ATTENDANCE NOTE

DAVIES ARNOLD COOPER

SOLICITORS

CLIENT	NHSLA
MATTER	Dr Barbara's statement
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FEE EARNER	GDada
DATE	7 December 1999

Attendance on Dr Barbara at our offices from 12:25 to 16:30.

I briefly explained the purpose of the meeting, why we needed a statement and the areas I wanted him to cover in his statement.

He was aware that there had been some settlement proposal and I explained that although the case might be settled, we had to take into account the possibility that it might not be possible to settle the cases without a trial. Dr Barbara said that he understood.

He said that he felt that they were an open target because he thought that they could make an issue of the decision not to use anti-HBC and ALT, again about the decision not to use the first generation tests. He thought that the gap between the introduction of the second generation tests and screening which had been introduced was indefensible. He did not know what he could say about that.

They did not go for first generation tests because of the cost benefit, the lack of scientific evidence and the disruption to the blood supply.

First there were the first generation tests and there was a lack of confirmatory tests and then the second generation tests. There would not have been any reason other than a timetable as to why the second generation tests were not used and he found that hard to justify.

He would say that they never believed that Hepatitis C was that serious but he thought that it would be difficult to hold to that view when the "rarities" were in front of him.

I asked him about Australia and he confirmed that he had made a witness statement which he thought may have been served but the claims had not materialised and he had not had to give any evidence. Both he and Dr Gunson had been approached by the Canadians but had decided not to get involved. He confirmed that he did not have any big slots of holiday within the next few months.

We discussed the timetable and the possibility of a trial in October 2000.

I explained that we would need a copy of his curriculum vitae and to identify his role at the MBA. We would also need to discuss surrogate testing and the HCV tests.

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Dr Barbara said that surrogate testing would cover the period from 1978-1989 and between then and 1991 the HCV test.

He said that he had a large CV which he had done when the MBA was first reorganised and that it had not recently been updated. This is about 4-5 years ago. He would ask Marina to send me a full copy. It included a detailed list of his papers, but that his recent publications were not included. He would ask the research fellow who worked with him to dig out his recent publications.

I said that it was important to have all his publications and published letters to show that they were consistent with his statement or at least to explain the differences. I explained that it was important that if there were any difficult areas in relation to his evidence that we had the opportunity to consider them now and to cover them in his statement rather than hope that the Claimants would not pick up on the published article.

He said that he thought we should get a statement from Marcela Contreras because she was very vocal in her reluctance to introduce screening. He suggested that Patricia Hewitt should also give evidence because she was logical and clear. I asked if she had been involved in the decisions at the time and Dr Barbara thought that she may have been having children at that time. He said that Marcela Contreras still believes that Hepatitis C infection was overrated.

He referred to a paper by **Leonard Sieff** to an update which showed that there was no change in the death rate after a couple more decades study.

Dr Barbara wanted to know who else was on our side and I mentioned that we were obtaining statements from Professor Zuckerman, Dr Craske and Dr Gunson. We did not know whether Professor Zuckerman would be entirely supportive, but we would obtain his statement and take it from there.

Dr Barbara said that Marcela would give a vigorous account of the perception at the time that Hepatitis C was not worth the candle. He wanted to know if we were obtaining statements from anyone from abroad. I said that we'd considered Holland, but that we had decided against it.

Dr Barbara said that I should watch the Panorama programme and that it was important to note that the responses he gave in the programme were responses to the wrong questions. I said that if this was the case that this might have to be covered in his statement.

Dr Barbara said that he started in service in 1974 and from his recollection, Hepatitis B surface antigen testing started around 1971. It was not introduced uniformly but over the year was introduced to the centres. At the time there was a broad national approach but there was no national policy. He thought that the MBA could be criticised for that.

I explained that there were a number of points which Counsel had noted from the draft statements prepared by Simon Pearl following a meeting with Dr Barbara. I will deal with those first.

There was a reference to a paper by Moira Briggs. Dr Barbara thought that this would be in his references and that if I couldn't find it then I should give him a ring. I said that I had not been able to find it and he said that he would look for it.

I asked him about the NIH studies. He explained that these were a series of test looking more prospectively at post transfusion hepatitis and recipients. This included for example a paper by Moseley et al on TTVS. He said that this paper was still tapped into to answer questions on post transfusion infection.

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The other source of the perception that non a non b hepatitis was a mild infection was from conversations, conferences, from talking to people. He said that in the basic reviews of non a non b a figure of 90% was cited as being asymptomatic. He could not remember the references off hand but suggested that we speak to Marcela.

On 4.4, the question as to who thought non a non b was more prevalent abroad and that the incidents were low in the United Kingdom, Dr Barbara referred to a study at North London by the Medical Research Council, a paper by Zuckerman in the 70s and the paper of Collins and Bassendine.

I asked about the prevalence of Hepatitis C infection in donors in the early 1980s. Dr Barbara did not know what the prevalence was but referred to the Collins and Bassendine paper. He said that there were not many papers on this issue. The HIV questionnaire, which reduced the number of Hepatitis C infected donors presenting for donation was started in or soon after September 1983. He said that the question initially asked if people were rampantly homosexual or if they injected drugs, that they were not to give blood. He worked in North London where they had one of the highest rates of homosexual donors and they noted that the question they did not change the number of homosexual donors presenting to give blood and therefore the questionnaire had to be revised to say that if they had ever been homosexual they were not to donate blood.

Dr Barbara explained the history of his association with North London and the fact that at North London because of the larger homosexual population they had more experience of Hepatitis B. He had started counselling for people with acute Hepatitis B and this was the first in the UK.

I asked if there was anything in the Panorama programme that he was concerned about. He said that he was not. With hindsight he thought that if he was asked about the introduction of screening now that his response might be different but that his decision would probably have been the same if hindsight was not involved.

Another paper on the prevalence of non a non b outside the UK was the paper of Cossart. This was in Sydney. It showed a 2% post transfusion rate.

Dr Barbara then referred to the paper by Henke Resink on non a non b which showed a predictor value of 17% using the first generation HCV test. He said that in the UK we had got a rate of 16.4%. This meant that for every real positive result there were several false positive, the test had a predictor value to the tune of 15-16% only.

The papers which supported the view of a change of perception of effects on the liver of non a non b were the papers by Harvey Alter and Dame Sheila Sherlock also at meetings.

The papers which had a high prevalence of post transfusion hepatitis by those who'd been transfused were the Japanese papers, paper by Esteban in Spain and Harvey Alter's textbook references. The paper by Sheila Pollikov was in fact the paper by Wood in 1989. Pollikov was not the first author.

The independent studies which showed a relationship between non a non b and ALT levels were the papers by Stephens in New York. This paper had the clearest exposition of the relationship between ALT and non a non b and it also showed increased levels of ALT were even more predictive - query the ..... It showed the combination of the two, ALT and anticore had a 50% predictive value. This approached the predictor value of the first generation test in a New York population.

It was important to appreciate that the predictor value depended upon the prevalence of the condition and the population and where there was low prevalence this would affect the predictor value.

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There was a multi centre trial by the NBA but only part 1 of the trial was carried out, not part 2. This showed a much lower rate, an anticore of 2.7%. The part 2 results were noted by Harold Gunson and they showed that only two patients were anti core positive and that only one of them was HCV positive so the predictor rate was 50%. This meant that of 9,125 people tested only 2 had anti core and only one of them was anti HCV positive. This was a rate of 1 in 9,000 for HCV positive which was a bit lower. A 1 in 4,500 for anti core.

The problem was that these results did not tell you those that had been missed by the assay and that he would say that they had missed 8 if the rate was 1 in 9,000. He thought this because of the data at the time which indicated the incidents.

Dr Barbara said that the question of anti core ALT were discussed regularly at ACTTD advisory committees. It was formally looked at in the study by Anderson.

North London had published earlier studies, by Tedder, Barbara and Cameron on anti core and anti HB surface antigen. They showed a 2% were anti core positive before HIV risk donors were excluded and afterwards this went to 1%.

He explained that ALT studies were performed from the mid 70s onwards at the North London. At the North London a lot of microbiological studies were performed because of him, he was the only microbiologist in the blood service. He had a PhD in Microbiology and a remit to conduct microbiological research and development. On the other hand, other blood centres had senior technical staff and no remit for research and development. Cleghorn had arranged this because of Professor Dane who was at the Middlesex and an Honorary Consultant at North London. Dr Barbara researched at the Middlesex.

Dr Barbara said that he would send me the ALT papers.

They had not used the ALT papers because Gunson had said that they applied to North London and not the NHS and so they had to do a national survey because the risk of Hepatitis B in North London were higher. Dr Barbara said that North London had 75% of the homosexual community in the whole country. The higher Hepatitis B rate was attributable to the homosexuals and to the fact that there were more ethnic groups in that area. From 1974 ALT and protein levels were done, even before he started because Cleghorn did regular plasmapheresis and bled donors frequently. He thought it might have been to monitor the donors and that if there was a sustained significant rise in the Alt to do more detailed Hepatitis A and B tests and if ALT levels were high to exclude the donors and retest them in a year's time.

I asked if the ALT test was used to exclude the donors absolutely and he said that it was not. He said that if a donor had a high ALT and then it went down the following year they would use the donor again

The studies which showed ALT to be a non-specific indicator were Stephens and the studies which showed that the majority of people with raised ALT this was due to alcohol or obesity were the papers by Alter. The UK study which showed an incidence of Hepatitis C of 1-2.4% before the introduction of self exclusion for donors at risk of HIV was the Collins and Bassendine paper. Dr Barbara said that this was a very small study and very selective but was as good as it got because there weren't others. There was also a paper by Zuckerman.

The Glasebrook paper in 1982 Dr Barbara thought was important and he said that he would obtain a copy.

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He said that the other important paper was the paper by him and Marcela Contreras in the Lancet in 1991 which looked at the lower incidence of post transfusion hepatitis in the North London domain. The Glasebrook paper was a paper which showed how the Hepatitis C clone was defined and it was important because they were able to definitive work to check the confirmatory tests.

I explained to Dr Barbara that I had tried to work out a chronology of the different studies that were done at different stages and how they related to the introduction of the various HCV tests including the confirmatory tests and that I had found it quite confusing. I had the impression that some studies were started using a particular test and then if another test was introduced during the course of that study the study was changed to include the new tests. Dr Barbara said that this had happened.

He confirmed that he had done some tests on some of the Elisas when they became available such as the Ortho Abbots, RIBA and Welcome. There was no unified programme, they responded to the latest novelty.

There was no unit or transfusion research, the research depended on people working for the NHS who were interested in trying to do more.

Most of the studies performed by the MBA on the HCV tests were not published, the Scottish had carried out more research and had published their research. He suggested that we spoke to Eddie Follett and to B Dow.

He thought that we had a list of when the different assays became available and we considered his handwritten notes on this. I said that we needed to understand when the different studies were done and what the results showed, how they affected the MBA's decisions.

Dr Barbara said that the problem was that a chunk of his filing had gone and that he was relying on slides of lectures he'd given to show what studies had been done. These studies were not as he said published, but reported at specially convened review meetings or national meetings. It was the Scottish that tended to publish.

He thought that Eddie Follett would be useful because he would attest to the non-specificity of the tests and that he would be able to provide a chronology of what was available when. He described him as his opposite number in Scotland.

Dr Barbara said that he thought the dates of the introduction of the different tests as set out in the ACVSB memo in 1992 were correct.

Dr Barbara recognised that there was a confusion about the studies and the fact that it was not always clear if the references to the studies in the minutes were to the same studies or to additional studies. He said that some of the studies were multi centre studies to spread the load but that this had resulted in confusion when trying to map out what had happened. He suggested that we address this later when he had had a look at his Lancet article with Dr Contreras in 1991. He thought this might clarify.

I asked when he concluded that it wasn't possible to detect Hepatitis C by the same method as Hepatitis B. He said that this was based on the experience of people who had tried assays for Hepatitis C and they had all failed. He said that Alter had a cartoon slide showing people falling off a cliff and these were meant to represent the number of researchers who had tried to find an assay for Hepatitis C. He had understood as a Microbiologist that it was accepted wisdom that non a non b was not the same as Hepatitis B and that his appreciation to some extent was personal because he was the only Microbiologist in service and his perception had been that b surface antigen was an exception because of his history of working with smallpox and vaccinia that you could not use the same method. He

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would never use a gel to detect the virus because there would not be enough antigen. He saw Hepatitis B as different. It is an exception because Hepatitis B produces a large excess amount of surface antigen. He noted however that Ortho had recently announced an HCV antigen assay.

He referred to a study by Skidmore with haemophiliacs who had received inactivated factor 8 concentrate. They were tested with the HCV assay almost like a confirmatory test. This study was exciting because they had tested two variables at once. The variables were 1) does heat inactivation work and 2) is the assay seeing something different.

He said that the assay was quite effective when used on selected people who were known to be HCV positive and that all of them in the study had been positive with the HCV test.

I asked why there had been a reluctance to use the first generation HCV. If there were no confirmatory tests at the time, how did they know then that the test was of a low specificity and sensitivity.

Dr Barbara said that at the first meeting with Ortho, they'd been told that the assay was an antigen assay to a non-structural component. He thought that it was therefore likely to be insensitive. Traditionally, one would want most assays to be destructural antigens. He predicted that because the assay was globulen based that it would probably be non-specific. At the first training at the AVB meeting, he recorded that they had seen a video with Harvey Alter who had said that he didn't think that a confirmatory test would be necessary. He recalled that that had made him annoyed and that he had said that until they had a confirmatory test they couldn't tell if one was necessary. They could not assume that the tests would be completely specific because it was well known that anti globulen assays could result in false positive results.

Dr Barbara said that if you took the people with all the clinical indications that they were infected, you would expect them to be positive and normals to be negative. The clearest example of this was the paper of Reesink and North London 1991 in the Lancet. A follow up of post transfusion Hepatitis looking at elevated transaminases on two occasions, this was the classical definition of post transfusion Hepatitis and then testing the donors in cases of positive donor implicated.

Dr Barbara said that it was important to remember that although the papers were published later, they would have been discussed earlier than that. His concern about Hepatitis C first generation test was a theoretical concern and then there was the Reesink paper.

He also referred to the Garson paper in 1991 on the PCR test. The PCR test was used as a research tool but gives some useful information about the specificity of the test. He also said that the Van Poel study was important. His paper on the for and against introduction of HCV screening at an earlier date was also important.

He said the problem was that the service did not want to screen and that they were making up the reasons for it retrospectively. They need from the previous Bassendine & Zuckerman papers that the prevalence of Hepatitis C was lower. The transfusion services perception of Hepatitis C would have been different from that of the Hepatologist at the time. They always felt that America was more at risk and from the TTV Moseley paper showed a 10% post transfusion rate.

We discussed the incidents as described by Bassendine which seemed to show that there was an incidence of 7 in 1000. Of these, Dr Barbara said that 1-2 per 100 would become infected. He said that because there were no reports of post transfusion Hepatitis like the US and in hospitals, that if we were getting rates of complications as predicted by the worst case then the wards would have been littered with non a non b due to transfusion and that there was a bias in the perception of Hepatitis C as a

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problem, depending on practice. He thought that the papers would help to show what they were doing at the time.

He referred me to the MIC working party on post transfusion Hepatitis in 1974 by Ari Zuckerman. This would cover the incidents. They considered the post transfusion hepatitis to be low. This was on the figures for pre-1983, there were none for afterwards. Taking into account the self-selection questionnaires they would expect the prevalence to be even lower.

Dr Barbara asked if we would compare his statement with Dr Gunson's for consistency and I said that we would.

In relation to the 1990 doctor study I asked why we had taken a different view from Holland on testing with the first generation when we associated our situation with Holland and considered the US situation to be entirely different. Dr Barbara said that he did not recall meetings where they look collectively at the studies from Holland. He thought that the momentum was so that they were not going to introduce the tests that either they didn't think of it or that it was a question of costs. I would have to ask Marcela. He said that Marcela influenced the decisions at the RTD and that he was only invited by invitation.

He thought they may also have felt that it was less clinically relevant. He said that anti core was used in the US for non a non b but it was not FDA requirement but it was an APB recommendation.

Going through the further discovery questions with Dr Barbara and noting his responses on attendance note of 26th November 1999.

I said that I would consider the references that Dr Barbara had recommended and that we would arrange to meet up within the near future while our discussions were fresh in both our minds to see if we could make some headway with the chronology and with his statement. I will discuss with the team his suggestions for obtaining a statement from Marcela and from Eddie Follett.

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