was a view that non-A non-B hepatitis was rarely transmitted by the parenteral route."

Was that a view you would have held in 1986?

A. No.

Q. We have perhaps also to take into account in that regard that the reports from really, I think, starting in 1982 but then perhaps published in 1983/1984 that almost all haemophilia patients who received Factor VIII concentrates for the first time developed NANBH

regardless of whether the concentrates were commercial or voluntary NHS concentrates. So, again, that presumably would be fairly convincing evidence that NANBH was transmitted by the parenteral route.

A. Yes.

Q. To pause at this stage, we have looked a little at the studies into the prevalence of NANBH in the UK. Could we perhaps look at some of the literature regarding the seriousness of this disease? Before I do that, could you perhaps indicate just in general terms your understanding of how serious NANBH was regarded in the 1980s, perhaps starting at the beginning, taking us to the middle and then taking us to the end of that decade, just in general terms?

A. That's a very difficult question to answer in any useful way. I think all that I could say was that over that period, from the beginning of the 1980s to the end of the 1980s, you know, I would have been aware of a growing body of evidence that in some cases the disease characterised by transient and fluctuating elevations of liver enzymes could in some cases progress to serious and possibly life-threatening liver disease. I think over that decade very far and away the bulk of that understanding would have been derived from what was happening in the haemophilia community, which were the

most -- obviously the most intensively exposed, we now know in retrospective would have been at high risk of being exposed to several different genotypes of the virus and, therefore, would be the group in whom severe liver disease would I think -- common sense would have told one that was the group that was most likely to develop severe liver disease.

I honestly cannot recall whether in that decade I was aware of severe progressive liver disease leading to cirrhosis occurring in recipients of blood components derived from, you know, small or relatively small number of individual donors.

Q. Thank you. I think what I would like to do now, doctor, is to turn to some of the particular items of literature and see if they generally represent what would have been the understanding at the time, and you have mentioned Dame Sherlock's book. We should perhaps start with that, the 1981 edition. It's [LIT0012431].

This is chapter 9 of your preliminary report, which contains an extract, in particular it's at page 2453.

THE CHAIRMAN: Which edition is this, Mr Mackenzie?

MR MACKENZIE: This is the 1981, sixth edition.

In paragraph 6.110 there is a reference to Professor Sherlock's book, and the end of this paragraph states:

"In terms of the clinical course of the disease it indicated that a 'mild chronic hepatitis' develops in about a quarter of patients but this usually improved with time although cirrhosis could develop."

Then over the page to the next paragraph, please, paragraph 6.114, the final quote where Professor Sherlock stated:

"Non-A non-B Hepatitis often progresses to a mild chronic hepatitis. The prognosis of this is, at the moment, uncertain but probably benign."

Then the next publication, please, is Professor Mollison's book in 1983, the seventh edition, and it's [PEN0171734].

Doctor, was this the standard textbook on blood transfusion in the UK at the time?

A. Yes.

Q. Were there any other textbooks on blood transfusion at the time?

A. Sorry, what date was this?

Q. This is a January 1983, seventh edition.

A. There certainly wasn't another major textbook, UK textbook in 1983 that I can recall.

Q. Yes. Then over the page, please. The author states under "Non-A non-B Hepatitis":

"This rather clumsy term is used to describe

hepatitis in which both HAV and HBV have been excluded. The term Hepatitis C is not used because there is evidence that there is more than one kind of non-A non-B virus and because no specific tests have yet been developed. The mode of transmission of non-A non-B Hepatitis may sometimes be similar to that of Hepatitis B. Non-A non-B Hepatitis is prevalent following transfusion or other percutaneous exposure; it is commoner in populations of low socio-economic status and is probably spread by close person to person contact; it is associated with a chronic carrier state."

What was meant by that, a chronic carrier state?

A. I think that would have been considered to be an analogy with the -- what happens, for example, with Hepatitis B, which is that some patients who become infected with the virus continue to have the virus in their blood for long periods. Even though their body may make some form of immune response, that does not successfully remove the virus from the blood, so there is a risk that the blood may be infectious, even during a period when the individual is showing no clinical signs or symptoms of the disease associated with that virus.

Q. Thank you. Returning to the passage:

"Non-A non-B PTH has a slightly shorter incubation period than Hepatitis B, ie between six and ten weeks

with a peak of about eight weeks ... As a rule non-A non-B Hepatitis is symptomatically mild. Patients seldom need to be admitted to hospital, nevertheless up to 60 per cent of cases have abnormal alanine aminotransferase (ALT) (previously called SGPT) levels for more than one year. If a liver biopsy is taken, most of the cases show histological evidence of a significant chronic liver disease and approximately 10 per cent show features of cirrhosis (Alter, 1980). A striking feature in non-A non-B Hepatitis is the tendency for serum hepatic enzyme levels to fluctuate markedly over a relatively short time. Although typical non-A non-B Hepatitis differs in several respects from typical B hepatitis, there is a substantial overlap and the two forms cannot be differentiated solely on clinical grounds."

A reference -- the paragraph at the bottom of the page -- to the Aach study in 1981, which I'll come back to in your statement in due course, about the possible use of ALT as a surrogate test for screening donors for non-A non-B Hepatitis.

Then over the page, please, at page 774, under "Frequency of post-transfusion hepatitis", the author states:

"Anicteric cases of PTH are commoner than icteric

cases."

Does that mean in short, doctor, that jaundice is unlikely in post-transfusion hepatitis cases, as at this time, anyway?

A. I think the majority of cases did not go yellow.

Q. Yes:

"For example, in a study reported from the USA in which 2,204 patients were followed and in which PTH was diagnosed in 241 patients, the disease was icteric in less than one-fifth of the cases. It follows that repeated sampling of recipients is necessary if all cases are to be detected and that only prospective studies are likely to give a true indication of the frequency of PTH."

A reference to studies reviewed in America, I think. The final paragraph:

"In the UK no prospective survey, carried out exclusively with HBsAg negative blood has been reported. Nevertheless there is evidence that non-A non-B viruses play a smaller part in the UK than in the USA."

Et cetera.

There is a reference to Dane personal communication. Who is Dr Dane?

A. Dr David Dane was virologist of the Middlesex Hospital -- I can't tell you exactly what dates -- but

he was eminent -- the research for which he was most famous in relation to Hepatitis B, and he actually discovered -- he was one of the first people to visualise the virus in the blood by electronmicroscopy, and that observation led to it being called the Dane particle. He was a mentor of virological testing group, which one of his students was Dr Richard Tedder, whose name has featured quite prominently in the Inquiry.

Q. Just looking at the passages we have read from Professor Mollison's publication in 1983, do these passages reasonably set out what would have been the knowledge of a transfusionist about non-A non-B post-transfusion hepatitis at the time?

A. I think very reasonably, yes. And this is what most people would have read.

Q. Now, the next publication, please, may we go to is over to America, Harvey Alter in 1985. It's [LIT0010811].

This is a chapter in a textbook, I think, "Post-transfusion hepatitis clinical features, risk and donor testing". Really again just sticking at the passages, looking at the state of knowledge as to the seriousness of the disease, if we go to page 49, please, it's 0813 -- and under "NANB clinical significance" -- I won't read out what's stated but I think much of what's set out chimes with what Mollison had set out.

The top of the next page, please, we see in the second line:

"Very characteristic of NANB is the fact that these ALT elevations tend to fluctuate considerably."

Then the paragraph beginning:

"Because of the asymptomatic nature of chronic NANB hepatitis, the clinical significance of chronic ALT elevations in these patients has been questioned. Although NANB hepatitis is indeed generally a clinically benign disease, there is accumulating evidence that some cases progress to severe chronic liver disease."

There is then reference to various studies, which I won't read out, but over the page, please, page 51, about ten lines down, there is reference to the Realdi study in Italy, reported in 1982, and then Alter picks up a "composite of existing data suggests that at least 10 per cent of patients that develop chronic ALT elevations following acute PTH will progress to cirrhosis. However, this estimate is based on a very small sampling of biopsied blood recipients and must be reaffirmed by continuous prospective follow-up of patients developing chronic hepatitis following blood transfusion. If these findings are validated, then the clinical implications of NANB are somewhat greater than previously anticipated."

A. May I just say, though, that I think there is -- buried in the first paragraph there is a very important line:

"... since the selection of patients for biopsy is not random but skewed to those with the most severe biochemical or clinical abnormal amounts."

So any study -- liver biopsy is not a benign procedure.

If you think about it for a moment, having a large needle stuck into your liver is not pleasant and not entirely safe. Particularly at this time was not entirely safe. So it would be ethical to restrict the procedure only to patients in whom there was really material, other evidence that their disease was actually quite severe.

So any study that's based -- any inferences drawn from liver biopsy studies includes a very large element of bias. And the preliminary report it does mention some very important population-based studies in which actually looking at large populations of patients who have been exposed to non-A non-B Hepatitis over very long periods, one gets a very different picture of the severity of the disease. So the element of selection I think one should never forget.

Q. I understand that, doctor, although I suppose at least for that category of patients who had the most severe

biochemical or clinical abnormalities, the biopsy results were beginning to suggest that NANBH may be a more serious disease than previously thought?

A. Absolutely.

Q. But the question perhaps was whether those biopsy results were truly representative of all patients who suffered continuing elevated, fluctuating ALT levels.

A. Yes, exactly.

Q. Yes. The next item of literature please, again, sticking with Alter but one year later, 1986, is [LIT0011675].

This is a publication by Dienstag and Alter, "Non-A non-B Hepatitis, evolving epidemiologic and clinical perspective", published in 1986 in "Seminars on liver disease".

If we could go to page 71, which is 1679, the right-hand column under "Chronic NANB hepatitis", I wonder whether we see a slight hardening in the view of Alter. He states:

"In the decade since its discovery the concept of NANB hepatitis has evolved from that of a benign elevation of aminotransferase activity to that of a serious disease with significant long-term consequences. The longer patients are followed the more obvious it becomes that CAH ..."

Is that chronic active hepatitis?

A. Yes.

Q. "... and cirrhosis are a very real part of the natural history of NANB hepatitis."

Over to page 72, please. In the left-hand column, about half way down, after considering the various studies of biopsies, the authors stated:

"These studies demonstrate that the histologic pattern in patients with non-A non-B Hepatitis who are selected by biopsy ..."

That's the point you made:

"... connotes a more serious outcome than is suggested by either the amplitude of the ALT elevations or the severity of symptoms. Note has been made of the fact that generally the CAH and NANB hepatitis is not extensive and that the diagnosis is subject to the variability of histologic interpretation. Nonetheless, the diagnosis of cirrhosis is histologically unequivocal and the frequency with which it occurs suggests that the CAH observed is not a benign or static lesion; indeed it can progress to cirrhosis in a substantial proportion of cases. Such progression has been well documented by serial liver biopsies."

Then towards the bottom of the left-hand column it's stated:

"Progression to severe symptomatology may be very protracted taking 14 to 18 years in two patients analysed retrospectively in the NIH series. Because the maximum prospective evaluation time for chronic non-A non-B Hepatitis is now only ten years, we may find increasing non-A non-B Hepatitis related morbidity and mortality occurring in the patient population over the next decade and beyond."

Then sticking with the right-hand column, towards the bottom, commencing:

"Thus one decade ..."

The authors make various predictions based on the evidence available.

At the end of that paragraph they say:

"The accuracy of such a prediction remains to be substantiated. Prospective evaluation of newly developing NANB hepatitis cases and continued long-term follow-up of existing cases is essential to define more precisely the chronic consequences of NANB hepatitis."

I think I'll leave that paper there, please, and then come back to Britain and to Professor Mollison again. This is in his eighth edition textbook in 1987, which we find in the preliminary report. It's [LIT0012543].

We see that paragraph 9.40 of the preliminary

report:

"In 1987 the eighth edition of the standard UK textbook on blood transfusion was published ..."

By Professor Mollison.

Then over the page, please, paragraph 9.41. We can see the quote at the top of the page. The quote was that:

"NANB PTH is usually mild and asymptomatic during the acute phase ... However, prospective studies in the USA have shown that the chronic sequelae of NANB PTH may be serious. Over 50 per cent of patients develop chronic hepatitis as judged by persisting or fluctuating rises in ALT levels lasting for at least one year after onset of the disease and in most for more than three years ... although the chronic phase of NANB PTH, like the acute phase, tends to be mild, some patients develop severe chronic liver disease and 10 per cent of these patients progress to cirrhosis, which is generally milder than alcoholic cirrhosis."

In the next paragraph:

"It was noted that the available data was based on biopsy in very small numbers of patients."

Finally, just to complete the decade, if we can go back to Professor Sherlock please. This is at paragraph 9.104 of the preliminary report. It's page 28

of [LIT0012543]. This is the seventh edition of Professor Sherlock's textbook, published in 1989.

We can see the quote:

"The causative agent of NANBH has not hitherto been identified, although a viral genomic clone has been isolated from infected plasma and liver ..."

That's perhaps a reference to the Chiron discovery, I think, which we will hear about in the next topic.

The next paragraph, 9.105:

"As regards the clinical picture of the disease [they state that] 60 per cent of patients will have raised serum transaminase one year later. In 68 per cent of the disease becomes chronic and in 20 per cent cirrhosis develops. Hepatocellular carcinoma ... is a rare complication."

Then later the authors stated:

"[Prognosis] is very variable. In some the diseases are benign with spontaneous biochemical improvement over one to three years. In others, chronic persistent hepatitis and chronic active hepatitis can convert to more serious disease and even go on to cirrhosis. In general, however, in spite of biochemical disease the patient is asymptomatic and the development of hepatic failure is rare. Hepatocellular cancer has been recorded but is exceedingly rare."

Doctor, that completes my review of the literature. Do you think that's a reasonable portrayal of the state of knowledge of the seriousness of non-A non-B Hepatitis in the 80s?

A. I think that's very fair.

Q. Thank you. Returning to your statement, please, we are about to go back to America and their studies into surrogate testing. I think we had reached page 4 and your subheading "Surrogate testing as a means of reducing the risk of transfusion transmitted hepatitis".

You explain that:

"Much of the early information comes from the United States, whereby as early as the 1940s it was recognised that patients often developed jaundice after blood transfusion."

You explain what jaundice is, that it's a manifestation of liver disease:

"A subset of liver disease, hepatitis, is inflammation of the liver. It may occur with or without jaundice."

In paragraph 2.2:

"Understanding of hepatitis grew as better tests were developed ... In 1955 tests were introduced that detected raised levels of enzymes in the blood that are released from liver cells. There are many causes of

increased levels of liver enzymes in the blood; they include damage to liver cells caused by, eg alcohol, drugs, including some anaesthetics and antibiotics in association with obesity or as a result of an infection."

I think some of the other causes we looked at in the MRC study report.

Over the page, please, paragraph 2.3 you explain that:

"A commonly used liver function test is based on measurement of the concentration of the ALT which is present in normal liver cells and is released when liver cells are damaged. It is important to say that tests like ALT were developed to help diagnosis of patients. They were not developed for screening populations of healthy individuals."

Paragraph 2.4, we can see what you say there.

Paragraph 2.5 you explain:

"The term surrogate has come to be used in the context of NANB PTH to denote a test that may be applied to blood donors or donations and that detects a property that indicates the presence of some form of transmissible hepatitis, presumed to be due to the transfer of an infectious agent."

In the next paragraph you explain:

"In the United States, the transfusion-transmitted viruses (TTV) study was started in 1974 and collected samples from transfused patients and from blood donors up to 1979. An interim report in 1978 indicated that transfusion hepatitis (diagnosed by the presence of elevated ALT levels) occurred in 12.6 per cent of transfused patients and 2.6 per cent of control non-transfused hospital patients. Of the patients who received only volunteer donor blood, 7.5 per cent developed PTH, whereas 43 per cent of those who received only paid donor blood developed PTH."

You go on to say:

"Analysis of information about the donors' blood revealed that the risk of PTH in the recipient was associated with the level of ALT in the donated blood. Where the donor ALT was normal, the attack infection rate for PTH was 3.4 per cent. Where the ALT level in the blood was elevated, the infection rate was 43.3 per cent."

We should perhaps pause briefly to look at this 1978 report. It's [PEN0170870]. I think it's set out in the first page, the objectives of the study. There were four in total.

Firstly:

"To determine in a prospective fashion the incidence

and aetiologies of transfusion associated hepatitis at different medical centres and relate these to different blood donor populations."

Secondly, we can see for ourselves.

Thirdly:

"To establish a bank of well pedigreed serum samples..."

Fourthly:

"To evaluate the effectiveness of present methods of donor screening ..."

Just for interest, I think we can see the next paragraph, the four participating centres, initially at Los Angeles, St Louis, Missouri, Houston Texas, and then later on the study in January 1976, the New York Blood Centre joined the study. That gives us a little background.

Over the page, please, we can see the diagnosis of PTH used. This is at page 384, about half way down in the paragraph commencing:

"All participating centres ..."

About six lines down from that towards the right, the sentence commencing:

"The upper limit of normal was considered to be 45 international units, a value two standard deviations above the geometric mean."

Then the next paragraph:

"The diagnosis of hepatitis was made if within 14 to 180 days after transfusion, or surgery for the control group, two sequential ALT levels greater than 45 IU were observed in the absence of other probable causes. These abnormal samples had to be drawn three to 17 days apart with at least one sample equal to or greater than 90IU two times the upper limits of normal."

If we could then, please, go to page 388, which is 0875, we should look, I think, at the source of blood. I think one often sees the comment, "Well, in America, of course, they were using paid donors and that's different to here", but I think we can see in this study, under "Relation of post-transfusion hepatitis to the source of blood", it's stated:

"Blood from volunteer donors was used exclusively in St Louis and in New York. Whereas both commercial paid donors as well as volunteer donors ..."

Was used at Los Angeles.

Then:

Baylor Houston, "donor units collected by a hospital blood bank, usually family or friends of hospitalised patients ..."

Were used.

So certainly paid donors used at Los Angeles but not

seemingly, I think, at the other centres.

Then, please, page 395. 0882. This is under the discussion part of the paper.

The paragraph commencing:

"Since the TTV study is an ongoing effort, our sample size will continue to grow. Although our study suggests that screening donor units for ALT levels might be useful in reducing the incidence of non-A non-B post-transfusion hepatitis, the data must be interpreted with caution since the number of patients analysed to date is small. Also, there are a number of causes for an elevated ALT other than viral hepatitis, one possible reason why 41 of the 75 patients given blood with an abnormal ALT level did not develop evidence of hepatitis in serial follow-up. Furthermore, 30 of the 65 non-A non-B cases received blood with normal ALT values."

Then, finally, the very last line on the page, the authors state:

"Screening volunteer donor units for ALT may be useful in reducing the incidence of hepatitis although further study is warranted."

Doctor, was this study to do with the first report suggesting that ALT screening of donors may be useful in seeking to reduce the incidence of post-transfusion non-A non-B Hepatitis?

A. It certainly was the first work that I became aware of very -- around about the time I was appointed to BTS actually, appointed as a consultant, and I actually remember obtaining this paper, which is taken from a published conference proceedings, I think, from Dr Aaron Kellner at that time in 1978, I think.

Q. Did that spark an interest in you?

A. That was really what triggered my interest in it, yes.

Q. What was your reaction to that paper?

A. Well, all I can say is what I did, what is documented that I did in reaction to it, which was this was the sort of basis of this and subsequent discussions with people in the New York Blood Centre and others involved in the study led me to propose that we should actually do what is suggested here in the UK and try to set up the prospective study based on the sort of model and techniques that had already been developed in the United States.

Q. Why did you think that should be done here?

A. Well, because we had no data. We had really no useful data about the UK to compare the incidence of -- however we defined it, the incidence of non-A non-B Hepatitis in blood recipients, apart from the early studies that we have already been through this morning, all we had was the data from the United States, which was, you know,

considerably more recent and nothing at all really in which -- a belief that non-A non-B Hepatitis was much rarer in the UK but no serious factual evidence on which to base our policy.

Q. Sir, I'm about to move on to another paper. I could carry on or I could --

THE CHAIRMAN: That would be a good time.

(11.02 am)

(Short break)

(11.20 am)

THE CHAIRMAN: Yes, Mr Mackenzie.

MR MACKENZIE: Thank you, sir. Dr McClelland, we had looked before the break at the 1978 report from America. If we go back to your statement, please, paragraph 2.7. We then, I think, see that in 1981 the same group in America issued a report which confirmed and extended their findings and led the authors to conclude:

"That ALT testing was a potentially useful method of screening donors to reduce incidence of non-A non-B Hepatitis. The observations in this report suggest that about 40 per cent of the cases of non-A non-B post-transfusion hepatitis in this study could have been prevented by discarding units with an ALT level in the upper 3 per cent of the distribution."

We should perhaps again briefly look at that report.

It's [LIT0010753].

On the next page, please, page 990, if we can note in passing the source of the donors, in the right-hand column, under "Characteristics of donors and recipients", we see again that the blood from St Louis and New York was obtained from volunteers, and between 1974 and 1976 the hospital in Los Angeles acquired most of its blood from a similar population but some units were also obtained from three commercial collection agencies that depended on paid donors. And at Houston blood was obtained from volunteers.

On, please, to page 993. This is the authors' discussion in the left-hand column, the second paragraph commencing:

"We also conclude, on the basis of the results in this study that ALT testing in a potentially useful method of screening donors to reduce the incidence of non-A non-B Hepatitis."

Then sticking with the left-hand column, second last paragraph, the authors state:

"The benefits of initiating ALT screening must be carefully weighed against the number of potential donors that would be excluded, the overall incidence of hepatitis in recipients and the severity of the disease. Although non-A non-B post-transfusion hepatitis is most

often subclinical, approximately 20 to 40 per cent of patients who contract this disease are asymptomatic. At least 25 per cent of all affected patients have amino transaminase elevations lasting longer than six months ... The development of chronic hepatitis and progression to cirrhosis have been observed, although the precise frequency of these complications is uncertain.

"Other considerations must be taken into account if widespread ALT testing of blood donors is to be initiated. These include the uncertainty about how long to defer a donor whose blood was rejected ..."

Et cetera:

"Advising donors of the implications of the ALT level would also pose a special problem. In addition, adjustments might have to be made for the observed differences between ALT levels in male and female donors and for the ages of donors. Nonetheless, it appears from this study that screening donor blood to eliminate units with elevated ALT levels would result in a substantial reduction in non-A non-B post-transfusion hepatitis.

"Although ALT screening lacks the sensitivity to detect all infectious units and lacks the specificity to detect only infectious units, the high correlation

between an elevated ALT level and infectivity of transfused blood provides a compelling argument that such screening should be instituted."

Et cetera.

I take it, doctor, you would have been aware of that report when that came out?

A. Yes.

Q. Returning to your statement, please, we are then on to page 6.

You then tell us about another surrogate test which came along, namely antibody to the Hepatitis B virus core antigen. In paragraph 2.8 you explain:

"The use of a test for antibody to the Hepatitis B virus core antigen (anti-HBc) also emerged as an alternative or complementary approach to surrogate testing. In 1984, the TTV study group reported that the presence of anti-HBc in donor blood was also associated with a rate of non-A non-B Hepatitis in the recipients."

The reference for that, without going to it, is Stevens and others, 1984. Our reference [LIT00013755].

You go on to state, doctor:

"A parallel study published in 1986 reported that 'of 193 recipients of blood positive for antibody to the Hepatitis B core antigen ... 23 (11.9 per cent) developed NANB PTH compared with 12 (ie 4.2 per cent) of

288 recipients of only anti-HBc negative blood.' Both these studies concluded that an elevated ALT value and the presence of anti-HBc acted independently on the attack rate for PTH."

I think in short, doctor, either it was known at that time or came to be known that the two different types of surrogate testing, ALT and anti-HBc, seemed to identify two different groups of donors.

A. That was the conclusion from this study, and I think later on I'm sure we will refer to a study carried out much more recently in Scotland by Dr Jack Gillon and colleagues, and they found exactly the same thing that these were really independent -- they existed in two populations of donors and both appeared to independently have some association with the risk of PTH in the recipient.

Q. Another paper I should perhaps refer to for completeness, we looked at the TTVS papers 1970 and 1981 on ALT testing, and I think Harvey Alter at the National Institute of Health in the US had their own prospective study on ALT as a surrogate marker for post-transfusion hepatitis.

If we go to that report, please, it's [LIT0011817]. This is Alter's report in 1981 and just reading the abstract it's stated -- I won't read it but in short,

I think, Alter's group also found an association between elevated ALT levels in donors and an increased risk of recipients contracting post-transfusion non-A non-B Hepatitis. Is that correct?

A. Yes.

Q. Again looking at the source, blood, in the middle paragraph, we can see just on our screens:

"Blood donors were all volunteers in the NIH study."

We should also, perhaps just for completeness, see in the right-hand column at the top "The criteria for diagnosis of post-transfusion hepatitis" used in this study. I think similar but a little different to the TTVS:

"In this study hepatitis was diagnosed when between two and 26 weeks after transfusion a patient with a normal pre-operative ALT level demonstrated a rise in the level of ALT to 2.5 times upper limit of normal, ie 110IU, followed one or more weeks later by an elevation at least two times upper limit of normal, ie 88IU."

Perhaps interesting to look at the author's comment at the end of the paper, the very last page, please, page 634, our reference 1821. In the middle column, please, at the bottom, the authors state:

"For the blood recipient the ALT test offers new hope for hepatitis prevention. For the donor it offers

new information but perhaps information that is not really desired. For the blood supplier it increases the complexity and cost of blood delivery and reduces the available amount of a product already in critically short supply. ALT testing of donors is thus in a tenuous balance between risk and benefit. The balance shifts towards testing when one considers that approximately 30 per cent of PTH might be prevented but this is tempered by the realisation that 70 per cent will not be prevented and that even the prevention of 30 per cent is in some doubt unless confirmed by randomised clinical trial. The balance also shifts away from testing when one considers the estimated additional cost and the potential loss of donors. It is a difficult equation whose solution will require thought and planning."

So that was the view of the authors in 1981.

Presumably, would that also have been your view in 1981 as well, that a proper trial was required rather than a rush to introduce surrogate testing?

A. Yes, absolutely.

Q. Returning to your paper, please, doctor -- your statement, rather, at page 6, if I may, in paragraph 2.9, picking up again anti-HBc as the test you state that:

"The observed association between an antibody to the Hepatitis B virus and donor blood and transmission of NANBH has not been explained although it has been suggested that individuals who have anti-HBc may be more likely to have exposed themselves to a variety of blood-borne infections and are therefore more likely to be infected."

Essentially, is anti-HBc identifying donors -- or more likely to identify donors who have injected drugs at some point?

A. Yes, or people, particularly gay men, who have large numbers of sexual partners would be the other group.

It's a little more complicated than that because, of course, Hepatitis B is very prevalent in some parts of the world and in some ethnic communities, so it also -- Hepatitis B core antibody is quite common in certain racial groups and that poses -- that's probably more a reflection of the endemicity of Hepatitis B in those populations than it is a reflection of particular behaviours, but from a blood donor point of view it raises a whole extra lot of problems, which we can touch on if you wish to.

Q. I don't think we have to just now, doctor. Returning to your statement, please, in paragraph 2.10, you explain:

"As late as 1986 Dienstag and Alter described the

important limitations of both ALT and anti-HBc as surrogate tests."

You provide a quote. It might be worth us going to the paper to see the full quote, if we may. We looked at this paper earlier. It's [LIT0011675]. At page 76, which is our page 1684.

In the left-hand column, please, about half way down, the sentence commencing:

"Both these indirect assays have the disadvantage of relatively low sensitivity and specificity (both in the range of 60 per cent) and a very low positive predictive value (12 per cent in the NIH study)."

Could I pause, doctor? What's meant by a "positive predictive value"?

A. It's a measure of efficiency of the test in predicting a particular outcome in this case, the development of non-A non-B Hepatitis in the recipient.

Q. Okay. Returning to the passage:

"If adopted, the anti-HBc test will result in the loss of 4 to 8 per cent of the donor population and the sustained loss of probably 2 to 4 per cent. Cost and time are other detrimental elements to the adoption of either/or both of these non-specific assays. Despite these negative features, however, the accumulating data that chronic NANB hepatitis leads to cirrhosis in 10 to

20 per cent of cases has served as compelling evidence for the need to rely on indirect assays as an interim measure until such time as specific NANB hepatitis assays are developed. The major components of the blood delivery complex are currently considering the adoption of either the anti-HBc test or both the ALT and the anti-HBc test. Because of the cost and significant donor loss engendered and because of recent introduction of mandatory screening of all donor blood for antibody to HTLV-III, adoption of yet another one or two donor blood screening tests represents a very complex and difficult decision. Nonetheless, increasing documentation of the chronic sequelae of NANB hepatitis and the continued high incidence of this disease after transfusion have tipped the balance in favour of adopting indirect assays for NANB hepatitis carrier detection."

So it seems that in the mind of Alter, at least, as at 1986, while he recognised that the introduction of surrogate testing was a balancing exercise looking at the pros and cons, in his mind at least by this time the balance appeared to have tipped towards introducing such screening tests, in particular having regard to the increasing documentation of the seriousness or potential seriousness of the disease and the continued high

prevalence. Is that a fair representation?

A. I think that's exactly what he was saying, and I think elsewhere at the same time, I think he had also expressed the view that possibly the time, while prospective trial was still important, the time for doing that had possibly passed.

Q. I think I have seen that reference somewhere else as well. We will come on to look at this in due course but we know that in 1986 I think blood banks in America did start to introduce surrogate testing.

A. That's correct.

Q. Thank you. Then, please, returning to your statement in paragraph 2.11 you explain:

"Low test specificity ... has serious consequences when a test is used to screen a member of a healthy population. A substantial proportion of the individuals who test positive and who therefore will be rejected as donors because of the risk of transmitting NANBPTH will not in fact have NANBPTH, nor will their blood contain the relevant infectious agent. Nevertheless, such individuals have to be informed that their donations can no longer be accepted and the risk that their blood could transmit hepatitis must be part of the explanation. This can have the effect of converting a person who correctly considers themselves to be in

good health into one who has been given information that indicates that he may be afflicted with a serious infection. This problem can only be avoided if there is some form of additional test (often termed a confirmatory test) that can reliably demonstrate the presence or absence of infection."

Of course, if one is using a surrogate test for non-A non-B Hepatitis, there won't be a confirmatory test.

A. By definition there was no specific test.

Q. Yes. Thank you. Then over the page, please, in your statement, we have, I think, ranged quite far and wide this morning but I would now like to really follow essentially in a chronological fashion what happened in Scotland and the UK in respect of considering the question of surrogate testing.

At page 8 of your statement under your subheading you state:

"The consideration given by the SNBTS in the 1980s to whether or not surrogate testing of blood donors should be introduced ..."

I should explain, of course, that now in your statement you are answering a series of standard questions that we asked all the witnesses.

Before we go to your answer, doctor, I think the

starting document is perhaps this, [PEN0171737].

This, doctor, is a minute of an ad hoc meeting held at the Medical Research Council on 12 February 1979. You weren't present at this meeting, doctor, we can see those who were. Professor Mollison chaired the meeting and some other names we recognise there as well, including perhaps Professor Sherlock, Professor Zuckerman and others. No, I think, Scottish representation at that meeting, though.

A. No.

Q. I think in short the meeting was convened to consider the question of non-A non-B Hepatitis, and if we go to the final paragraph, Professor Zuckerman referred to an outbreak of parenterally transmitted non-A non-B Hepatitis in a dialysis unit at Fulham. And Dr Cleghorn said that his impression was that PTH must now be rare and it would be difficult to find many cases.

Over the page, please, the minute records:

"One and a quarter million units of blood were transfused last year and very little had been heard of NANBPTH. Professor Zuckerman pointed out however that much non-A non-B associated PTH might be anicteric and that the risk of progression to chronic liver disease remained however mild the initial infection. Professor Sherlock, agreeing with Dr Cleghorn, that PTH

was rare in the UK was nevertheless concerned about the continued use here of blood products of commercial origin."

Then two paragraphs down:

"Sir William Maycock --

THE CHAIRMAN: Sorry, is it one and a quarter or one and three quarters. I think one and three quarters.

MR MACKENZIE: Oh, I see, one and three quarters. I wonder if I could blow up -- I think, sir, it is one and three quarters, thank you:

The paragraph commencing:

"Sir William Maycock asked whether plans for the formal follow-up of cases of post-transfusion and post blood product hepatitis might be made. Dr Craske confirmed that there was continuing follow-up of haemophiliacs under treatment."

In the next paragraph a few lines down:

"The chairman suggested and Professors Sherlock and Zuckerman agreed that until there were such markers a survey of PTH as suggested by Sir William Maycock was not warranted."

Doctor, have you seen this minute before today?

A. Yes.

Q. What did you understand was being discussed in these two paragraphs where Sir William Maycock asked whether plans

for the formal follow-up of cases of PTH might be made but Professors Mollison, Sherlock and Zuckerman agreeing that until there were such markers a survey of PTH was not warranted? What was your understanding of that passage?

A. I assumed that Sir William Maycock would have been talking about some form of surveillance of transfusion recipients, and they obviously were aware of the importance of elevated liver enzymes at that time, probably not aware of anything of relevance to Hepatitis B core antibodies. So I assume that's some form of -- it's pretty vague. I think Sherlock and Zuckerman were expressing the view that probably the markers, such as ALT, were probably too non-specific to be used, and you have already taken us through a lot of evidence that gives some, you know, credibility to that opinion.

Q. Yes. Thank you.

PROFESSOR JAMES: Could I just perhaps add to that very briefly? It looks to me as if what Maycock was suggesting really was just a sort of survey of the old sort, and formal follow-up of cases of post-transfusion and blood product hepatitis doesn't suggest a prospective study of the sort that had been done in America. Therefore, I imagine that the reason that

Professor Sherlock and Zuckerman and so on really felt that wasn't very helpful was because that was precisely the not very informative study, for the reasons that have been rehearsed before, that the not very informative study that had not really yielded anything very useful and, for example, to get the MRC to embark on such a study would be a waste of time.

MR MACKENZIE: Thank you. Returning to your statement, please, doctor, at page 8, just developing things chronologically you say you:

"... first became interested in this topic soon after I joined the SNBTS in 1979. On 14 February 1980 the UK Medical Research Council convened a meeting of a Working Party on Post-Transfusion Hepatitis, being a subgroup of the MRC Blood Transfusion Research Committee. Dr Cash asked me to attend. One of the agenda items were was NANBH."

You say:

"During that discussion I proposed the idea of a prospective study to demonstrate the rate of non-A non-B Hepatitis in blood recipients and the relationship of infection in recipients to putative markers of the infection in the donor's blood."

If we could perhaps then look at some documents relating to this committee?

Firstly, the membership, please, [PEN0171715]. We can see for ourselves the membership.

Doctor, you were a member of this working party, chaired by Dr Gunson, and other names we recognise again, Professor Sherlock and Professor Zuckerman.

If we go to the minutes, please, of the meeting, PEN0171478, at page 3 of the minutes, please -- I'm sorry, I have gone to the wrong minute. It's the one before that. It should be [PEN0171710].

We see these are the minutes of a meeting of this working party on 14 February 1980, the names have been redacted of those present, but we can see Edinburgh and Southeast Scotland RBTC. So that must have been you, Dr McClelland.

Discussion under paragraph 2 of the purpose of the working party. We can see that it's stated:

"The DHSS Advisory Group on Testing For The [Prevalence] Of HBsAg and its Antibody advised on methods and policy with regard to the screening of blood donations and the preparation of national standards. An ad hoc group had met at the MRC at the request of DHSS in February 1979 as a result of discussions in the advisory group, and this had resulted in the establishment of the MRC PTH WP."

So I think you can see the genesis of that working

party.

Then it was agreed that the function of the MRC working party was to promote research to assess, and then over the page, a little hard to read but I think it says:

" ... the nature and size of the problem of PTH in the UK with particular reference to changes in transfusion practice, eg the use of products prepared from pooled plasma from large numbers of donors and the introduction of commercial products from abroad. Studies should include, 1, an assessment of any further need for research into Hepatitis B ... 2, investigations to assess the incidence of non-A non-B Hepatitis in the UK, particularly with the risk of introducing the infection by blood transfusions, and, 3, the position of research to characterise the agent(s) [and reagents] associated with this form of hepatitis and to derive diagnostic tests."

Under 3, the subheading "The problems of non-A non-B Hepatitis viruses" it's stated:

"There was a wide-ranging discussion regarding the incidence of PTH in the UK. There was agreement that the reported cases of Hepatitis B were very few. No cases of non-A non-B Hepatitis related to whole blood transfusions had yet been reported despite enquiry of

hospitals in London where open heart surgery was carried out."

The second last paragraph -- this must have been you, Dr McClelland -- said:

"Work was proceeding at the Southeast Scotland BTC into the problem of non-A non-B hepatitis associated with blood transfusion. He suggested that a multi-centre study might be sponsored by the WP. It was agreed however that this matter should be deferred until candidate laboratory tests were available."

Pausing there, doctor, do you have any recollection of the discussion at this meeting?

A. Not really but I clearly fell asleep at that point or the minute is slightly creative, because I certainly behaved as though that agreement had not been reached at the meeting.

Q. Because for the second meeting you had produced a draft protocol for such a study --

A. Yes.

Q. -- which would be slightly inconsistent with you having agreed that no such study was required.

A. Entirely.

Q. I understand. If we just complete this minute, at the bottom of the page it states:

"It was decided that the following problems needed

investigation: (a) the identification of donors and units of blood associated with possible cases of non-A non-B Hepatitis, (b) research into methods of identifying the viruses associated with non-A non-B Hepatitis, and (c) epidemiological surveys to assess the size of the problem in relation to blood transfusions."

Could one have properly investigated (a), (b) and (c) without carrying out a multi-centre study of the type you proposed?

A. Not really, certainly not (c). I mean, methods of identifying the viruses could have gone in many technical directions.

Q. Lastly, in this minute, over the page, please, again it's a little hard to read but somebody -- a redacted name -- said --

THE CHAIRMAN: "That as a result of the meeting ..."

MR MACKENZIE: "As a result of the meeting of the ad hoc group in February 1979 three special project grants had been approved for research into the incidence, epidemiology and clinical features of non-A non-B Hepatitis and a fourth would probably soon be approved too. It was open to the working party to initiate fresh projects in this field."

Put that minute to one side, thank you. If we turn then to your statement, please, at page 8, about half

way down paragraph 1.1 you say:

"In the second meeting of the MRC working party on 25 June 1981 I put forward a draft protocol for a prospective study of surrogate testing for non-A non-B Hepatitis which drew on the protocol of the US transfusion-transmitted viruses study. The need for such a study was challenged by Professor Zuckerman on the grounds that it would merely be repeating a completed study that had been funded by the MRC and published in 1974. He suggested that retained samples from the patients who had participated in the earlier study would be available and could be used in studies of markers of infectivity."

As we will come to see:

"It later emerged that these samples had been mislaid or destroyed."

Again, doctor, do you have any recollection of the meeting on 25 June 1981?

A. Yes, a vague recollection.

Q. Did you go into that meeting feeling a need for a prospective study? Do you remember that?

A. Yes, I also had -- from the previous minute that you just took us through, referred to, you know, it was open to the working party to produce further proposals, which I took as a very strong steer that we should be

producing further proposals. That was very much, you know, in my mind when I drafted this thing out for the committee. So I felt strongly that it was really important to do this.

Q. And how was your proposal received at the meeting?

A. I think Harry Zuckerman was, as I recall, quite miffed because I think in my proposal I hadn't read -- I wasn't aware of the 1974 study when I wrote the proposal and I made a statement which implied that it didn't exist, and he wasn't very happy about that, and I think basically I came away with the feeling that he thought he had done it and that it didn't need to be done again, and that all these samples had been laid down and at least could be used for one important part of the work, which was to evaluate some of the candidate markers, as they were called, some of the things that people thought might be specific markers for non-A non-B Hepatitis. That would have been a useful exercise because if that had actually yielded evidence that could lead relatively quickly to identifying a specific test, then obviously there would be no need to go ahead with testing surrogate tests, which everybody knew was going to be a real pain to do. It was never going to be an easy study.

Q. That was Professor Zuckerman's reaction to your proposed

study. Do you remember the reactions of any of the other members?

A. Not really. I do remember his reactions. I think it's also fair to say -- he was very eminent, he was a very big cheese in the field at that time and I was a complete upstart. I had only just come into transfusion and I wasn't -- I didn't know anything about hepatitis. So I think he felt a bit superior really. I certainly felt he was behaving very superior.

THE CHAIRMAN: You would remember being put down by him.

A. I do, yes, you remember those things.

PROFESSOR JAMES: If I could just add to that that as a matter of fact the samples were almost certainly destroyed by a cleaner turning off a refrigerator, a deep freeze, where the samples had been stored some years earlier.

MR MACKENZIE: I think there is reference to that.

PROFESSOR JAMES: My friend did the study.

MR MACKENZIE: I thought you were going to confess your friend was the cleaner.

PROFESSOR JAMES: I don't know who he or she was. But my friend was very sad when he discovered this.

MR MACKENZIE: If we could perhaps, doctor, look briefly at the minutes, if I may, it's page 8 of [PEN0171478]. We see unredacted minutes. I think these perhaps were

produced by yourself, doctor, for which we are grateful, of the meeting of June 25th 1981. We can see who was present.

Page 3, please. We can see under the subheading at 3.3:

"Identification of donors and units of blood associated with possible cases of non-A non-B Hepatitis."

And:

"Screening of donors for transaminase levels."

We can see reference, doctor, to your tabling a protocol for:

"A prospective study of blood transfusion associated hepatitis in Edinburgh and Manchester."

I think importantly this study would follow up both donors and recipients.

Then we see the next paragraph:

"Professor Zuckerman pointed out that a study already had been undertaken ..."

You have referred to that.

The next paragraph states:

"An evaluation of the value of ALT screening of blood donors had been carried out at the BTS at Edgware (Northwest Thames). Problems had been encountered as it had proved difficult to trace the fate of found donors

to who have raised ALT values. The value of this procedure in the UK at the present time was agreed by the working party to be of doubtful value."

What's meant by "this procedure"? Is that simply looking at donors?

A. I think it probably refers to the ALT test specifically.

Q. So ALT as a surrogate test for NANBH being of doubtful value?

A. Just on the basis that the first line says:

"Evaluation of the value of ALT screening of blood donors ..."

You know, this procedure of doubtful value, I think that's what it refers to.

Q. So a scepticism towards ALT testing perhaps?

A. Yes. I have to say I don't recall, and I don't recall seeing in the course of preparation for this, the report of that study. I may have seen it but I don't remember it.

Q. Over the page, please, at page 4, we see Dr Polakoff suggested:

"An effort should be made to follow up the patients involved in the original MRC study and enquiries should be made to see if the original collection of sera ... were still available ... this was agreed to by the working party and the chairman (Dr Gunson) said that he

would write to Professor Sherlock and Professor Zuckerman who had left the meeting to see if the patient records and serum specimens were still available. Dr McClelland's project could then be reconsidered in the light of the specimens and clinical data available from the earlier study."

We should very briefly, I think, doctor, look at your proposed study. It's [PEN0171486]. This is entitled "Proposal for a prospective study of post-transfusion hepatitis in the UK". You have written a handwritten note more recently.

Over the page, please, at 1487 under "Summary":

"There has been no prospective study in the UK of the incidence of subclinical hepatitis following transfusion of blood or single donor blood products."

Is that perhaps the statement that provoked Professor Zuckerman.

A. I would think so, yes.

Q. You go on:

"This information is essential to assess the importance of this problem and as a basis for the planning and evaluation of future donor screening strategies."

Why did you say that?

A. Well, because I believed it was factually correct. We

didn't have the information needed to plan anything.

Q. Your position perhaps was that it's self-evident that you need such information before you can properly assess the importance of the problem and decide on planning and evaluation of future donor screening strategies?

A. Absolutely. As I say, I wrote that I was not aware of the findings of the MRC study published in 1974, but when I read it, I realised it didn't really tell us what we needed to know, not least because it was done over the period of introduction of Hepatitis B testing.

Q. Yes.

And you say:

"An outline proposal is presented for a prospective study which would involve two UK centres and enrol 600 patients over a three-year period, with matched controls."

Could we perhaps just go to for reference, without looking at it in detail, page 1491, we can see you set out the objectives of the study. I won't read them. We can read them ourselves.

Over the page, please, we can see:

"These objectives are broadly the same as those of the USA TTV study."

I think in fact, doctor, you had been in correspondence with some of the participants in that

study and had received their study protocol?

A. I had the documents, yes.

Q. If we could perhaps for completeness go to[PEN0170884], we can see this is a letter, 10 February 1981, from Dr Kellner of the New York Blood Centre to yourself, doctor, second paragraph:

"To get started on the information you requested, I am enclosing a copy of the clinical procedures manual for the TTV study and an early interim report."

So presumably, doctor, you had been in contact with those at the New York Blood Centre and had asked them about their study and asked for documentation relating to it?

A. Exactly. Dr Kellner had actually visited us in Edinburgh on a different matter and I had chosen to, you know, raise this question with him because I didn't know any of the other -- I was a very new boy in transfusion and I didn't know any of the other people but that gave me the opportunity to get in contact with them.

Q. Thank you. Then returning to your statement, if I may, at page 8, so essentially there have been two meetings of the MRC working party on post-transfusion hepatitis but then paragraph 1.2 you explain:

"This working party had no further meetings and was disbanded in 1982. I do not know why that happened."

One explanation may be this, doctor, if we go, please, to [SNB0025864]. This is a letter from Helen Duke of the MRC to Dr Cash of 19 July 1982, in short advising of the disbanding of the MRC Blood Transfusion Research Committee.

Now, the Working Party on Post-Transfusion Hepatitis was a Working Party of the Blood Transfusion Research Committee. So it may have been with the disbanding of the parent committee, then the daughter working party would also be disbanded. Is that a possible explanation?

A. It's a possible explanation. I mean, it's a very anodyne letter. It's quite an extraordinary letter actually. I haven't seen this before. At least I don't recall seeing it before.

Q. I see. Take a second to look at it.

A. For the MRC board to conclude in mid-1982 that there was no more research to do in transfusion is quite bizarre actually. So I suspect that possibly the real reason for the disbanding is not quite as simple as -- not quite as reflected here, but I have no idea what it may have been.

Q. And the author states that the work of the committee was being duplicated elsewhere, so not perhaps that there was no more work to do in research into transfusion but

rather that the work was being duplicated elsewhere. What would your view on that have been?

A. Well, I think that for the MRC as the sort of prime responsible state body for medical research to delegate this to whoever they were delegating it to -- and it's not clear to me -- the British Blood Transfusion Society was a newly-formed professional society, which had no funds, it had absolutely no capacity to initiate major research. It doesn't make sense.

Q. One can speculate there may have been politics at play but --

A. I'm absolutely sure there were but I have no idea about what.

Q. No. I won't invite you to speculate any further, doctor, thank you.

Returning to your statement, please --

THE CHAIRMAN: Could we just have a look at the manuscript note at the bottom briefly? It might be ...

Yes. Clearly, someone at PFC is wondering whether something should be done about it or whether it should just be filed away quietly.

A. The note is addressed to Mr Watt, that's Mr John Watt, and the Irene will have been his then secretary, Irene McKinney.

THE CHAIRMAN: Yes.

A. I think she is simply saying that she doesn't have a file for this and she's asking where to file it.

THE CHAIRMAN: She doesn't have a file for it? Right. That's not a file for lost causes then at this stage?

MR MACKENZIE: Returning to your statement, please, doctor, at page 8 -- so that's the end of the MRC Working Party on Post-Transfusion Hepatitis and indeed the end of the MRC subcommittee in blood transfusion research.

A. Yes.

Q. So what we then see is, you say:

"Because post-transfusion hepatitis was seen to be an important topic, Dr William Wagstaff, then regional transfusion director in Sheffield, called together a group chaired by Dr Gunson to continue work on hepatitis. This was called the regional directors' Working Party on Transfusion Associated Hepatitis."

I think if we can go to a letter, please, [PEN0171502], we will see a letter from Dr Wagstaff to yourself of 14 May 1982 inviting you to join this new working party.

The second paragraph of the letter states:

"We are all very much aware of residual problems in the field of Hepatitis B. Added to this, of course, we are waiting with keen interest the development of reliable and useful tests for non-A non-B virus."

Returning to your statement, please, the bottom of page 8, you say:

"This new working party first met on 27 September 1982 and the working party set its own terms of reference as 'to promote the investigations of the epidemiology of transfusion-associated hepatitis, to promote research into the methods of prevention, and to make recommendations to the directors of the UK transfusion services regarding procedures and screening tests necessary for its prevention.'."

You again agreed to provide an outline study protocol for the next meeting:

"... for (a) determining the incidence of recipients with 'transaminitis' ... so that a library of putative non-A non-B recipient samples could be collected, (b) determining the incidence of PTH in recipients of blood positive for existing putative markers for non-A non-B Hepatitis."

We can look first at the membership of this new group, page 4 of [PEN0171716], please, chaired by Dr Gunson.

We can see the members: Dr Barbara from Edgware, Dr Lane, Dr Howard Thomas, Dr Craske, yourself, doctor, Dr Mitchell, Dr Bruce Cuthbertson, many names we are familiar with now.

The minutes, please, of the first meeting are [PEN0171716]. We can see these are the minutes of the inaugural meeting. The terms of reference were set out, as you have set out in your statement.

Page 2, please. Under paragraph 5 "Discussion of transfusion-associated hepatitis":

"Dr Gunson felt that the quarterly TAH reports were an inadequate estimate of true incidence of TAH."

Then scrolling down, please, to "Prospective studies":

"These would be considered in the light of the above information."

It's a collection of existing data and evidence.

Then:

"Dr McClelland will produce an outline study a protocol for the next meeting for either (a) determining the incidence of recipients with transaminitis so that a library of putative non-A non-B Hepatitis samples could be collected or (b) determining the incidence of PTH in recipients of blood positive for existing putative markers of non-A non-B Hepatitis. This might also include non-specific markers like ALT level and/or presence of anti-HBc in the donor."

Doctor, what's the difference between (a) and (b)? Are they two different studies?

A. I was trying to produce something that the committee would go with and there are two quite different studies. One is much simpler. The first study is substantially simpler. It doesn't involve -- the first study was designed purely to collect a lot of samples from a lot of patients who had received transfusion, measure the serial samples, measure the frequency of elevated liver enzymes and then keep the samples archived, because, as I have already said, there were several candidate tests being developed in the UK and elsewhere and this was the sort of material that one needed to test them.

The second study was much closer to the one which we already looked at, which was a prospective study, looking at both the recipients and the donors in terms of the consequences of blood that was either positive for or negative for a particular test result.

Q. Okay. If we look over the page, please, at the top we see the latter type of studies are option (b). It would be preferred by Dr McClelland and Dr Thomas. So was your preference at that stage still something closer to the TTVS study?

A. Absolutely.

Q. Then we see for completeness under "Library of putative samples":

"Although the American TTV study was originally

supposed to be able to provide samples for analysis in the UK, this has not materialised. Dr Gunson will therefore write to the MRC to ask if the samples from the 1974 study could be made available ..."

That's that meeting.

Could we then, please, return to your statement at page 9 now?

In paragraph 1.3 we see that this second meeting of the working party was on 18 January 1983 and you presented a study protocol, and the members agreed to send comments to you, and the comments were in due course favourable.

Can we look at the minutes of this meeting, please, page 4 of [PEN0171507]? Over the page, please, at page 2, under 6 "TAH studies", a listing of the different types of study one could have.

At the bottom of the page:

"It was agreed that some form of study was needed so that the UK is equipped to answer queries about any specific or non-specific test for non-A non-B offered from abroad. Also prospective comparative studies are only feasible ethically when the outcome is unknown and we are still at that stage."

Then:

"Fate of the 1974 MRC study:

"Dr Gunson will again ask MRC if samples are available ..."

6.5:

"Dr McClelland circulated a draft proposal for a prospective study of non-A non-B Hepatitis."

There was to be contact with Newcastle to ask about availability of samples from their study. That's the Collins paper of 1983.

Perhaps this important paragraph:

"If MRC samples are not available, the working party will put forward proposals for some form of study to the MRC and DHSS".

I will come to look at your proposed study in a second, doctor, but we can also see item 8 "AIDS". I think this is the first reference to the minutes of this working party to AIDS, which perhaps on one view might be surprising, given this is a working party on hepatitis but, on the other hand, is completely unsurprising, given how AIDS really exploded on to the scene at this time.

If I could briefly, please, look at your outline proposal you presented to this meeting. It's [PEN0171514].

If we go first to page 5, please, the last page, 1518. We can see the date in the bottom right-hand

corner, it's 10 January 1983. You are the author, doctor.

Back to the first page, please. Doctor, without going through this in detail, can you tell us really in summary what you proposed to do?

A. Well, there were two types of study and what I was proposing was not recommending the first one but recommending the second one, which was essentially the same as the study we have already looked at. It was a study to look at the consequence -- test donors and test patients and look at the consequences in terms of Hepatitis, ALT elevation in the recipients of receiving blood that had been tested or blood that had not been tested. So it was essentially the same study.

Q. I'm not sure if I understand the difference because the first study at 1.1:

"A prospective study of a large number of transfusion recipients and the respective donors."

A. I think it's not -- looking at it now, it's not correct actually because the logic of that -- it should be just a study of recipients, looking at the objectives, to measure the current incidence of PTH in the selected areas and provide a library of patient samples. So I think the reference to donors is an error quite honestly.

Q. Right.
A. It's confusing, I agree.
Q. I wondered whether option 1 was a large-scale, ambitious study like the TTVS study, whereas option 2 was a more modest, perhaps more feasible study, but is that a wrong understanding?
A. Actually question 2 is the more difficult one because question 2 implies studying the consequences of an intervention, ie testing, and comparing that in some controlled way with the consequences of no intervention, which is current practice, no testing, and that's technically a lot more difficult to do than the first one. I think I made a mistake. It was probably done in a hurry.
Q. Okay. Certainly if we go then to --
THE CHAIRMAN: I'm not sure. If you look at the second group of paragraphs, it was 1.2 that you decided to pursue or recommended to pursue, and the first study was not done because of its scale and potential costs and the fact that you couldn't even set out to prepare it.
I'm just wondering if Mr Mackenzie wasn't right in suggesting to you that 1.1 was effectively the TTVS scale study. I'm not sure it's important, Dr McClelland, I just don't want to leave the evidence in a slightly confused state if we can clarify it.

A. Sure. I'm not sure that I can clarify that, sir. Looking at it again, I hadn't really spotted this inconsistency, to be honest, when I re-read this.

THE CHAIRMAN: Perhaps it's one of these cases where the ignorant reader can interpret the words better than yourself.

A. That is highly possible, sir.

THE CHAIRMAN: I don't want to worry about it. If you are not sure yourself, that's fine.

A. I'm not sure at this moment in time, no, I'm not.

MR MACKENZIE: What perhaps is important for your purposes, Dr McClelland, is that your proposal was still to follow up recipients.

A. Yes, that is a common feature of both the studies.

Q. Yes, and the objective is set out in paragraph 3.1 and plan of the study in 4.1. And then, page 3, 1516, we can see in paragraph 4.3 the laboratory tests that are proposed to be undertaken, including ALT, anti-HBc and then markers of putative non-A non-B systems being developed at Edinburgh and the Royal Free hospital.

Perhaps, just out of interest, if we go again to the last page, we can see the estimated cost of this study. We see the figure of -- I think, is it? -- £63,000. Or is it 83? -- £63,000 over an 18-month period.

PROFESSOR JAMES: Sorry, Dr McClelland, I just missed this.

It was on a previous page. Was that a proposal to actually test for ALT and core antibody and exclude those people -- their blood -- from the recipients?

A. The proposal was to randomise into a group who received blood that had been tested and blood that had not been tested, and because we were concerned about the ethics of transfusing blood that we knew had markers that had already been associated with possible increased risk, we would test the donation samples after the blood had been transfused. So at the time of transfusion all the blood would have the same knowledge associated with it.

PROFESSOR JAMES: I think it's rather important to emphasise that this suggested study was precisely the effectively controlled trial of the examination of the putative surrogate markers that had been suggested earlier by Alter in the States but actually which hadn't been carried out. So effectively what Dr McClelland was suggesting was sort of two for the price of one. It was to try and find out the prevalence of probable non-A non-B Hepatitis following transfusion, using parameters like the transaminase being twice the upper limit of normal et cetera, that really had not been done hitherto either in the original MRC study nor for that matter in the Newcastle study. And, second, to see what the utility of excluding blood with those markers, those

putative markers was. So in my view, sitting here now, it was a very good study.

MR MACKENZIE: Thank you. Do you agree, doctor, with the explanation of the study?

A. This was what I certainly was wanting to achieve. You have asked a supplementary question about this study, which I have addressed in that second statement, which I didn't realise until this morning you hadn't received but which you now have, so we might want to just come back to the adequacy of the study design and resources. It's a question you have asked.

Q. I think we will come back to that maybe at the very end of your evidence, perhaps.

A. Yes.

Q. Thank you. Back to your statement now, please, if I may. At page 9, paragraph 1.4 -- we are now on to the third meeting of this working party on 20 April 1983, at which Dr Gunson had been informed by the MRC that samples from its 1974 study were no longer available. I'll give the references without going to them. It's [PEN0171505] and [PEN0171507]:

"The proposal for the proposed prospective study on post-transfusion hepatitis was discussed. Dr John Barbara, microbiologist in North London NBTS undertook to prepare a joint proposal that would include

the North London RTC, where the incidence of PTH was expected to be higher than in Edinburgh. It was minuted that this might then be submitted to the MRC on behalf of the working party."

We should, I think, look at the minutes for this meeting. It's [PEN0171522]. In paragraph 4 "Availability of 1974 MRC ... study samples":

"Dr Gunson had received letters ... duplicate sets of study samples ... had both been lost or destroyed."

Then:

"Prospective TAH studies."

A discussion there, including Dr James, as he then was, having sent yourself, doctor, the results of the Newcastle prospective study.

Then the bottom of the page, "Dr McClelland's TAH study proposal":

"So far a source of funding has not been found. In the light of Dr James results the problem of Edinburgh's likely low incidence of non-A non-B Hepatitis numbers was raised."

Over the page:

"It was therefore suggested to Dr Barbara that Edgware might provide a higher incidence area. He agreed to ask Dr Davies (director, NLBTC) and will submit a draft concerning the possibility of this.

Plans for a joint study with Edinburgh might then be submitted to the MRC by the working party."

Doctor, do you remember the discussion at this meeting, doctor?

A. I don't honestly remember but it was -- I think we were impressed by the apparent low incidence in the Newcastle study, which I think had not been published at that time. I think you sent me the results. It certainly was believed, possibly incorrectly, we now know, that there was more post-transfusion hepatitis in North London. So it seemed like a reasonable idea to include that as one of the centres in the study.

Q. And what was the view of this working party on the need for a study of the type you proposed?

A. Well, I think I said somewhere in my statement actually -- and possibly the next paragraph -- that there was really very little enthusiasm. There was polite interest. But when it says on the previous page of the minutes,"No source of funding has been found", no source of funding had been seriously sought. Nobody had gone back to the MRC, and I wasn't going to go back to the MRC at that stage myself as an individual because I knew I wouldn't get anywhere. I was depending on -- and, of course, the MRC had disbanded the subcommittee to which it had sent an invitation to submit more

proposals. So it was perfectly clear there was going to have to be a major effort made to obtain major funding for this study and other resources, which we may come back to.

Q. Obviously, you were of the view that there should be such a study.

A. I was strongly of the view but I was beginning to get a little bit worn down by that time actually because, you know, there is only a certain amount one can do as an individual and it wasn't lighting fires for anybody else.

Q. By anybody else, do you mean the other members of this working party or do you mean more widely?

A. Well, I mean other members of this working party because this was the first jumping-off point to get something done. If the working party had -- looking at the membership of the working party, if those people had all put their shoulders behind this, something probably would have happened but that didn't happen.

Q. So you were largely driving forward this proposal by yourself?

A. I was endeavouring to, yes.

Q. Thank you. Then back to your statement, please. At page 9 of your statement, paragraph 1.5, you say:

"Despite searching for any documentation, I have no

recollection of the subsequent fate of this study proposal and it was the Inquiry's preliminary report that drew my attention to a statement made by Dr Harold Gunson referred to in the judgment in the case of A & Ors v The National Blood Transfusion Authority, that he had submitted the proposal and that it had been turn turned down."

I think it's a point of detail -- we won't go to it, but it is paragraph 122 of the judgment where the judge, Mr Justice Burton writes:

"The working party had 'petered' to an end in 1983 when no grant was obtained for the studies into surrogate testing that they wanted to implement."

So it's possibly not entirely clear what the judge means by "no grant was obtained for the studies". It may be implicit in that a grant was applied for but it may not be. Do you have any recollection?

A. No, I can't remember, and I think I couldn't work out when I came to write this why I had kind of given up because, you know, my teeth were fairly firmly into this, and I think my next paragraph is what I recall as being the reasons. Basically we were taken over by HIV.

Q. You do say that you were awaiting information from Dr John Barbara to see if he could shed any light of the fate of the proposal.

A. I wrote to him subsequent to submitting this statement and he eventually replied, he confessed to no recollection whatsoever.

Q. Okay. Then paragraph 1.6 of your statement you say:

"I have thought about why a prospective study was not pursued at this time. I do recall being surprised and dismayed by the notable lack of enthusiasm to commit any resources to undertake what I believed was a necessary study to try and determine if surrogate testing had any value in reducing NANB post-transfusion hepatitis."

You explain:

"I believe the main reason that the SNBTS lost sight of NANBPTH for a period is that by early 1983 concern about AIDS was increasing."

You:

"... became increasingly preoccupied with the actions that the BTS should be taking to protect patients against any possible risk of being infected by locally collected blood donations."

The reference to:

"... May 1983 SEBTS prepared the first donor information leaflet on AIDS ..."

Et cetera.

You say in paragraph 1.7:

"Looking back, I think it is the case that the work related to AIDS ... distracted the attention of both the SNBTS and the [service in England] from non-A non-B Hepatitis for about three years. The working party did not meet after September 1983 until it was reconvened on November 24, 1986."

I take it, doctor, what you set out in paragraphs 1.6 and 1.7 remain your view about AIDS essentially coming on to the scene and distracting attention from hepatitis?

A. I think that must be the explanation because I know we were -- most of my personal effort and attention was focused on this for many months, certainly in 1983/1984.

Q. Yes.

A. I don't think that excuses a failure to grind on with the other study, but I think it explains it.

Q. As an observation on my part, I think it's certainly the case that our documents relating to post-transfusion hepatitis are fairly scarce and possibly nonexistent for years 1984 and 1985 and then we see more documents reappearing again in 1986.

A. Yes.

Q. If I could then just complete this working party's meeting in 1983, I think there was a final meeting on 27 September 1983. If we could start with the agenda,

please, which is [SNB0143029].

This is the agenda for the fourth meeting of the working party. We can see item 4 "AIDS". So that's now the priority.

Beneath that item 5, "Transfusion-associated hepatitis", and we can see that it was proposed to discuss various topics to do with hepatitis.

And in particular, 5.3 "Prospective TAH studies", I think including particularly your one.

But if we then go to the minutes of the meeting which are [SNB0143030], and in short, doctor, I don't think there is any reference at all in the minutes to transfusion-associated hepatitis. Do you remember the discussion at this meeting?

A. No.

Q. But from looking at the minutes in any event, it seems to me that AIDS was the subject which took up most of the time of the committee -- I'm sorry, of the working party.

A. That's absolutely my impression.

Q. Yes. There is also discussion of immunoglobulins but certainly not hepatitis. Then, as we have just noted, this meeting -- this working party, rather, went into abeyance or fell asleep or stopped meeting, until it was resurrected at the end of 1986.

A. Correct.

Q. Thank you, doctor. What I would like to do, if I may, is to put your statement to one side, please, and look chronologically at events in 1986 and 1987. I think the next main development, perhaps, if we can go to America and [SGF0010783]. This is a publication from the American Association of Blood Banks on 21 February 1986. Go over the page, please.

We can see under the heading "FDA advisory panel recommends surrogate testing for NANB".

We can see:

"The Blood Products Advisory Committee of the FDA will recommend that both ALT and anti-core testing be performed on donated blood to reduce the incidence of transmission of non-A non-B Hepatitis through transfusion. In a February meeting the panel received reports on two studies showing that recipients of blood from donors with elevated ALT and anti-core had a higher incidence of NANB hepatitis. While questions were raised about the data, it was noted that the carrier rate of NANB is higher than previously thought [and] that cases are underreported and that NANB is now considered to be a much more serious disease."

Then three paragraphs down, please:

"The advisory panel makes its recommendations to FDA

staff; the recommendations are not binding at this time."

So I think that's the start of the change in America towards recommending surrogate testing of donors.

Then the next document, please, coming back to Scotland, a meeting of the directors on 25 March 1986, [SNF0010135], please.

We can see a meeting of the directors on that date. And on the last page, please, at 0142, item 5, "Surrogate testing for NANB", reference to the FDA's recommendation:

"Dr Forrester of the SHHD said it was highly unlikely that the UK departments of health would fund testing based on data from the USA. Certainly clinicians and haematologists in this country had felt that the transfusion services had been slow to commence AIDS antibody testing and others had similar views in relation to non-A non-B Hepatitis surrogate tests. Dr McClelland said he would be able to provide data about raised ALT levels in blood donors by the autumn of 1986. Dr Forrester will be glad to hear of any research but could not guarantee funding. After a full discussion, the directors agreed to give consideration to funding someone to undertake research. Dr Cash would think about the possibilities in association with

Dr Fraser and make some proposals to the directors."

Dr McClelland, the reference to the study in Edinburgh, we will come on to that later but essentially I think it was restricted to a study of ALT levels in donors --

A. It's a donor study, yes.

Q. What was your reaction at the time to the directors would give consideration to funding someone to undertake research? Can you remember?

A. I can't remember, but looking at the minutes, it sounds like probably I didn't expect an awful lot of action.

Q. Why not?

A. Well, giving consideration to funding, it's pretty vague, it doesn't look like a commitment to me but I don't remember the discussion.

Q. Was there an element on your part perhaps of having been there, seen it, done it, and got the teeshirt in trying to provoke a study in this area?

A. We hadn't got any tee shirts. That was very frustrating. But I can't tell from the minute. There is nothing there to indicate what kind of research was envisaged, whether it was returning to some sort of epidemiological study, as we had wanted to do, or something else. I really don't know.

Q. This may be wrong but there is possibly a whiff, reading

this, of the matter appearing for the first time or being considered for the first time, whereas, as far as you are concerned, obviously, you had looked at this in some detail way back in 1980, I think.

A. Yes. I mean, I had certainly discussed it -- and I'm sure Dr Cash will say the same thing. It was at his request that I had originally joined that, or he had proposed me to be a member of that MRC working party, and I certainly felt that I had his support in pursuing the idea of a prospective study.

Q. I should perhaps have asked, doctor, when you attended the meetings of the MRC working group and then later the blood transfusion services working party on hepatitis, did you report back to Dr Cash?

A. Yes.

Q. So Dr Cash knew at all times what you were doing, what you were proposing?

A. Yes, I probably reported to him in writing. I usually provided him with a note but I certainly would have informed him of what was happening.

Q. Thank you. The next document, please, [DHF0021290]. We go south of the border to the English directors' meeting on 24 and 25 April 1986. The name, suitably redacted, but we can see SNBTS. Am I right in thinking Professor Cash was usually the SNBTS representative at

these meetings?

A. Yes, I think so.

Q. Can we, please, go to page 7, which is 1296? Item 16:

"Should NBTS carry out a study on NANBH? The chairman reported that this had been discussed with the Scottish directors and that he had agreed to raise it with RTDs. [Blank] reminded directors of two previous attempts, one by the MRC and one by the transfusion-associated hepatitis working party to study this problem. After discussion it was agreed that this should not be pursued because of lack of time and resources."

So that's the initial view of the English directors to the suggestion that the matter should be studied.

Could I then, please, go to document [SNB0024077]? I simply mention this as a further step in the chronology.

We had mentioned, doctor, the Edinburgh study of donors, and I think this is a document setting out that proposal. We don't see the date but we see a date stamp of April 1986 and we see the document is entitled "A proposal for a prospective study of blood donors with abnormal liver function tests possibly indicating carriage of non-A non-B Hepatitis."

And the authors are Dr Gillon, Dr Beckett and

yourself.

What was the purpose of this study, doctor, being restricted to donors against the background that your preferred study was the much larger-scale one, including recipients?

A. Actually, I think part of the -- if you look at the body of the study, there were actually two types of liver enzyme tests being utilised in this study, ALT and another one, which I'm ashamed to say I can't remember at the moment.

Q. GST?

A. GST -- which was new and was the research interest of Dr Beckett, and I suspect that the initiation of this study was at least 50 per cent an attempt to establish some more information about the relative significance of these two enzymes in a fairly healthy population. It didn't go anywhere to addressing the questions that we had been interested in in the earlier proposals.

Q. Yes.

A. I honestly can't remember now what were the factors that led us to feel this study was worth doing but I suspect an interest in the other enzyme test was a significant part of it --

Q. I think, out of fairness to you, doctor, that's absolutely right. If we go to page 4083, headed,

"Background to the present study", I won't read it but perhaps take a minute to read it, to satisfy yourself. (Pause)?

A. Yes, I think this was probably what drove it and I think that may well be why it got funded because this was a novel test and that's always much easier to get funding for than a bit of epidemiology.

Q. Thank you. The next document, please, is [SGH0016286], the minutes of a Scottish directors meeting on 25 June 1986, please. Page 5, which is 6290, item (i), "Surrogate testing":

"Increasing evidence that the USA and several European countries were introducing anti HBc and/or ALT testing ... Dr Cash believes that the SNBTS would soon come under pressure from clinicians to introduce testing."

Reference to the limited study at Edinburgh. And:

"Dr Fraser had advised Dr Cash that he (Dr Fraser) and Dr Marcela Contreras (Edgware ... ) were keen to set up a small group to explore the feasibility and practicability of this development and that it was their hope that a Scottish RTC would contribute."

Then the next document, please, takes us to America and the introduction of screening. It's an article from Nature of 4 September 1986. It's [SGF0012108]. We can

see the article, headed, "Hepatitis screening extended". The first paragraph:

"Spurred by growing concern that non-A non-B Hepatitis may represent a more serious health hazard than previously thought, the AABB announced last week that its members will begin screening all donated blood for evidence of non-A non-B Hepatitis but, as AABB officials are quick to acknowledge, such screening leaves much to be desired, as no direct testing for non-A non-B Hepatitis exists."

Then the third paragraph, lefthand column:

"The debate over whether to use one or both of these tests to screen donated blood has been raging for years."

The next paragraph:

"The American Red Cross is also implementing ALT testing at its blood banks ... AABB expects to implement testing ... by 30 November. A third organisation for blood banks, the Council for Community Blood Centres ... has not officially declared a position on ALT testing. But its president ... says most members will go ahead with ALT screening.

"Far more contentious is the use of anti HBc screening."

Right-hand column, please, second paragraph down:

"Robert AuBuchon of the American Red Cross says the Red Cross is planning to start an anti-HBc screening programme of its own but not until after the ALT test is implemented. Counts feels that the Food and Drug Administration should play a larger role in certifying the usefulness of anti-HBc."

In the second paragraph in the right-hand column:

"What everybody is hoping for is a direct test for the agent ... but that seems a long way off. Several candidates have been suggested but none has held up."

Last paragraph:

"A major concern for all blood centres will be the loss of donors from false positives."

At the end:

"The AABB president ... says the tests are 'essential to increase the safety of the blood supply'."

That sets out the position in America. I take it, doctor, that at some point you became aware in 1986 that the American blood banks --

A. Yes, we knew exactly what they were doing.

Q. Could I then look at the next meeting of the English directors, please? It's [SNB0113106]. 8 October 1986. Can we go to page 7, please, which is 3112, item 14, "Anti-HBc and/or ALT testing". A few lines down we can see:

"Developments in America meant that this topic must be considered again, as anti-HBc/ALT was soon to be essential for the accreditation of blood banks in the USA. The chairman proposed that the RTDs should approach the DHSS to fund a prospective study of 10,000 donations ..."

Over the page, please. The last sentence in this paragraph. We can see:

"The introduction of anti-HBc/ALT screening seemed very likely."

So really in quite a short period -- the English directors -- from the meeting in April 1986, when there was no interest really in a study, to a meeting in October 1986 and it being recorded, at least, that the introduction of screening being very likely.

Did you have a view yourself at the time, doctor, once the American blood banks had introduced the test -- did you have a view as to how likely it would be as to whether the Scottish and UK Transfusion Service would have to introduce the test?

A. I honestly can't remember but I'm sure I would have felt at the time that the fact that the whole of the United States had no option but to do this would have influenced thinking in the UK. It would have been very surprising if it didn't.

Q. I suppose the mere fact that the Americans have introduced it, but also, secondly, I suppose, it would provide an opportunity for working through the various problems and objections which had been raised to the screening. For example, the loss of innocent donors, the effect on donors, how to counsel and that sort of things, the Americans really would be forced to address these problems and --

A. I do recall that we became aware very quickly that particular the ALT testing was causing very considerable problems for the American services, as we knew was inevitable. But the fact is that they didn't fall over, they didn't stop providing blood and it didn't cause a crisis, but I think it probably caused a lot of stress and probably cost a lot more than they expected it was going to cost.

Q. Can you clarify a little what you mean by the problems that were caused in America with ALT testing? What type of problems?

A. There were the very obvious problems of loss of donors, very obvious problems associated with deciding which donors were to be informed and who was going to do that and how it was going to be done and what was going to be said to them, all very difficult questions, and then what is not terribly obvious from the outside is the

extent to which in a very large -- you know, it's a mass production operation and by that time parts of it were quite heavily dependent on automated systems and computers and things like that. But introducing a new test and particularly one which requires a lot of donations of blood to be taken, as it were, out of circuit can destabilise the whole system and actually creates a lot of -- something that's not really talked about very much, but it creates a lot of new risks; it increases the risk of other essential test results not getting attached correctly to the donations and so on. I don't think anybody measured this but I think I would be quite confident that during the period of the introduction of ALT testing many mistakes were made in blood services where this was done, and some of them undoubtedly would have compromised patients. There is no free lunch.

Q. I see.

THE CHAIRMAN: Could you follow up just a little bit, just to see what the mechanics were that resulted in that? Did the records get dislocated in some way from samples or was there a breakdown in recording or what?

A. There is a myriad things that can go wrong, particularly in a system which is partially automated, where you are depending on, for example, manual procedures to withdraw

physical blood units and put them in a quarantine position so that they don't get transfused once a positive test result has come out and then to ensure that those units are correctly disposed of and don't, as a result of somebody going to the wrong refrigerator, find their way back into the blood supply and so on.

There are infinite possibilities for anything that causes a partially planned or an incompletely planned change to the system to produce downstream problems. That's not unique to blood transfusion; it occurs in every large complex system.

THE CHAIRMAN: Yes. Thank you. I think just the more procedures there are -- because of the number of opportunities for things to go wrong.

A. If it is important, we could easily produce some very specific examples of how complexity has contributed to errors.

THE CHAIRMAN: I don't think I want to go into the whole range of possibility, Dr McClelland, but just at this moment to get a little bit of a feel for what it was that created the risk of error, rather than to pursue particular examples.

A. Yes.

MR MACKENZIE: Thank you, sir.

Dr McClelland, could I finally look, before lunch,

at another minute of the Scottish directors? It's [SGF0010268]. It's a meeting of 9 October 1986. If we can go to page 0272, please, page 5, under little "(g) Surrogate testing ... ":

"Dr Gunson reported that three English centres (Edgware, Bristol, Manchester) were to study the incidence of raised ALT and hepatitis core antibody levels in their donor populations."

I think this is the start of the UK multi-centre trial.

A. Yes.

Q. Looking at surrogate testing but only studying donors. Is that correct?

A. That's correct, yes.

Q. "Dr Fraser indicated that it would be helpful if an SNBTS centre could be included in the study."

Do you remember, Dr McClelland, what was your view at the time of the usefulness of such a study?

A. I really don't remember, but I don't know that there are any documents in which I committed myself to that.

I can't see how I would have thought it was going to help very much. It did seem rather like a way of buying time actually. It's an easy study to do because all these donor samples are completely under the control of the blood service. The only problem they have is to

actually do the tests and also to decide on what is going to be done in terms of are donors going to be informed that these extra tests are being done and so on. But it's relatively very, very quick, easy and inexpensive to do a large study of this sort on donors. Moving to doing a study on patients, that requires them to be followed up and have repeated samples taken after they leave hospital is orders of magnitude more difficult.

Q. I think later in your statement you refer to this study as essentially being an irrelevance if one wants to assess the efficacy of surrogate testing in reducing the incidence of post-transfusion non-A non-B Hepatitis?

A. That sounds rather rudely dismissive but I think it's true.

Q. It seems true as a matter of logic, I think.

A. Yes.

Q. How can one properly assess the efficacy of surrogate testing without studying the recipients?

A. I agree.

PROFESSOR JAMES: The only use of that study would have, presumably, been to see how much blood would have to be put aside because it failed those tests.

A. Absolutely, yes. It has a utility in that respect.

PROFESSOR JAMES: Sort of a financial management-type of

utility but not much else.

A. We already had quite a lot of information about prevalence in donors and I am not aware of any reasons why it should have changed dramatically in this relatively short time period.

MR MACKENZIE: Finally before we break, if I may, can we also see reference in the minutes to it being agreed that:

" ... the UK Working Party in Transfusion-Associated Hepatitis was the most appropriate body to pursue the issue of implementing surrogate testing and Dr Cash would write to Dr Gunson formally requesting that this working party be reconvened with a view to make proposals to the Department of Health."

The note says:

"The UK working party last met in 1981."

I think that's inaccurate. I think it was 1983, the last meeting.

A. Yes.

MR MACKENZIE: Thank you. That may be an appropriate point to adjourn.

(1.05 pm)

(The short adjournment)

(2.00 pm)

MR MACKENZIE: Doctor, before we look at events in late

1986, there was one paper from 1983 that I did mean to put to you earlier. Could we go to that please? It's [LIT0011837].

I think you will recognise this as being Vox Sanguinis' publication and we can see the title in short, the question was asked:

"Based on your analysis of the benefits and costs the pros and cons of surrogate testing, would you recommend it?"

I think, Dr McClelland, your response is at page 57, 1846. We can see top left-hand corner your name, doctor. I think in short your position is that you recommended proper research first rather than a rush to introduce surrogate testing.

A. Yes.

Q. We see you say:

"The only action which I would recommend at present is that there should be a thorough prospective study to determine the frequency with which post-transfusion hepatitis occurs in the regions served by this centre or in a closely comparable population.

"If the results of such a study indicate that post-transfusion hepatitis due to non-A non-B viruses (PTH) occurs sufficiently frequently to cause concern, I would recommend further study be carried out to

determine whether the introduction of a donor ALT screening programme does in fact reduce the attack rate for PTH. As an alternative it may well be possible to estimate simultaneously the attack rate for PTH in the recipients of ALT screened or non-screened blood."

Is that essentially consistent with what you were proposing at the time?

A. Yes. Oh, yes, absolutely.

Q. You say that:

"I consider that without undertaking thorough studies along these lines, the potential and actual scale of the benefit side of the cost benefit calculation is unknown and therefore no rational decisions can be taken."

Finally:

"I would therefore recommend that we are careful to establish the benefits before we become committed to the costs. We must know what improvement in the quality of our blood and blood products we are asking the community to pay for."

I think, as we will come to see shortly, doctor, I should say this passage was written at a time obviously when a proper prospective study remained a live issue in the UK.

A. Well, yes.

Q. But things were to change, as we will come on to see very shortly. So that's that paper.

Then could I, please, revert to events in late 1986, which I can pick up, please, at the bottom of page 10 of your statement, 0763. In paragraph 1.8 -- so we are now talking about the reconvening of the UK Blood Transfusion Service's Working Party on Transfusion Associated Hepatitis and a meeting on 24 November 1986. We haven't been able to find or recover minutes of this meeting.

A. I am aware of that.

Q. Doctor, I think you have provided us with your handwritten notes of part of the meeting and we also have a typed-up note from Dr Forrester of the SHHD, and we will consider each in turn, but sticking with your statement, you say you missed the first part of the meeting due to travel delays. You have your own contemporaneous notes for the second part of the meeting but have been unable to locate the minutes:

"A working paper had been prepared for the meeting by Dr Gunson and is informative. I have reproduced below part of the text that details the matters that Dr Gunson proposed for consideration at the meeting, following his review of the literature from the USA and the UK."

Over the page, please, this is an extract from Dr Gunson's paper. I'm not going to go to his paper. I'll give the reference number for the record. It's [PEN0170806].

You set out an extract from it:

"Incidence of transfusion-associated NANB hepatitis in the UK. The best estimate of incidence from published data is 3 per cent."

Et cetera:

"2. Projected value of ALT and anti-HBc screening in prevention of transfusion-associated NANB hepatitis.

"If 30 to 40 per cent of NANB hepatitis could be prevented by the use of the above tests, then the reduction in the number of cases would be 6750-900 per year and by extrapolations; 670-900 cases of cirrhosis."

You point out there is a typographical error, when it states that "the reduction in the number of cases would be 6750-900 per year", the 900 should be 9,000?

A. Yes.

Q. And then Dr Gunson went on:

"Some qualifications should be made to 1 and 2 above:

"(a) the course of chronic disease in NANB hepatitis is mild and therefore many cases probably remain undiagnosed even when cirrhotic changes occur.

This, I feel, is why we have not been aware of what appear to be quite serious statistics."

Et cetera:

"(d) one must question ... whether the incidence of transfusion-associated NANB hepatitis is as high now as the estimates suggest.

"3. Effective ALT and anti-HBc screening and blood collection from the evidence available in the UK, one might expect that ALT screening will cause the loss of .07 to .09 per cent of donations and anti-HBc in order of 1 per cent. Presumably there will be some overlap in the ALT and anti-HBc results but one might expect a loss of donations of approximately 1.5-1.75 per cent."

There is a comment later in your statement, I think, that is probably an underestimate if both tests had been introduced, we may have been looking at loss of donations in the order of perhaps 4/4.5 per cent?

A. Yes.

Q. We will come back to that. In your statement you go on to say that:

"Despite the estimate that a substantial reduction in NANBPTH could result from the introduction of surrogate testing the committee did not proceed to recommend that it be introduced. Instead a multi-centre study of surrogate markers in blood donors was

proposed."

We will come on to that.

As I say, we haven't been able to recover the minutes for the meeting on 24 November 1986.

We do have, doctor, your handwritten notes which are [PEN0171540]. They run to one and a half pages, doctor. I don't propose taking anything from these notes or putting anything to you.

Is there anything you feel we ought to know from the notes?

THE CHAIRMAN: That's putting a terrible burden to Dr McClelland.

A. These ones I have seen them before recently.

THE CHAIRMAN: Not only has he to read them but he's got to decide on the --

A. I don't think there is anything material here that doesn't come out in the statement actually. I think the Inquiry team did ask me to send any notes that I had. So I did so.

MR MACKENZIE: I think, with no disrespect, perhaps of more assistance to us would be Dr Forrester's note of the whole meeting, and that's SGH0028137. If nothing else, it's more legible.

It may be a different number. Can we try perhaps [PEN0171554]. I apologise.

If we go on to the next page, we will see that this note was produced by Dr Forrester on 1 December 1986. We see that there.

Back to the first page, please. It's a note from Dr Forrester to Dr McIntyre of the SHHD, copied to Dr Scott and Mr Murray. Dr Forrester explains in the first paragraph that:

"This working party was established in 1981 and has been inactive for some time ... it was convened on 24 November 1986 to discuss screening of blood donations for ALT ... and anti-HBc."

There is reference in the next paragraph to Dr Gunson's written presentation, and then Dr Forrester says:

"They considered the following issues:

"1. Is the American experience of frequent non-A non-B Hepatitis in the recipients of blood and blood products reproduced here? If so, a 40 per cent reduction in it would follow the screening. The answer is no. Such evidence as exists does not bear out the American experience but to examine the question properly would be a long and expensive business."

Do you agree with that, doctor?

A. Oh, yes. I mean, there is no doubt that the sort of study that would have been required to do this would

have been expensive, complex and taken several years.

Q. There would have to have been sufficient will and resources?

A. Oh, yes. Quite a lot of both.

Q. Yes. Both of which I think you found lacking from our discussion this morning?

A. Well, the will was lacking and the resources would only follow.

Q. Paragraph 2 here:

"Is ALT screening the application of a straightforward yes/no test? The answer is no, it is an arbitrary decision on where to draw the line ... Dr McClelland put the proportion of local donations showing an ALT test in excess of 45IU (a credible place for the line) at 34/1008 ie 3.4 per cent. The proportion excluded by Hepatitis B core antibody screening is put at 1 to 1.8 per cent ... It is clear that much innocent blood would be excluded."

I think already from the discussion in the meeting perhaps a more realistic estimate of the percentage of donations which would be excluded than we saw in Dr Gunson's paper.

Paragraph 3:

"Will better solutions emerge?"

No response to that really:

"4. Is research indicated? The meeting felt that a prospective study to discover the present burden of transfusion-associated non-A non-B Hepatitis was impracticable on grounds of cost and huge sample size."

Would that have been your view at the time, doctor?

A. No.

Q. Would your view have remained as at the 1983 meetings?

A. Yes, at this stage absolutely.

Q. Do you have any recollection of this meeting, doctor?

A. Well, not really, no. I do know I missed -- there was weather problems and I arrived late. No, I clearly was there because I made notes but I really don't remember the meeting.

Q. Okay:

"... and they proposed instead a study to identify in three centres (one Scottish) donors positive for ALT or core antibodies and search for other risk factors in them."

This is again a reference to the UK multi-centre study involving only donors rather than recipients. Does that seem reasonable?

A. The statement is reasonable, yes.

Q. Over the page, of interest, I think, paragraph 3:

"There was some discussion of the cost of screening all donations (perhaps £8 million). I asked the

chairman ..."

Dr Gunson:

"... whether he would advise screening if it were free of cost. He said no."

What would your reply to that question have been at the time, doctor?

A. I have no recollection of this. It's a most extraordinary line. It really is. I think my -- 1986 -- I think by 1986 my view probably would have been that, you know, being aware of what was going on in the United States and so on, the fact that they had reluctantly concluded that the evidence was sufficiently strong that they had little option but to introduce screening, my answer to this would have been, yes.

Q. And then the last paragraph:

"The position explicitly reached at the meeting is to recommend research of no great significance or scientific interest because the prospect of research would serve to counter pressure from, for example, haemophiliacs and haemophilia directors, to embark on an indirect and largely infective form of screening, which would also lose us a certain amount of perfectly harmless blood."

Do you have any comment on that passage?

A. I think it's -- I agree with the dismissal of the

1 further study on prevalence in donors, which we have
2 already discussed. I have absolutely no -- as I say,
3 I do not recall the meeting. I do think this is
4 a things of John Forrester's. I don't think -- that's
5 very uncharacteristic, it's not the sort of discussion
6 that would have taken place typically at this sort of
7 meeting, I don't think to just say cynically we will do
8 some research to shut people up. When I read this, when
9 I first saw this document fairly recently, I was really
10 quite surprised by that actually.
11 Q. So you would disassociate yourself with the second part
12 of that passage but perhaps agree with the first part,
13 namely that the research was of no great significance or
14 scientific interest?
15 A. I don't think it would have added very much to our
16 ability to make a rational decision on what to do.
17 Q. For the reasons we discussed this morning?
18 A. For the reasons we have already discussed.
19 Q. Thank you.
20 PROFESSOR JAMES: Sorry, before we leave, could I just ask
21 about the second part of that last paragraph, which
22 seems very odd, and I don't know where Dr Forrester can
23 have got what was patently extremely false information,
24 which says:
25 "Figures were produced for the total number of non-A

non-B cases encountered annually among haemophiliacs."

We know that virtually every haemophiliac was affected by non-A non-B Hepatitis. So that seems a very curious misapprehension and, of course, it may have informed his and hence other people's views in a very unfortunate way. Do you know where that might have come from?

A. I don't. I know where it might well have come from, but without the minutes of the meeting we don't actually know who was present at the meeting, I don't think. The person who was most au fait with this information and responsible for generating a lot of it was Dr John Craske from the Public Health Laboratory Service, but John Craske knew what he was talking about and would not have made a statement like this. I think this must be a -- not a misrepresentation but a misunderstanding of what was said at the meeting.

PROFESSOR JAMES: Yes, I agree, thank you.

MR MACKENZIE: And again, thank you, it's speculation but one perhaps has to bear in mind the number of reported cases of non-A non-B Hepatitis and perhaps the number of actual cases. They may be two very different things.

A. Oh, absolutely, yes.

Q. I would like to, doctor, just again put your statement to one side, please, and continue to look at a number of

other documents which just follow things chronologically. 1987.

The next document, very briefly, please, is [PEN0170814]. You will see this is the document setting out the proposals for the multi-centre study, and I see, doctor, you are listed, obviously, as one of the members of this committee. Does that mean that you supported this multi-centre study or you were neutral or against it or what?

A. Yes, I was quite surprised to see my name on the front page of this study. I really don't remember. I don't think I was very interested in it actually. I think it just sort of seemed to be something that was going to be done for whatever reason, and I wasn't particularly against it but I didn't -- I certainly can't imagine that I would see much value in it.

But there is some other correspondence with the -- the Scottish Home and Health Department about applications for funding for this. I have really tried very hard to remember where I stood in relationship to this study and I can't.

Q. Yes. Certainly, you were a member of a committee which proposed this study and, as you say, in due course, you, I think, and Dr Gillon jointly applied for money for a research application for the Scottish leg of the

study. So to some extent, I assume you were supportive of this study, albeit it wasn't the study you really wanted to carry out?

A. That's the only conclusion I can draw.

Q. The next document, please, is an important one. It's a meeting of the SNBTS directors on 3 March 1987. It's [SGH0016653]. Can we go to page 5, please?

At the bottom of page 5, reference to the UK Working Party on Transfusion Associated Hepatitis had been reconvened to pursue the issue of surrogate testing:

"A proposal for a study which would include the Glasgow and Edinburgh centres had been modified and no Scottish centre was now being asked to participate."

Over the page, please:

"It was noted that some commercial plasma collectors and non-profit blood collectors in the US had begun surrogate testing in 1987 and that in Britain the Haemophilia Society may adopt a position which put pressure on BPL to ensure surrogate testing was introduced:

"The doctors discussed the options open to Scotland and agreed the following."

I should have paused, doctor, do you have any recollection of this meeting?

A. I don't.

Q. Then to return to the minutes, they say:

"To recommend to the SHHD that surrogate testing for NANB should be implemented with effect from 1 April 1988 as a national development requiring strictly new funding."

Et cetera.

Do you remember, doctor, why the directors made that recommendation at that time?

A. Certainly not clear from the minutes. It just sort of appears out of the blue. I think it must have been primarily motivated by the awareness of what was going on in the United States.

I can't think of any other factor that would have sort of produced that decision at that sort of time. It's very surprising that none of that is minuted. I mean, there was a separate issue, which is alluded to in the paragraph above, which is the testing, specifically in relation to plasma for the manufacture of Factor VIII and other plasma derivatives, and that was a separate theme that appears in the correspondence from time to time, but it's really quite a different issue.

Q. Yes.

A. Although it impacts, of course -- because if you are going on test blood donations -- if you are going to

test -- have plasma that has been tested, ALT tested, shall we say, before fractionation, then, as a by-product of that you have those results for the donation from which that plasma came, but I think it's important to separate the implications of the two questions.

Q. Can you help us, doctor, with who is likely to have led this recommendation for the discussion on this topic? On the face of it, it seems slightly odd, as you say, for this just to appear out of the blue in the minutes. It's a fairly strong and clear recommendation. Can you remember which, if any, of the directors were pro surrogate testing or more pro than others?

A. My recollection is that there wasn't much enthusiasm among the Scottish directors. I mean, it may have been me, I don't know. I really do not remember. I was very surprised to see the clarity of this recommendation, amidst all the other fudges.

Q. What do you mean by "all the other fudges"?

A. We have already looked at several examples today of minuted commitments to go and investigate or set up a committee or await somebody's discussions with somebody else, which this looks more likely a call for actually doing something.

Q. The next document in the chronology, please, is

[SNB0113548]. We will see it's a letter from Dr Cash to yourself of 30 March 1987. I'm sorry, I have jumped the gun slightly. The preceding document is [SNB0113548]. I apologise. This is the correct document. I think the document manager actually corrected my mistake for me.

So this is a letter from Dr Cash to Dr Gillon of 30 March 1987 and obviously Dr Gillon has produced a draft article, a manuscript, following his study on ALT anti-HBc testing.

A. Yes.

Q. Dr Cash enjoyed the draft but, paragraph 4, he had one major worry, the final conclusion, I think in short, we will come to see Dr Gillon didn't recommend the introduction of surrogate testing on the information available, and as Dr Cash states in the letter:

"My problem is that it runs quite contrary to the decision made by the SNBTS directors (to seek funds to establish routine testing in mid 1988). The proposal, to which the directors agreed, was made by one of the co-authors of your paper."

Yourself, Dr McClelland. Do you have any recollection of this?

A. Yes, I remember this very well. It may also remind me of part of the answer to your previous question about that minute, if we can go back to that in a moment.

Yes, the study which we have already alluded to, the blood donors study, had been really driven by Dr Gillon and Dr Beckett of [The Department of] Clinical Chemistry and I think had been an author, my name had been on the original application but I had had very little to do with the study. So when they produced the draft, the first draft of the paper for publication, they very decently left my name on it, although I hadn't done very much.

Very shortly before that, if my time sequence is correct, I had drafted a letter, which all the transfusion directors signed, which appeared in the BMJ or the Lancet and that, I think, is linked to the decision that was minuted that we just looked at and that letter was saying really, "We have got to get off the pan and just start doing testing", for a specified number of reasons for expressing that view and, of course, Jack's paper, concluded on the basis of the donor study that testing wouldn't help.

It wasn't actually a totally sound conclusion, for all the reasons we have discussed in the morning, because it didn't look at patients. It just purports to explain the fact that there were lots of reasons for these donors havinv elevated ALT tests but it didn't exclude the possibility that they actually had

hepatitis.

So it was an embarrassing situation. I just took my name off the other paper because I hadn't done anything about it anyway, and it was noted, you know, that the SNBTS appeared to be facing in several different directions about this. It actually didn't worry me very much because I felt it was a matter that was highly controversial and there was nothing particularly wrong with having a lively debate in the organisation. Not everybody felt that way about it.

Q. We will go on just to look at the chronology. The next item is [SNB0060676]. This is a letter of the same date, 30 March 1987, from Dr Cash to yourself, Dr McClelland.

Dr Cash states:

"I feel, as a matter of some urgency, we need to have a chat -- either about modifying the conclusions of the paper or reversing the directors' meeting decision. Both options are likely to be painful."

Your response, doctor, is [SNB0060715]. A memo by yourself, doctor, to Professor Cash, 15 April 1987, and then you say:

"Yes, there is undoubtedly a problem of facing in both directions.

"The obvious difficulty is that on commercial

competitive grounds we need to introduce screening but on scientific and value for money for the health service grounds, we should be opposing it. I don't know if there is any way out of the dilemma. I am happy to remove my name from the paper but I don't really think that would solve anything."

I think what in fact happened was I think you did remove your name from --

A. I took my name off the paper.

Q. Yes. Then I think the next contribution in this debate comes from Edgware, if we can go, please, to [LIT0011854]. That is a letter in The Lancet dated 18 April 1987 from Dr Anderson and others from the North London Blood Transfusion Centre on the question of surrogate testing for NANBH.

In the left-hand column about half way down, the paragraph commencing:

"We collect more than 190,000 units of blood per annum and reports of post-transfusion hepatitis are received from hospitals and investigated to try and identify the type of hepatitis and its source. Since 1974 the number of cases reported has been 3-9 per annum, most being attributed to Hepatitis B virus. No association has been reported between cirrhosis and previous blood transfusion, nor do we have evidence in

the UK of a high prevalence of post-transfusion NANB hepatitis or its severe clinical sequelae."

In the right-hand column the authors state:

"The above data raise the following questions:

"1. Is there any evidence that the incidence of post-transfusion NANB hepatitis in the UK is similar to that in the USA?"

Other questions.

They say, the second last paragraph:

"Before we are forced to accept two screening tests of unproven benefit, which have high revenue implications, we need a national study to assess the incidence of raised ALT and anti-HBc in donors in different part of the country. Also, and perhaps more importantly, a study is needed to assess the incidence of acute post-transfusion NANB hepatitis and to assess how many of those affected develop evidence of chronicity and serious clinical sequelae:

"If the true incidence of post-transfusion NANB hepatitis and its serious clinical sequelae are at a much lower level than reported from the USA, then the screening of donations to reduce the incidence of NANB hepatitis may not be cost-effective in the UK."

Do you remember seeing this letter, doctor?

A. Oh, yes.

Q. What was your reaction or response?
A. Well, Dr Contreras was basically saying we still need a prospective study and then she went on and did it on a relatively small scale, and we referred to it this morning, and got the answer that she was hoping for, which was that it was a non-problem. It was interpreted as a non-problem.
Q. But at the time in April 1987 what was your response to the suggestion that a prospective study was needed rather than introduction of the tests?
A. Well, I honestly can't remember. I mean, I think I was in one sense probably glad that somebody was saying what I had been trying to say for quite a long time but at the same time, I mean, I was aware that the study would take several years and I think I would probably have felt it was a bit late and in fact the study that was started was not -- I think was not completed until after Hepatitis C testing had actually begun.

So we were running -- I mean, I didn't obviously know at this time that Hepatitis C -- a test was going to become available at the end of 1989 or early 1990 but I felt that we had been prevaricating about this for a long time, and to sort of prevaricate for another three years, which was the minimum time it would have taken to do a decent prospective study, we were too

late, and I think that was the burden of the letter that was signed by the Scottish transfusion directors.

Q. We are almost at that letter. The next document is [SGF0010127]. This is a meeting of the SNBTS directors on 10 June 1987.

If we can go to page 6, please, which is 0132, item g, "Surrogate testing":

"It was confirmed that the minute of the previous meeting was incorrect and that the Edinburgh centre was contributing to this study."

Then:

"Directors noted the need for synchrony with England and Wales."

What was your position at the time, doctor? Did you consider Scotland could introduce surrogate testing by itself or did you consider that any such testing could or should only be done in conjunction with the English transfusion service?

A. I think I accepted that ultimately we had absolutely no option but to proceed -- we could proceed with something as costly as this only with the support of the Scottish Home and Health Department because we were accountable to them for the expenditure of public money. So we couldn't just sort of stand back, "I'm a doctor" and start testing. So we had to have their support.

That's a very different question to did I think that we had to do the same thing as England. I'm sure my feeling at the time was that there were many obvious advantages to having a coordinated approach through the United Kingdom but if it meant that something that I believe was really important for patient safety was not going to be done, as it were, on my patch, I would give that a higher priority than, you know, keeping things tidy and avoiding problems of cross-border differences in practice.

Q. At the time, so in the summer of 1987, would you have put the issue of surrogate testing into that category where you felt so strongly about it that you would have been prepared to recommend its introduction in Scotland, even if the English directors had no plans to do the same?

A. Oh, yes, I wouldn't have had any compunction about that at all.

Q. But you would have sought the support of the government, the SHHD?

A. Yes, basically, if I, as an individual director, had tried to make a UDI and spent money that I did not have, I would have very appropriately have been given the sack or disciplined or something. There were certain rules about the expenditure of public money and ultimately,

you know, one accepted that one broadly speaking had to comply with them.

Q. So who did you consider was ultimately responsible for whether surrogate testing should be introduced in Scotland?

A. I think the decision probably rested with the -- it would have been the Scottish minister responsible for health, ultimately, as it were, delegated down the line through the department and the Common Services Agency, which was the channel through which our funding arose. But I think that's oversimplistic. I think the minister would inevitably be heavily dependent on the burden of the advice that he or she was given, and if there was very strong, clear, consistent, well-argued and rational advice coming from, say, the clinical and scientific community through the Home and Health Department to the minister, I find it hard to believe that most ministers would not have acted according to it. And it's perfectly clear that the advice that was, as it were, coming from the relevant professional community was not clear and consistent.

Q. On that very topic, the next item I would like to look at, please, is [LIT0010346]. We will see these are letters in The Lancet of 13 June 1987 from Dr Gillon and Dr Dow in Glasgow on the question of surrogate testing,

and in short these doctors were not recommending the introduction of surrogate testing at that time based on the information available.

We will see, left-hand column is headed "Non-A non-B Hepatitis surrogate testing of blood donations."

We can see this is a letter from Drs Dow, Mitchell and Follett from Glasgow and West of Scotland Blood Transfusion Service.

The second paragraph, left-hand column:

"Like Dr Anderson and colleagues ..."

In Edgware:

"... we have found a very low incidence of reported cases of post-transfusion NANB hepatitis in West Scotland with only 23 case in the past eight years, a period when over 800,000 units of blood have been transfused."

Down a little bit:

"Thus if ALT and anti-HBc tests had been done routinely for the past eight years at an estimated cost of more than £1 million, and with a loss of around 4 per cent of the blood supply, only five of the reported cases might have been prevented. That presupposes that the donors with surrogate markers were indeed the source of NANB infection."

The final paragraph:

"It would be prudent to do a UK study to assess the real incidence of acute post-transfusion NANB hepatitis and to assess the proportion of those chronically affected, before considering following the American surrogate testing policy."

Presumably, doctor, by this stage you are getting a sense of deja vu when you read a recommendation that it would be prudent to do a UK study to assess the real incidence?

A. Yes.

Q. Then the other letter, if we go over the page, please, this is the one from Edinburgh, Dr Gillon, and colleagues. I'm not going to read the details of what they say in terms of reporting their findings but, again, the top of the left-hand column, page 2, we see that the authors state:

"We conclude that the introduction of ALT/anti-HBc screening tests, an indicator of non-A non-B hepatitis carrier status in blood donors cannot at present be justified."

So that's that.

The next item, please -- I think we now come to the letter you drafted -- is [SNB0040672]. These are the minutes of an extra meeting of the coordinating group of the SNBTS. What was the coordinating group?

A. There were two -- there were essentially two sets of meetings which were a very closely similar group of people attended, one was called the board and the other was called the coordinating group, and that one was the coordinating group was supposed to sort of concentrate on sort of medical and scientific-type matters, and the board was supposed to be more managerial, administrative matters. In practice, because it was the same people meeting around the same table, things got a bit blurred most the time.

Q. Thank you. Page 3, please, of these minutes. Paragraph 5. Again we see "Testing blood donors for non-A non-B Hepatitis."

The minutes state:

"Dr Brian McClelland tabled a draft letter to The Lancet in expansion of the SNBTS view of the need to commence surrogate marker screening of the blood donations for NANB in the context of product liability and of competition from commercial producers who would be introducing it. Certain SNBTS staff had already written to The Lancet that surrogate testing was not justified on scientific grounds and the directors acknowledged this.

"It was known that the United States had declared blood transfusion to be a service, not a product, thus

escaping product liability. Dr Cash had done his best to persuade the UK departments to follow suit but they were not willing to apply for exemption from EEC legislation.

"After a few editing points were made, each director signed an amended copy of the letter which Dr Cash would submit for publication."

So it appears, doctor, that you were the author of the letter we will shortly come to and really no major revisions were made to your draft.

A. As I recall, very little revision.

Q. Do you recall at this meeting or at about the time of this meeting how strongly the various SNBTS directors felt about the issue of surrogate testing?

A. I think most of them were still pretty lukewarm about it. I mean, as you can see, quite a number of them had put their names to letters saying we shouldn't do it, one at least of whom actually signed this letter as well, which was interesting. But I don't think they were enthusiastic. I think the thing -- and part of the reason why -- we can come back and look at the letter, but having repeatedly failed to get anywhere with -- on grounds of patient safety, you know, I thought it might be worth deploying some other arguments, because people were worried about this new -- it was the European

directive on strict product liability, which was about to be translated into the Consumer Protection Act, and that was quite exercising people in the transfusion service at this sort of time.

Q. Thank you. So we now, finally with that long build-up, come to the letter, please, it's [LIT0010328]. This is the letter published in The Lancet on 4 July 1987 and we can see over the next page, please, in the right-hand column at the top, please, it's signed by all of the Scottish directors, including Dr Perry, and your name is stated first, Dr McClelland, presumably reflecting the fact that you were the lead author of the letter?

A. Yes, I assume that's -- I'm not sure what The Lancet's convention is but I imagine -- it's not alphabetical so it must mean that.

Q. Professor Cash, I think, was going to send the letter to The Lancet. It may be that he put your name first, I don't know.

A. That's why I'm hesitating --

Q. We can always ask him tomorrow.

A. -- because I'm not sure what exactly was submitted.

Q. You can take the flak from those down south. So we can see the title is quite striking, I think "Testing of blood donors for non-A non-B Hepatitis, Irrational perhaps but Inescapable," in the text of the letter --

sorry, we are back on page 1, I'm sorry.

We can see the first paragraph:

"In three letters in The Lancet Dr Anderson, Dr Gillon and Dr Dow and their colleagues point out weaknesses in the arguments which have been used to support introduction of blood donor screening to reduce transfusion-transmitted non-A non-B Hepatitis using ALT and anti-HBc as surrogate markers, while three letters suggest the use of UK transfusion services should not start donor screening until prospective controlled studies have been done in the UK to find out how many cases of post-transfusion hepatitis would be prevented. No large study to answer this critical question has yet been presented and we agree that the size of the benefit to be gained from surrogate testing cannot be accurately established without such a study. However, the time for this study has already passed. Starting now will give us an answer in three to four years -- and that is probably three to four years too late. The introduction of surrogate marker testing for NANBH just now is virtually inescapable for three reasons:

"1. In 1988 European legislation on strict product liability comes into force in the UK. If harm should come to the recipient of a therapeutic product the producer will be held liable unless he can demonstrate

that he used all known methods and information to avoid the risk."

Et cetera.

Then 2, the question of pooled plasma fractions:

"Even if surrogate marker screening would only modestly reduce the level of infectivity in these products, many would argue that some improvement is better than none."

Thirdly:

"The UK blood transfusion services, although the major suppliers of blood and blood products in this country, cannot afford to ignore the wishes of consumers to be supplied with non-A non-B tested products, even if it is believed that the real benefit in safety which is offered to the patient is marginal."

Then the question of -- the letter goes on to look at the assumption that surrogate marker testing was necessarily a bad buy in comparison with other tests.

And the top of the second column, please, the authors conclude:

"Looking at these three factors -- producer's liability, competition and value for money -- we suggest that the decision which has to be made is when, rather than whether the UK transfusion services follow the lead of the United States and other European countries in

donor screening."

Doctor, I think it's clear from this letter and from what you have said today that you were in favour at this stage of simply introducing surrogate screening.

A. Yes.

Q. Would that have been with the ALT test, the anti-HBc or both?

A. Probably both. Probably both because anti-core testing would have been fairly -- would have been really quite simple for us. We probably could have started anti-core testing literally within days, and we had done all the groundwork -- as the Inquiry knows, we had done all the groundwork on ALT testing in a big, well-conducted study. So we knew exactly what the scope of the problems with that would be as well. So we could have started quickly.

Q. What was the main or the determining factor or factors which led you to recommend that surrogate testing should be introduced?

A. Well, I felt there was -- even in the absence of a proper -- you know a definitive prospect of randomised controlled study to provide a real answer, that there was sufficient evidence -- the evidence which had convinced the Blood Products Advisory Committee of the FDA that surrogate testing needed to be introduced and

led to the decision in the United States was, while not complete and not definitive, very, very difficult to ignore and I had no conviction that the epidemiological situation, the sort of prevalence, the amount of Hepatitis C -- or non-A non-B Hepatitis infection in the UK was really that much less than it was in America, in 1986, because, you know, commercial paid donors had stopped. They had introduced similar changes in donor selection in relation to AIDS that we had, and I felt if, in the light of, you know, those two major changes, the United States felt it had to introduce this testing, we were in a very, very poor position to not follow suit in the UK, unless we had convincing evidence that it really genuinely wasn't a problem.

Q. Yes.

A. And we didn't have that.

Q. The American prospective studies, the TTV study and the NIH study, in short, I think, showed a correlation between elevated ALT in a donor and increased chances of a recipient getting NANBH, at its very simplest.

A. Yes.

Q. And, therefore, presumably the argument was that at its very simplest to introduce surrogate testing would lead to an increase in patient safety, an increase in the safety of the blood being transfused to a patient, at

a very simple level.

A. Yes.

Q. What's perhaps interesting, doctor, is that that point doesn't appear in your letter. Instead, the letter talks about producer's liability, competition and increased safety of plasma products, pooled plasma products, and the question of value for money.

A. It possibly doesn't appear in the text but it certainly appears in table 1.

Q. Yes.

A. You know, I have specifically -- okay, it's the fourth point in the letter but -- and there is a reason why I drafted it that way, but I have made the point that actually some of the testing that we currently do, specifically testing repeat, reattending donors for Hepatitis B surface antigen is a very expensive way of providing very little increment in safety because donors virtually never seroconvert for Hepatitis B, and I made the comparison between the cost of that and the cost of -- and the number of cases of cirrhosis that could be prevented by an even partially effective screening programme. I was using different arguments because I had spectacularly failed on numerous previous occasions using the patient safety argument. So I thought let's try something else. It was my sort of

last throw on this topic.

Q. At this time in July 1987 to what extent was patient safety a factor in your consideration --

A. It was the factor in my consideration.

Q. And perhaps we should --

A. The objective was to try and get testing started.

Q. Yes. Really, should we read into this letter that it almost goes without saying that your whole purpose in seeking such testing was to increase patient safety?

A. Oh, yes. There was no other substantive reason for it. I wasn't that fussed about product liability and so on. I thought these arguments might work.

Q. Thank you. Could we then next, please, look at [LIT0010326]. This is the reaction from the transfusion directors down south.

We can see again, top right-hand column, a letter in The Lancet of 1 August 1987, and the question of surrogate testing. Over the page, please, we will see this is a letter from Contreras and Barbara in Edgware North London.

Do you remember getting any reaction to your letter at the time?

A. I obviously read the correspondence in The Lancet and I'm sure some people phoned me up and said, "We disagree". But I recall that in terms of my working

relationships with people like Contreras and Barbara and so on I think it was accepted that there was a difference of opinion, and we were using the correspondence columns, and I think appropriately, to air that. I personally still feel that was a very appropriate thing to do.

Q. If we go back to the first page of this letter, please, just to give a flavour of the views of the authors, in the right-hand column, two-thirds of the way down, a paragraph commencing:

"Transfusion services must not bow to irrational pressure for measures whose efficacy is unproven. In the UK, transfusion centre directors resisted commercial pressure for premature introduction of unsatisfactory screening tests for anti-HIV; this should show the same resolution with NANBH."

That's just an example, I think, of there being room for argument as to which position you agree with or disagree with?

A. They clearly weren't subscribers to the precautionary principle.

Q. Yes. So to develop that a little, how would you describe their approach?

A. I think it was quite unscientific, actually. I really don't -- despite that I have a lot of respect for a lot

of these people. I think the arguments that were used around this, really, right the way through the saga, I think the sort of lack of scientific rigour failed the patients to some extent. I think, you know, the balance between the focus on patient safety, which to me was always a reason for -- well, at a given point for trying to establish the facts and then at a later point, when history had moved on, I felt became a driving reason for actually doing something that you had reasonable grounds for improving patient safety.

And remember Harold Gunson's paper that he produced for that 1986 meeting, when he estimated that we could avoid 6,500 to 9,000 cases of Hepatitis C. These are massive numbers. 675-900 cases of cirrhosis. This was the transfusion service national medical director putting these numbers down and then deciding not to do anything about it. I couldn't compute that.

Q. Yes. So your position is that your position was evidence-based. It may not have been complete evidence but, as you put it, there were reasonable grounds for believing that surrogate testing would increase patient safety. So you would say, "There was some evidence for my position, certainly sufficient for me to hold the view I did"?

A. Yes.

Q. And there's perhaps a certain --
A. It wasn't entirely satisfactory evidence but there was a lot of it and it all pointed -- all the evidence from studies that were fairly substantial and fairly well done, even though they weren't proper randomised prospect of trials, pointed in the same direction. As I recall, the only studies that looked at surrogate testing and concluded that it didn't have any effect, if you look carefully at them actually, the number of patients enrolled was very small and probably not sufficient to draw any conclusions from at all as a statistical basis.
Q. Perhaps the question is, how much evidence does one need before one acts, which would then lead on to perhaps undertaking a cost/benefit analysis of acting and not acting?
A. Well, this is where -- you know, this enters -- divides into the health economic view and what I call the Krever view, which is that if something might make a patient safer, then you have to do it. That is in a very crude way, as I understand, what he articulated as the precautionary principle. And depending on whether you are a health economist or concerned primarily with the nations economics or whether you're concerned with the public health or you are concerned with the health of an

individual, you will view those things in different aways. There ain't no right answer.

Q. Dr McClelland, I'm about to move on from this particular point. I think we have covered in quite some detail the views you held on surrogate testing at the time and the reasons for it.

Just as one point of detail, the question of the UK multi-centre trial and the involvement of Edinburgh in it and Edinburgh submitting the grant application but that being, I think, refused or rejected on 25 September 1987 by the Chief Scientific Officer's Biomedical Research Committee, essentially, it appears on scientific grounds that, because the proposed study didn't include follow-up of recipients, there was little scientific value in it. I don't propose, doctor, taking up a lot of the time going through all the documents on that. Instead, what I propose doing is simply listing the main four or five documents for the record so they can be examined if anybody wishes, but it does seem as though it's not a central matter to this topic.

So if I may do that, we do have your grant application dated 6 August 1987, which is [SGH0028080]. We also have a letter from Professor du V Florey of Dundee, to the Chief Scientist's Office of 4 September 1987, [PEN0160167], essentially pointing out

the problems with the study.

We also have a letter from Dr Forbes of the Chief Scientific Office in Scotland to the DHSS of 13 November 1987. That's [PEN0160152].

We have another set of letters to the CSO of 27 October 1987, which is [PEN0160210].

And finally on this point, we have a letter from Professor Hedley of Glasgow, who was either an assessor, I think may have been actually a member of the committee who assessed the application to the CSO, 2 November 1987, [PEN0160156], but I have to say I don't propose taking up further time on that particular line.

Sir, I'm happy to carry on going. It may be an appropriate time to pause.

THE CHAIRMAN: It might be an appropriate time to pause.

(3.14 pm)

(Short break)

(3.30 pm)

THE CHAIRMAN: Yes, Mr Mackenzie.

MR MACKENZIE: Thank you, sir. Doctor, we had looked at the letter in July 1987 to The Lancet in which the Scottish directors set out their support for the introduction of surrogate testing. I would like now to look at events in Europe, please. We have a document [SNB0019445].

We can see it's headed "Council of Europe,

Strasbourg 18 June 1987". It appears to relate to the European Health Committee, its 21st meeting, June/July 1987, and there is an extract from the report of the Committee of Experts on Blood Transfusion in Immuno-Haematology, their tenth meeting at Rome, 19 to 22 May 1987.

If we go, please, to 9447 -- it's the third page into this document -- we can see Dr Gunson was a member of this committee and he told the committee:

"In the UK a study on a cohort of donors in four centres had been proposed ..."

Then:

"Proposals for a prospective study on patients transfused with blood with normal and raised ALT levels had not received ethical approval."

I haven't seen any reference to that in any other document. Are you aware of what Dr Gunson is referring to there, doctor?

A. I had never noticed that before. That's complete news to me. I have no knowledge -- I'm sure I have no knowledge of such a study ever going to an ethics committee in the UK.

Q. Yes. Certainly I think your proposal in '83 involved studying recipients of screened blood and unscreened blood. Is that correct?

A. Yes, in the second proposal we -- I can't honestly remember whether we had addressed it in the first iteration but in the second iteration what we had proposed was that the donated blood would only be tested after it had been transfused.

Q. Yes.

A. Whether that would have passed muster with an ethics committee or not I don't know, because we never got to the stage of going through the ethics committee hoops.

Q. I was going to ask, if that study, proposed study, had been submitted to an ethics committee in 1987, may there have been ethical difficulties?

A. I'm sure there would. I mean, I think there would have been probably quite a lot of coming and going. I don't know what the outcome would have been in 1987. It has got progressively more and more and more difficult to get anything through an ethics committee. In 1987 we probably would have got it through.

Q. Even though in 1986 US blood banks were screening?

A. Ethics committees always get themselves into a very -- we have been through this many times but if the study -- let us say the Americans had started doing ALT testing, so all patients are getting ALT tested blood and no patients in Britain are getting ALT tested blood and you propose a study in which half of the recipients will get

it and the other half will get standard practice, what is generally considered in the design of randomised trials to be a base position that you can take to an ethics committee is current practice versus something that may offer some advantages. So we could have argued very strongly to get it through. Whether we would have succeeded or not, that's pure speculation.

Q. This document sets out discussion among these experts on the question of surrogate testing, but we can then see the outcome on the next page, please, at the bottom, the very bottom. We can see:

"After ample discussion on this topic it was decided that a working group comprising Professor Van Aken, Dr Gunson, Dr Habibi and Dr Leikola would prepare a brief report and if possible define recommendations."

Over the page again, please, we can see at the top:

"Later this working group reported as follows."

I won't read that but the next page again, please, we will see the conclusions of the working group, and we can see, on the basis of this information, the working group concluded that:

"1. The use of non-specific tests for the purpose of reducing the incidence of transfusion-associated NANB hepatitis and its possible value as a public health measure remain controversial issues."

We have seen that in terms of the differing views within Scotland and between Scotland and England.

And:

"2. If a stance is taken that blood should have maximum safety, then the tests would be introduced but the benefits derived from this testing would not be uniform throughout every country."

Dr McClelland, was that essentially your position, that you took the stance that blood should have maximum safety?

A. Yes, that was part of my job.

Q. Yes. Thirdly --

A. I mean, it's not completely -- it's not -- I could qualify that slightly. There have to be some limits around this and to take the example, a real example, which was when you take acid testing for Hepatitis C, which came up later on, we know that the cost of that is enormous and the number of patients who are spared exposure to Hepatitis C-positive unit across the whole UK is of the order of one or perhaps half per year.

I would have been comfortable with the decision to stop doing NAT testing because I think that feels to me like an inappropriate use of resources which I wouldn't want to defend in the public forum. But the sort of levels of safety gain that with the best guess that we

could make about surrogate testing were much greater than that and the cost was actually much less.

Q. There was no other step which could have been taken at that time in 1987 to try and reduce the risk of NANBH transfusion transmission?

A. I don't think there was. I think the steps that we had taken in relation to AIDS -- there is evidence from some countries that those contributed through complications of donor selection, contributed some safety but I'm not aware now of anything other than some form of testing that we could have done to enhance patient safety in regard to NANB.

Q. Returning to these recommendations, we see:

"3. The question of compromise of blood supply," the relevant factor.

And then, 4, the need for counselling, et cetera, of donors.

And then 5:

"The committee cannot give a general recommendation on the introduction routinely of non-specific tests for evidence of NANB infectivity of blood donors, individual countries will have to assess the situation locally and decide on the appropriate action to take."

Is what is said here a reasonable representation of your understanding of views of your European colleagues

at the time?

A. I wasn't involved with this group at that time, so I can't directly answer that. But this is very consistent with the sort of very measured advice that I would have expected to come from that group. It did include one member, Dr Habibi, whose service had introduced surrogate testing. I think this was quite consistent with my understanding of these guys.

THE CHAIRMAN: Would you have considered the fourth item particularly important?

A. Oh, yes. I mean, this was one of, you know, very substantial concerns because, as I said this morning, you know, you take -- somebody walks in the door as well and you then have to tell them a few weeks later that, "Well, you are probably well but you have got this funny test in your blood and we can't accept it for transfusion", and if you have a clinical -- our view has always been we have a duty of care to the donor, whose wellbeing we compromise in this way to see that they are not just properly and appropriately informed of what has been found but they have the follow-up care, and it's something I feel very strongly about because when I went first to work in blood transfusion, for example, any donor who had Hepatitis B as a result -- was found to be a Hepatitis B carrier as a result of our testing could

not get dental treatment in Edinburgh.

THE CHAIRMAN: Do you think that at this stage the working group would have a clear idea of how they would inform, how they would counsel, people, given that a few years later, when tests for Hepatitis C came along, a fair degree of chaos resulted?

A. I'm not entirely sure that I recognise your characteristics of the Hepatitis C situation. In Scotland Dr Jack Gillon produced a very good -- with clinical colleagues working through the College of Physicians -- set of guidelines specifically for counselling, which basically were adopted and used. There were a couple of issues which were contentious, notably look-back, which I'm sure you will be returning to at some point, but in terms of the clinical, the sort of the content of the clinical management of the patients found to be Hep C positive, I think that was fairly well done.

But a similar sort of process would have been required here and it would have been more difficult because the finding was much less concrete --

THE CHAIRMAN: Positive.

A. It had a far wider range of potential interpretations, ranging from the very serious to the possibly trivial, you know. And you know, would have been a challenging

problem, but I have no doubt that it could have been managed. I share very little personal information about how this was handled in the United States but traditionally in the United States the blood collecting organisations took a much more cavalier approach to their donors and basically sent them the result through the post and left it to go and find their own doctor if they wanted to do something about it. We never felt that that was an appropriate way to handle these things.

PROFESSOR JAMES: Can I just add to that a moment? First of all, a million blood donations a year in the UK, I mean, more actually but let's say a million, 4 per cent for the sake of this argument with a significantly raised transaminase by general consent, so that's 40,000 individuals a year. Had you in Scotland, you and your colleagues, when proposing that there should be surrogate testing, thought, for example, not just chatting to the people but how many more investigations would be done, who people would be referred to? For example, would you be automatically doing autoantibody screens, MCVs, gamma GTs, in other words investigating possible liver disease? Had you kind of thought this through?

And just second and briefly, I mean, although with respect, although you say that Jack Gillon and indeed we

know he did, produce some guidelines, the evidence from the witness statements that the Inquiry has seen suggests that on the whole, to my way of thinking, and no doubt this will be properly explored later, but as a matter of fact, you know, people heard about their Hep C from their GP who then said, "I have not got the faintest idea what this means, you know, you can go and see somebody or you needn't". It was done in a very -- people learned about their Hep C status often in a very ad hoc fashion, let's put it that way, it wasn't extraordinarily well organised, although it was thought through. And I'm just asking really whether you had really thought through very carefully in retrospect what the implications were of making it recommending.

A. I think the honest answer to that is probably we did not.

PROFESSOR JAMES: I'm really asking these questions on behalf of the Scottish Government sitting over there, I should say.

A. I don't think that we followed -- when you talk about 40,000 donors having to be counselled, followed, retested, possibly requiring further investigations, I don't believe that we really took that on board. You see, the only experience we had before was two serious infections which were relatively a very low prevalence

in the community, Hepatitis B and HIV --

PROFESSOR JAMES: Exactly.

A. -- which were relatively easy to manage, and even with Hepatitis C the numbers were relatively small. We are talking about one in 1,000 on the first pass and falling considerably after that. So the numbers here, I think the answer to your question is, no, we probably didn't really -- I don't think I personally internalised the implications of that and that was probably a bit arrogant on my part. But, no.

PROFESSOR JAMES: Thank you very much. Thank you, sir.

MR MACKENZIE: Thank you. Doctor, I would like to carry on and look at some documents from 1988 and 1989 just to finish the factual chronology of the consideration given to surrogate testing.

We are in now 1988, document [SNB0027321]. This is the minutes of a directors' meeting of 12 April 1988.

If we go to page 4, please, 7324, and we see under "(e) surrogate testing", a few paragraphs down we can see:

"It was confirmed that it had been agreed not to introduce ALT testing in Scotland until it had become UK policy but directors wished to reserve their position on this matter in the light of reports of the commencement of ALT testing in at least one England and Wales RTC."

The question of "until it had become UK policy", what does that mean? Does that mean policy of the UK Government or policy of the UK transfusion services, do you know?

A. I don't know. It possibly wasn't even defined fully in the discussion. I can't answer that.

Q. But certainly some UK-wide approach rather than Scotland going declaring UDI?

A. That's the sense I take from it.

Q. And have you any recollection of when the English centre commenced the ALT testing?

A. Yes, I do have a vague recollection of one of the centres in the north. I think it may have been Liverpool that had -- but it's a vague recollection and it was -- it may have been more at the level of rumours, as is implied here, than an established fact.

Q. Yes.

A. It's entirely possible because, as the Inquiry will have heard, the English centres were managed by regional health authorities and each was financed quite independently of the other. So if a transfusion director quietly reached agreement with the appropriate people in his or her RHA, they could get on with it.

Q. But is it essentially in the realm of rumour and speculation rather than that being something concrete

which happened?

A. From my knowledge, it's in that realm.

Q. Yes. Thank you. The next document is [SGH0017505].

We will see these are the minutes of a meeting of the Scottish BTS and haemophilia directors on 5 May 1988. If we could go to page 4, please, under item 6 "Non-A non-B Hepatitis screening", the chairman, who is Dr Forrester, said:

"That a research project was being mounted in England and that a decision whether to introduce screening would probably wait upon its outcome. Dr McClelland and Professor Cash considered the delay unjustifiable."

So your position remained consistent, doctor, that surrogate testing should be introduced.

Then we know that in May 1988 Chiron announced the discovery in cloning of the NANBH virus, albeit scientific details weren't published until a year later.

We then go into 1989, please, document [SNB0061975]. We see the creation of a new committee, the UK Advisory Committee On Transfusion-transmitted Diseases. The first meeting on 24 February 1989.

We can see those present didn't include yourself, doctor, but Professor Cash and Dr Mitchell were members. I'm not going to dwell on this committee because it will

be, I think, considered in more detail in the next topic, HCV screening, but just to see what was said about surrogate testing, if we could go, please, to page 4 -- I should have said the meeting was on 24 February 1989.

Page 4, item 7, "Non-A non-B Hepatitis", a discussion of various matters. Then paragraph 7.4:

"It was agreed that there should be no recommendation to institute ALT testing until the current study was completed in England. However, there was a degree of inevitability about the introduction of the test which was required by regulatory authorities in other countries to determine the acceptability of fractionated plasma products. This would be discussed with BPL in the near future."

I think you touched upon that earlier today, doctor, about there being a parallel, but in some instances intertwining, point about the need for surrogate testing of donations going into pooled plasma?

A. Yes.

Q. I'll explore that with Professor Cash a little bit more tomorrow.

We also see in paragraph 7.5 reference to the Ortho Pharmaceutical Company and their test.

The next document, please, is [SNB0019416]. This is

another new committee, which again I think will be looked at more closely in the next topic but the Advisory Committee on the Virological Safety of Blood. These are the minutes of the second meeting on 22 May 1989.

Can we go to page 3, please, again consideration of non-A non-B from paragraph 16 on.

Paragraph 19:

"Plasma fractionators were considering funding ALT testing once the scientific basis was established. This would be necessary if excess products were to be sold to Europe:

"20. It was agreed NANB testing should not be introduced into the NBTS prior to the results of the UK BTS NANB trial...

"21. The Department would keep the issue of testing under review. The use of Chiron or surrogate testing would be influenced by the Chiron data once released; MRC might be asked to consider. Members regarded the matter to be a priority."

The next document, please, is SNF0011387. This is a report of the multi-centre trial into surrogate testing. I think it's SNF0011387. It may have another -- yes, if we try perhaps [SNF0011383].

This is Dr Gunson's report. If we go three pages

on, we can see it's dated 3 November 1989. We can see that there.

Could we go back to the beginning, please, 1387? So he reports on the results of the trial. I think we can go to the conclusions, please, over the page.

So 4.1:

"Taken overall, 3.2 per cent of donors would have been rejected for raised ALT and 0.63 per cent for anti-HBc seropositivity."

A reference to the Swiss Red Cross' policy:

"A disturbing finding was the variability of ALT testing in the three centres. There were some donors in Manchester who had normal levels of ALT who would have been rejected in Bristol or north London.

"4.2. It is difficult to conclude how many of the donors with a raised ALT or seropositive for anti-HBc may have transmitted non-A non-B Hepatitis. To determine this a prospective study would have to be performed.

"However, it is evident that the ALT test is non-specific since the correlation with alcohol intake and obesity is striking. Similarly, the significance of a positive anti-HBc result is unknown.

"4.3. Following the introduction of the anti-HCV test the only justification for performing the ALT and

anti-HBc tests routinely is:

"4.3.1. The possibility that ALT (in particularly) will identify a 'window' of infectivity prior to seroconversion for anti-HCV.

"4.3.2. The possibility that anti-HCV only identifies one of a number of viruses which cause NANBH.

"The introduction of other specific viral markers and increased sensitivity of the anti-HCV test in due course may render the subject of surrogate testing of academic interest. Meanwhile, the desirability of introducing these tests remains an issue of health economics."

Simply for the record, without going to them, there is a fuller report of the multi-centre study into surrogate testing in April 1990 at [PEN0160075]. And then a published report in 1992 by Anderson and others, [PEN0170831].

So that's the end of the UK multi-centre trial.

I think, finally, if we could then, please, look at document [SNB0019563]? These are the minutes of the Advisory Committee on the Virological Safety of Blood on 6 November 1989.

If we go to page 4, paragraph 23, we see a discussion of non-A non-B Hepatitis and discussion of the Chiron test. And over the page, please,

paragraph 29 starts:

"The committee's feeling was that there was no case for using surrogate tests for non-A non-B."

So I think by this stage there was sufficient confidence in the Chiron anti-HCV test that the view of the Advisory Committee was that there was then no case for surrogate testing, and I think that's largely the end of the question of surrogate testing in the UK, subject to one or two points we will discuss with Professor Cash tomorrow, to do with ALT testing of plasma for pooled products.

Thank you, doctor, that completes the chronology of documents and events. I would like now to return to your statement to complete that, please.

We have now largely, I think, covered most of the documents and events I would like to take you to, so we will be able to go through your statement more quickly. The only question which occurs, sir, is that it is a few minutes to four. I'm happy to carry on a bit. I know Dr McClelland has to leave by ten past four or we can simply stop now.

THE CHAIRMAN: What's the progress after that?

MR MACKENZIE: If we could continue until 10 past, it might be helpful, because we have Professor Cash coming tomorrow, and if we could start just after 11, I'm sure

he will take until lunch.

THE CHAIRMAN: I rather think that there is considerable interest on the part of Mr Di Rollo in what we have been dealing with. At least I can't imagine that there is none. And I think I have to have regard to the total amount of time that's likely to be taken.

MR MACKENZIE: Yes.

THE CHAIRMAN: Do you anticipate taking all day with Dr Cash.

MR MACKENZIE: No.

THE CHAIRMAN: Did you anticipate getting Dr McClelland finished today?

MR MACKENZIE: No, I thought it was unlikely.

THE CHAIRMAN: I think that we have to take a reasonable judgment. If ten minutes would make a material difference, then fine.

MR MACKENZIE: I think it would help, sir.

THE CHAIRMAN: If it's not going to make a material difference, and Dr McClelland has to come back tomorrow, the notion of starting Dr Cash right away really doesn't have much substance, because I don't think you are going to finish.

MR MACKENZIE: I certainly won't finish Dr McClelland today, certainly.

THE CHAIRMAN: Let's take one more topic and see how we get

on.

MR MACKENZIE: I'm grateful, sir, thank you.

THE CHAIRMAN: But make sure, if I don't look like I'm responding to the time that you do.

A. Okay.

PROFESSOR JAMES: Get up and walk out.

THE CHAIRMAN: I'm not encouraging that.

MR MACKENZIE: Thank you. Well, doctor, we will make what use we can of the time we have.

At page 12, please, of your statement. We are back to the standard questions that we asked all witnesses and we had asked:

"The research undertaken by the SNBTS in the 1980s into surrogate testing for NANBH".

And you explain that:

"During the 1980s, two groups within SNBTS attempted to identify factors ('markers') in the blood that could be used to detect blood likely to cause NANBH."

The first reference is to Hopkins, publication in 1982, which is [PEN0170931]. I think the other reference is Tabor, 1982, [PEN0170933]. I don't have to go to either because in the next two paragraphs you explain the work in Scotland.

In 2.2 you explain Dr Dow's work in the West of Scotland, part of which was to seek to identify

a test which could be used to detect blood likely to cause NANBH. Ultimately, I think that work was unsuccessful.

And similarly 2.3, Doctor Hopkins in Edinburgh, along with Miss Sonia Field, I think who similarly sought to identify a serological marker, which again was unsuccessful, but there was no shame in that because, as you go on to tell us over the page, at paragraph 2.4, you explain:

"[The] Research groups in other countries pursued the same goal and it has been estimated that 30 or 40 candidate test systems were reported."

The reference there is the Dienstag and Alter paper of 1986 we looked at today and that:

"None of these efforts were successful. In 1989 the discovery of the causative virus was reported and designated as Hepatitis C virus."

Et cetera.

Then standard question 3, we asked why the multi-centre study into surrogate testing did not include a Scottish blood centre. I think the answer in short, doctor, is because the application for funding was refused.

I think we will take paragraph 3.1 as read.

Paragraph 3.2 you explain:

"This study could never have provided any information about (a) the incidence in blood recipients..."

Et cetera, and I think we have covered much of that ground this morning.

We have also given the references earlier in the evidence as well to the protocol for the study and the final published report.

You also go on to say you can't be certain why there was no SNBTS participation in the multi-centre study but you go on to set out various factors. I think we can take that as read because we have covered all of this ground.

I think I'll simply take the paragraphs in 14 as read because, as I say, we have covered the ground.

Standard question 4 was:

"Why it took until October 1988 until the multi-centre study into surrogate testing commenced."

Again, we can see your answer 4.1 and perhaps take that as read.

At the top of page 15 -- I'll take Professor Cash to a DHSS funding document, which I think is of some interest. I think we will keep that for tomorrow.

Standard question 5, the question of funding for testing, I'll leave that for Professor Cash. I think

that will be more appropriate.

In question 6 we asked:

"Why the SNBTS first sought funding from the SHHD in 1986 for the introduction of surrogate testing in 1987."

You refer in your answer to the American blood collection organisations by 1986 returning to the question of surrogate testing, and you are sure that's a factor in reactivating interest in the topic in the UK.

At the top of page 16, if I may ask you a question, you say:

"There was still a belief in the UK that non-A non-B PTH was a less important problem than in the United States and many of the more influential professionals in the UK BTS were opposed to the introduction of surrogate tests. I imagine that such opinions would have influenced professionals officers in SHHD."

Who were the more influential professionals in the UK BTS who were opposed to the introduction of surrogate tests?

A. Well, I think we have seen their names on correspondence and various other documents today but, for example, Dr Contreras was fairly strongly opposed. Dr Barbara, who worked with Dr Contreras, was at best ambivalent.

They actually were between them extremely influential.

I think we saw in other patients that other transfusion doctors in both the Scottish service and the English service had expressed doubts about the benefits in letters to The Lancet and so on, some of which we have seen this afternoon. So I think across the piece you actually find quite a number of individuals in fairly senior professional positions voicing reservations about this.

Q. Thank you.

Perhaps the final question for today, doctor, question 7, we asked:

"Why the directors ... agreed at their meeting on 3 March 1987 that surrogate testing ... should be introduced ..."

Again we have covered that, I think. You do say:

"We were undoubtedly concerned that despite the persisting uncertainties about the real safety gains that might be achieved, failure to introduce testing could constitute a failure to protect patients from some degree of avoidable risk."

Does that really come back to your position as stated before, about seeking to maximise the safety of blood?

A. Yes.

Q. Sir that, may be a reasonable place to stop?

THE CHAIRMAN: Thank you very much. Yes. I have got another bit of business, Dr McClelland. So you are free to go.

Ladies and gentlemen, I have had an application that the evidence of potential witnesses should be taken by affidavit, dealing with certain aspects of Mr Tamburrini's history. I hope that I have made it clear that I want these matters to be dealt with in public, at least as a matter of record, but, of course, the deaths raise particularly sensitive issues in respect that in particular in those cases only individuals are named.

I want to be as helpful as I can in dealing with this.

I'm not prepared to take a final decision on the use of affidavits at the moment, I have not seen the affidavits or drafts of them and so I can't form any view on the extent to which there might be conflicts between the contents of affidavits and the evidence that I have already heard on oath or on affirmation.

What I am prepared to do is to consider drafts of affidavits and, having done so, and having shared that information with Mr Anderson and Mr Johnston, to take account of any submissions that are made and then, if

appropriate, to decide whether I can treat the affidavits as acceptable evidence while both maintaining the integrity of the final report and without subjecting the content to examination here.

So, Mr Di Rollo, I think I'm putting the matter back in your hands again. I don't require a new application but if you want it to be processed, I think I really need to see the affidavits in draft and to consider how I can handle them. As you know, I have got some idea about the possible content of some of them but not in any way enough information to reach a decision.

I don't expect you to rush this. I imagine that it will take a little time to be in a position to deal with the matter properly, but unless you have got some overriding reason that I should listen to at this stage, that is my intention as to the way forward.

MR DI ROLLO: Can I ask for one point of clarification, if I may?

THE CHAIRMAN: Yes.

MR DI ROLLO: That is in the application, the suggestion was that the affidavit should be taken by a member of the Inquiry team or a member of the Inquiry staff, as opposed to the solicitors at Thompsons, and I think the proposal was that an affidavit in draft form would be taken by such a person and thereafter it could be

considered. In the proposal that is being made just now, is it being suggested that the affidavit will in fact be gathered in draft form by a member of the Inquiry staff?

THE CHAIRMAN: I haven't thought that through. I'm concerned about it because if a member of the Inquiry team is to take this affidavit and in effect to become involved in an editorial process before I see it, then I think the exercise might be compromised.

I think on this occasion the drafts should be prepared by Thompsons and submitted. If we go on to have affidavit evidence in substitution for oral evidence, then the matter will be considered afresh at that stage. Because, as you will appreciate, I would not want there to be any significant problem as between draft and final affidavit stage. But at this stage I would not wish to have a member of the Inquiry team in effect put in the position of having to decide what should or should not go into the affidavit of any member of the family or any other witness who was tendered.

MR DI ROLLO: Just as a follow-up, in terms of it being a draft affidavit, that would mean that the affidavit wasn't in fact sworn, it was just simply --

THE CHAIRMAN: That is so.

MR DI ROLLO: Very well.

THE CHAIRMAN: It is strictly a draft.
MR DI ROLLO: I understand.
THE CHAIRMAN: Is anyone else inclined to suggest that that is not an appropriate way to go forward?

Very well, that's what will happen. I would like it, of course, to happen within a reasonable time, Mr Di Rollo, having regard to my interest in surviving this Inquiry.

(4.16 pm)

(The Inquiry adjourned until 9.30 am the following day)

I N D E X