CAL34 ResponseC5(011211)

Response to request of 16th November 2011 from the Penrose Inquiry for a

Witness Statement in relation to Topic C5 by

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Draft

Topic C5 includes

C5a) The information given to patients (or their parents) about the risk of non A non B Hepatitis and the severity of the condition before their treatment with blood or blood products;

C5b) the tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products; and

C5c) the information given to patients who might have been infected, or who were found to be infected, and their families.

The request for the Witness Statement includes questions in relation to Testing and Consent and Communication of Results and Implications of Diagnosis. The narrative set out below includes information which addresses these questions.

1. **Background**

   The topics C5a – 5c have been addressed in the Collective Response by the Haemophilia Service in Scotland. To this document are attached many annexes (which, to avoid duplication, will be referred to in the text of this Witness Statement). This was document was primarily developed by Professor Lowe, Dr Gibson and myself and therefore reflects much of the practise in Edinburgh (and elsewhere).
   In addition the following documents have been submitted previously to the Inquiry and these address issues in relation to the development of many specific aspects of the service and their content contributes to the documentation pertinent to Topic C5

   a. **Edinburgh Haemophilia Treatment Policy** (CAL16) reviews the risks of hepatitis including non-A non-B hepatitis (including the possibility that there may be more than one type (cause).
   b. **Development of the Edinburgh Haemophilia Centre** (CAL20) includes a description in
      i. **Section 4** of **Arrangements at Haemophilia Review Clinics.** The document reports the appointment to a newly created post of

Haemophilia Sister in 1982. She and her successors played a major part in interacting with the patients and their treatment on a day to day basis especially in the early 1980s when very many of the Edinburgh patients were still having to attend hospital for treatment of acute bleeds because of the limited supply of NHS concentrate preventing the wide uptake of home therapy.

ii. **Section 19** of the **Arrangement for Management of Hepatitis** which sets out the background to Hepatitis B and in particular the studies in 1986 with Dr Hopkins who had developed a possible test for non-A non-B hepatitis in 1986.

iii. **Section 20** describes **Treatment of non-A non-B Hepatitis from 1988** onwards before HCV was identified.

iv. **Section 21** describes the **Augmentation of the Service after the discovery of HCV.**

v. **Section 22** outlines the opportunities for **Liver Transplantation**.

c. **Long Term Safety Monitoring for Transfusion Transmitted Infections** (CAL21) describes the background and initial activities in relation to hepatitis B and non-A non-B hepatitis (although the major portion of the document relates to the emergence of AIDS in 1981/2 and the Edinburgh response to this perceived threat).

2. **Response to C5a** *The information given to patients (or their parents) about the risk of non A non B Hepatitis and the severity of the condition before their treatment with blood or blood products;*

a. The arrangements for informing patients about the risks of non-A non-B hepatitis before treatment are set out in the Collective Response. The large majority of individuals were infected very early in their lives, many in the 1970s and at a time when little was known about non-A non-B hepatitis and therefore little information was available. Within South-East Scotland up to the early 1980s patients with haemophilia were treated in a number of district general hospitals as well as small hospitals in Edinburgh, so it was impossible to know what the patients had been told about hepatitis.

b. It was our policy to inform patients (and parents of children) of all the risks of haemophilia as well as its treatment, including hepatitis because virtually all recipients of blood products were likely to be at risk or suffer from this complication. If an individual was known to have haemophilia some time prior to requiring treatment information about the condition including how bleeds

might present and be treated was offered. This would have included the complications of haemophilia itself and of its treatment. Discussion of hepatitis, like inhibitors, would be important topics. Information leaflets and contact with the Haemophilia Society was encouraged (see later).

c. About half of all children with severe haemophilia arise in families without any other individual in the family having the condition. Thus these individuals are only diagnosed once they bleed. By the time the diagnosis is made the child may have had the bleed, usually into a joint, for some time and be very distressed by the pain. Although it was our policy to inform patients, requiring blood product for the first time, of the risk of hepatitis, if diagnosis of haemophilia was concurrent with an acute painful bleed it is to be expected that information given might not be later recalled. Not only were (usually) parents having to try and quickly understand about the condition of haemophilia but they usually had a very upset child to comfort. In these stressful circumstances the chance of the information given being recalled would be reduced because of the stress. At an early stage patients and parents would be given booklets about haemophilia which included information about hepatitis and encouraged to join the Haemophilia Society (details set out in the Collective Response).

d. In the early 1980s I would have explained that we were using cryoprecipitate, for small children, to try and reduce the risk of hepatitis and that we were trying to avoid the use of commercial concentrates because of the perceived increased risk of hepatitis compared to NHS concentrates. My trying to avoid commercial concentrates was well known to patients (for instance because each patient was given a small statement to place in their Haemophilia Card to recommend that they should only receive NHS concentrates if they visited another Haemophilia Centre for treatment).

3. **Response to 5b** '*the tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products;*'

a. The narrative set out in the documents, itemised in the Background (para 1), describes the routine surveillance of patients for hepatitis viruses. This was part of the regular review of patients along with the other usual blood tests including liver function tests. In relation to non-A non-B we initiated treatment, under the supervision of Dr Peter Hayes, with interferon in Edinburgh in 1988

following the report of its successful use in this condition by Hoofnagle et al (NEJM 1986, 315; 1575). As this was prior to the identification of HCV, it was only possible to monitor the response to interferon by measuring the ALT (one of the routine liver function tests that is often raised in hepatitis).

b. Following the publication reporting the identity of HCV in 1989 (Choo et al, Science 1989; 242: 359-62) the initial antibody test was established at the Central Public Health Laboratory in Colindale. Our initial 'anonymous' testing of stored samples revealed that 85%% were antibody positive but this was less than anticipated from the studies of Fletcher and Kernoff in 1983-5 which suggested that virtually all patients who had received clotting factor concentrates became infected. It was interesting to note in this small study that none of 5 patients that had only been treated with heat-treated concentrate were anti-HCV negative (Ludlam et al, Lancet 1989, ii; 560-1). Over the succeeding two years we assessed not only different antibody detection methods (Watson et al Br J Haematol 1992, 80; 514-518) but Prof Simmonds set up a PCR based assay to detect HCV viral RNA in patients' plasma (Simmonds et al Lancet 1990, 336; 1439-72). This led on to his leading work on the characterisation of the different HCV genotypes (1 to 6). From these initial investigations it became clear that the first generation antibody test did not have a sufficient sensitivity to identify all previously or currently HCV infected individuals. Later it became apparent that the second generation assays had a higher sensitivity and specificity. By 1992 we had reliable and sensitive assays for detection of both specific antibody and the circulating HCV virus (by PCR) and these were offered by Prof Simmonds as a clinical service. It was at this point that we felt confident to provide the results of these tests to patients.

c. When reliable tests were available, and although some of the patients will have been tested from stored samples during initial studies to validate the techniques, in all cases a fresh sample was sought from the patient, after explanation and consent. The patients being told that we considered that we had a sensitive and specific test for both the antibody and virus which was responsible for the majority of cases of non-A non-B hepatitis. The result would be essential in deciding who might benefit from anti-viral therapy, e.g., it might be appropriate to offer therapy to PCR positive, rather than PCR negative, individuals. The patient would be given the result at the next clinic visit (or earlier if specifically requested). In most instances there was no need for the patient to receive the result urgently. The HCV tests were offered to all

patients who we identified as having been exposed to blood or blood products.

d. **Clinical service for HCV positive patients**

With Dr Hayes we developed an innovative programme for assessing the liver disease in those with haemophilia. He would come (and still does) to see patients when they attended the Haemophilia Centre (rather than the patients attending a separate gastrointestinal/hepatology service - initially this was at a time long before there was a funded and resourced formal 'HCV service'). Investigation included laparoscopic visual assessment of the liver and in some instances a biopsy (guided by laparoscopy). This led on to patients being offered interferon treatment. Endoscopies were offered to appropriate individuals (particularly to assess for the presence of oesophageal varices – which could be treated by 'banding', or a beta blocker to reduce the risk of catastrophic bleeding (both techniques pioneered by Prof Hayes). Ultrasound was also one of the routine investigative tests to assess the liver. Those with cirrhosis were, monitored initially 4 monthly (but now 6 monthly) in an attempt to detect hepatomas (cancers) early when treatment can be effective.

For the past 14 years we have been very fortunate to have had the generous commitment and ready availability of Prof Peter Hayes to see our patients in the setting of the Haemophilia Centre, when they attend for their routine or other appointments. We have monitored the individual patients (with alfa-feto protein, hyaluronic acid and abdominal ultrasounds), under his detailed supervision. He has been prompt with the introduction of new therapies, eg Ribravirin and pegelated interferon. We are about to start treating appropriate patients with the new ant-HCV drugs for those with resistant genotype 1 active hepatitis, e.g. Boceprevir and possibly Telaprevir.

4. ***Response to 5C*** *'the information given to patients who might have been infected, or who were found to be infected, and their families'.*

a. The Collective Response and other documents described in Background (para 1) contains details of information and how it was made available to patients and family members in Edinburgh. It describes in detail the various ways in information was disseminated. This was an continuous and ongoing process to keep patients abreast of developments because the situation changed during the 1980s quite substantially with the appearance of HIV, the realisation that non-A non-B hepatitis was progressive, that its transmission

could be reduced by some viral inactivation processes, that interferon was potentially valuable therapy and finally the identification of HCV and the development of specific tests at the end of the decade.

In Edinburgh patients were aware of my concern about hepatitis and its possible causes because there were frequent discussions about results of liver function test abnormalities especially at review clinics. It was also well known that we were storing small aliquots of blood for future investigations (as was customary with all samples sent from all clinics and specialties to virology). Furthermore we had a series of Lecturers from 1979 to 1996 (Dr Stirling, Dr Cuthbert, Dr Watson and Dr Hanley) whose principal responsibilities were the investigation and monitoring of viral infections in those with haemophilia. These individuals were very much in touch with the patients as they provided a great deal of the front line clinical care as well as monitoring the effects of viral infections and ensuring that patients were offered appropriate treatment. There was a very open policy of giving patients the most up to date information about hepatitis, their individual results and our assessment of their clinical situation.

The information given to patients with non-A non-B hepatitis was continually updated with the developments in knowledge and practise. For example in the late 1970s and early 1980s it was a puzzling condition of uncertain aetiology but not known to be serious. At this stage there was no evidence that it might be sexually transmitted. It became clearer in the mid-1980s that it was a potentially serious and progressive condition although it has taken many further years of study to begin to obtain a reasonably reliable estimate of the risk of cirrhosis, liver failure and hepatoma development. Once it became clear that it was progressive and after Hoofnagle's paper in 1986, patients were informed of this and we consequently initiated studies to use interferon treatment. With the advent of HCV testing it became clearer which patients were most suitable for interferon treatment so that it could be better targeted and response assessed by quantitative HCV PCR.

b. Whilst the Collective Response and its Annexes gives a good overall view of the information and the many ways it was made available the following highlights some of the more local documents in Edinburgh

i. The 'home treatment consent' form devised in the late 1970s makes very specific reference to the possibility that clotting factor concentrates may transmit infection. (Collective Response Annex 12)

ii. All patients who were in receipt of blood products were given a small statement to put in their Haemophilia Cards which requested that if the patient went to another Haemophilia Centre he should, if possible, be treated with cryoprecipitate or NHS concentrate rather than commercial products. The reason for this was explained to all patients individually when they were given the statement. (Unfortunately no copy of this is available).

iii. In 1986, in conjunction with Dr Hopkins, we were assessing a new test which was thought might identify those with 'non-A non-B hepatitis' and I wrote to many patients explaining that we might have a new test to seek their consent to assess blood samples. (Collective Response Annex 13)

iv. A Hepatitis C Patient Information Sheet and Investigation Checklist – these were developed in the early 1990s. (Collective Response Annex 18).

c. Other sources of information for patients are outlined in the Collective Response. Leaflets from the Haemophilia Society and British Liver Trust were readily available in the Haemophilia Centre waiting room and individuals were given information about contacting these organisations.