Witness Name: Professor John Stuart Lilleyman
Statement No.: WITN5095002
Exhibits: N/A
Dated: 24 February 2021

INFECTED BLOOD INQUIRY

SECOND WRITTEN STATEMENT OF JOHN STUART LILLEYMAN

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 10 February 2021.

I, Professor John Stuart Lilleyman, will say as follows: -

Section 1: Cryoprecipitate use

1. **In your first statement to the Inquiry [WITN5095001], you state that throughout the relevant period, you aimed to avoid treating patients with Factor VIII concentrates, instead preferring cryoprecipitate for its superior viral safety. Was this approach taken in relation to all patients at the haemophilia centre at Sheffield Children's Hospital, regardless of age? Or, did this approach depend on the age of the patient - for instance, was cryoprecipitate the preferred approach for younger children only? If it did depend on the age of the patient, please indicate the relevant age. Please explain in as much detail as you are able to.**

1.1 From 1975 (when I started as a consultant at the Sheffield Children's Hospital caring for children with haematological disorders) I used intravenous cryoprecipitate as the preferred routine treatment for boys with Haemophilia A who had spontaneous bleeds. This is because it contained a concentrated amount of factor VIII in a minimum amount of plasma, a major consideration in children whose blood volume was proportionately smaller than adults. Fresh

frozen plasma, effective in adults, would overload the circulating blood volume of (say) a six-year-old. The Regional Blood Transfusion Service supported our requests and reserved supplies of cryoprecipitate for our use.

1.2 In circumstances where higher circulating levels of factor VIII were needed, such as major injuries, emergency or elective surgery, we would have used the non-commercial Oxford NHS Factor VIII fractionated concentrate available at that time on a named patient basis for the Sheffield Haemophilia Reference Centre directed by Professor Eddie Blackburn. Such concentrates were just becoming available from academic institutions and pharmaceutical companies and were being used increasingly as first line therapy in many haemophilia centres. For our children, when cryoprecipitate was not considered adequate for more serious bleeds or to cover surgery, they would have received treatment with these agents, mostly from UK sources as available, but some from international commercial pharmaceutical companies as well.

1.3 By 1978 it was becoming clear from several studies that blood tests looking at liver function in haemophiliacs were sometimes persistently abnormal, and our small study at Sheffield Children's Hospital confirmed earlier reports from adult patients that liver biopsies from such patients showed chronic hepatitis, suggesting that viral hepatitis transmitted via blood products would seem to be the most likely source. Which viruses was not clear, but careful testing for related antigens and antibodies seemed to suggest that hepatitis A and/or hepatitis B were not the most likely culprits. Other viruses then vaguely referred to as Non-A Non-B were unidentified until Hepatitis C was discovered in 1989.

1.4 From our own and similar studies by others it became clear that exposure to Factor VIII concentrate fractionated from large pools of human plasma was a common factor in those with chronic hepatitis. Our conclusion in 1979 was that *'only brief exposure to FVIII concentrates (13-45 batches) is necessary to produce chronic liver damage in at least 25% of haemophiliacs requiring regular treatment. As children usually receive treatment in hospital until considered suitable for treatment at home, we recommend such patients should, if possible, be treated with cryoprecipitate in preference to large pool FVIII concentrates until the significance of the liver damage is better understood, or until such FVIII concentrates have been refined to exclude viral hepatitis agents.'* (See Document OXOUHOOO3758_006)

1.5 This therefore remained our standard therapeutic approach to treating young boys with haemophilia in hospital up to 1985. The volume of cryoprecipitate used in any one clinical situation would have depended on the post infusion level of factor VIII needed. As before our concern about hepatitis, cryoprecipitate would still not be first choice for a life-threatening bleed such as intracranial, or for a major injury, but would for the much more common episodes of spontaneous joint bleeds and minor injuries. Higher levels of factor VIII needed for longer periods of time would swing the decision towards the use of large pool concentrates but using cryoprecipitate for everyday events we hoped would keep the risk of virus transmission lower. Not zero, but much lower. This approach also serendipitously gave some protection to our young haemophiliacs when HIV unexpectedly appeared in commercial factor VIII concentrates in the early 1980s.

1.6 After 1985 and the successful heat treatment of all available fractionated Factor VIII concentrates to eliminate virus transmission there was no strong case for continuing to use cryoprecipitate as a first-choice therapy. However, up to that date, it had offered one of the safest options to avoid serious infections and in my view served its recipients well.

Section 2: Other Issues

2. Please explain, in as much detail as you are able to, any other issues that you believe may be of relevance to the Infected Blood Inquiry.

2.1 Pre-1985, before heat treatment for viral inactivation, the main factor that contributed to the likelihood of transmission of viral infections by blood derived Factor VIII concentrates was the health of the blood donors providing the plasma used for its fractionation. In the country that produced the most Factor VIII, the USA, the various pharmaceutical companies concerned paid their plasma donors, as many as 60,000 donors per batch, and these donors apparently included prisoners and drug addicts. Only a single donor from such a high-risk background would need to be carrying hepatitis C or HIV to contaminate the whole batch.

2.2 In the UK, the greatly increased demand for fractionated freeze-dried Factor VIII for home-based treatment in adolescents and adults with haemophilia meant that

the National Blood Transfusion Service struggled to supply enough plasma from its volunteer donor system for UK based products to meet demand, so imported Factor VIII was widely used, and the devastating outbreaks of HIV and hepatitis C followed.

2.3 After the advent of heat treatment for effective viral inactivation of plasma-derived Factor VIII in 1985, the incidence of transmission of HIV and viral hepatitis plummeted. Then in 1993 came recombinant Factor VIII, a laboratory made product not derived from human plasma, which has provided the most promise for trouble free and effective therapy so far.

2.4 For me, the story ended in 1995 when I left the Children's Hospital to take the chair of paediatric oncology at St Bartholomew's Hospital, and I have had no contractual responsibility for care of boys with haemophilia since that time. Now, in retirement, I occasionally read of real progress being made in gene therapy to correct the genetic aberration that produces this crippling disease and hope that soon the future will be very much better than the past for those with this disabling disease.

Statement of Truth

I believe that the facts stated in this witness statement are true.

Signed: **GRO-C**

Dated: 24 February 2021