Witness Name: Dr Vivian Eric Mitchell

Statement No.: WITN3174003

Exhibits: WITN317 4004- TBA

Dated:9th October 2020

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DR VIVIAN **ERIC MITCHELL**

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 29 July 2020.

I, Dr Vivian Eric Mitchell, will say as follows: -

Section 1: Introduction

1. My name is Dr Vivian Eric Mitchell, DOB GRO-C 1945, my address is known to the Inquiry. My qualifications are MB, ChB, FRCP, FRCPath.
2. Sheffield Hospitals Medical Rotation 1970 - 73:

   Training scheme in general medicine leading to the examination for membership of the Royal College of Physicians under the supervision of various consultants including Sir Robert (later Lord) Kilpatrick, Dr J D Ward, Professor D S Munro, Professor Sir Charles Stuart-Harris. Duties included care of patients on acute medical wards, emergency admissions and attending outpatient clinics.

   SHO Coronary Care and General Medicine

   Registrar Diabetes and Endocrinology

   Registrar Respiratory and Renal Medicine

   University Hospital of Wales and Llandough Hospital 1973 - 1975:

   Registrar in Haematology - Initial training in laboratory and clinical haematology rotating through the laboratories and sub-departments, care of patients with haematological disorders. I spent 6 months with similar duties at an associated hospital.

   Sheffield Royal Infirmary 1975 - 78:

   Senior Registrar in Haematology - Higher training in haematology leading to the MRCPath examination with duties in both laboratory haematology and care of in- patients and out-patients. This was mainly at Sheffield Royal Infirmary but included 6 months at Northern General Hospital and secondment to Sheffield BTS.

Sheffield University 1978 - 79:

Welcome Research Fellow - Research into smoking and thrombosis.

University Hospitals of Leicester November 1979 - November 2003:

Consultant Haematologist. Duties described below.

3. I was a member of the UKHCDO from 1980 and a committee member from 1995 to my retirement in 2003.

4. I have not been involved in other inquiries or litigation.

5. **Section 2: Decisions and actions of the Leicester Centre and your decisions and actions**

   . I was responsible with two colleagues for providing a full clinical and laboratory haematology service to three acute hospitals (Leicester Royal Infirmary, Leicester General Hospital and Groby Road Hospital - later Glenfield Hospital) and a population of one million. I was also responsible for developing a service in haemostasis and thrombosis including haemophilia.

   . Up to this time there had been no one with a specific duty to provide haemophilia care which had in fact only been available in Leicester for a few years. A new Haematology Department including a Haemophilia Centre was in the process of being completed.

   . After I arrived my consultant haematology colleagues Dr Wood and Dr Hutchinson had little involvement with haemophilia care. Professor Karl Nicholson and Dr Martin Wieselka, Infectious Diseases consultants were involved in the management of haemophilia patients with HIV and hepatitis and later a hepatologist Dr Grant also reviewed patients with hepatitis.

6.

   . The new centre opened in 1981 had a waiting room, a disabled toilet and two consulting/clinical rooms. It was on the same corridor as the Haematology Department and close to Blood Bank where treatment materials were stored and the Coagulation Laboratory. Soon after I took up the post, I met with Miss McGregor the hospital matron and discussed the possibility of appointing a haemophilia sister. The matron was very far-sighted and already exploring ways of extending the traditional role of nurses so that I was quickly able to make an appointment. The sister took up post early in 1981, one of the first in the UK. For personal and professional reasons, she was totally committed to the care and wellbeing of patients with haemophilia. The haemophilia centre remained on this site until 1999 when it was moved to the adjoining newly built Osborne Building. The new centre had more space and its own reception and clinic clerk, nursing assistant and a second sister.

   Prior to the mid-seventies and the appointment of consultant haematologists consequent on the development of the medical school there were no treatment facilities in Leicester. I have been told of families moving elsewhere to seek treatment for their children. Other patients travelled long distances to obtain treatment. I was the sole consultant in haemostasis until 1999 when Dr Sue Pavord was appointed part-time

consultant with duties in thrombosis and sharing obstetric haematology with me but no responsibility for haemophilia care at that time. The same year Professor John Pasi was appointed Professor of Haematology by the University of Leicester and did playa part in haemophilia care. I retired in March 2003 but returned as requested part time as there were no applicants for my post. Professor Pasi also left. I retired fully in November 2003 when Dr Pavord became Haemophilia Director.

. For many years I was combining my role in haemophilia and haemostasis with a full share of the clinical and laboratory haematology workload in the Leicester hospitals. Necessarily much of my time was taken up with these commitments. The appointment of a fourth consultant 10 years later (approximately 1990) did not materially alter this. It was not until 1996 that I was relieved of most of these duties. This was because of an audit report from the UKHCDO recommending this change, a large increase in thrombosis work and anticoagulation and the development of obstetric haematology as a newly recognised subspecialty. It was also contingent on the appointment of a fifth consultant specialising in malignant blood diseases and bone marrow transplantation.

. My work in haemophilia centred around improving the experience of patients with bleeding disorders. Obviously the fact there was from 1981 a physical centre was a major improvement. Twenty four hour ease of access, weekly new patient and haemophilia review clinics, paediatric review clinics and a joint clinic with a consultant orthopaedic surgeon and physiotherapist were set up in the centre. Dental care was provided by the oral surgeons. Home and school visits were carried out by the haemophilia sister. To reach out to the haemophilia community I encouraged the formation of a local Haemophilia Society group which the Haernophilia Sister joined as a committee member. There was a series of joint events and in 1987 the centre and the group were profiled in the Bulletin of the national Haemophilia Society. I developed a treatment policy which was designed to reduce risk and tailor treatment to the needs of the individual patient. Implementation of this policy would have been impossible without the efforts of the haemophilia sister. We tested and informed our patients of their HIV antibody results and initially followed them up but as treatment became available this aspect of their care transferred to Infectious Diseases. Essentially the same happened with Hepatitis C although some patients were initially treated in the centre.

. Professor Karl Nicholson provided care and treatment for haemophilia patients with HIV and later Hepatitis C. When a hepatologist Dr Grant was appointed he was also involved in the care of patients with hepatitis.

7. The figures from the 1983 annual returns [HCD00000150_002j which show only patients treated in the previous 12 months are Haemophilia A 31, Haemophilia B 9, von Willebrand's disease 6. The figures from the BMJ letter in 1985 showing the number of patients treated in the previous five years to be 76 but not clearly subdivided by diagnosis.

8. I formulated the policy described in the BMJ letter [PRSE0001555], it was applied by myself and the haemophilia sister. It was based on restricting the use of large donor pool factor V111 concentrates by using desmopressin and antifibrinolytic therapy whenever possible and using cryoprecipitate in von Willebrand's disease and mild to moderate

haemophilia when it was not. Children with severe Haemophilia A were also treated with cryoprecipitate until they went on to home treatment. I tried to limit the exposure of adult patients with severe haemophilia A by purchasing as much as possible of a batch from a single commercial supplier.

9.

- For some years I was largely responsible for selecting the products used. In the case of commercial products this would have followed discussion with the unit pharmacist and approval by the hospital authorities. Commercial products were purchased by the pharmacy and NHS products were delivered to Blood Bank. Eventually I believe because of EU laws and the value of the contract it was put out to tender.
- I was not aware of one commercial product having advantages over another certainly in the early years. I was more concerned with obtaining access to a single large batch and continued with the product in use on my arrival. Certainly, later with purer more expensive products cost became an issue for the hospital trust.
- Sourced from Cutter by pharmacy or direct from BPL.
- A change to a more expensive product required approval from the hospital authorities.
- I was largely responsible for selecting the products used.

10.

- As detailed above in 8 desmopressin and tranexamic acid were used wherever possible. Cryoprecipitate was used to treat patients with mild to moderate haemophilia and children with severe haemophilia. As much as possible adult severely affected patients were treated with NHS factor concentrates but commercial factor V111 concentrate was needed to make up the shortfall.
- Koate was the commercial factor V111 concentrate in use on my arrival. I had no reason to believe that other products were superior and to change to another product would have exposed the recipients to a completely different donor pool. All these choices were meant to reduce risk.
- I do not know if other products were used in Leicester in the 1970s, I arrived in November 1979. The returns show we replaced Koate with Koate HT in 1985. Later there will have been safer and purer products but I do not now have details of when these changes were made.
- We would certainly have used more NHS product if available. I did meet with Dr Wagstaff, Director of Sheffield NBTS and he did increase Leicester's allocation in view of the centre's growth in patient numbers.

11. We did meet with representatives from pharmaceutical companies, that did not change or influence my policy. The letter from Linda Firth to Mr Godfrey reducing the price from 13p per iu to 12p is probably the result of my discovering that another Haemophilia Centre was paying the lower price. Your included memo [BAYPOOOOOOB_056] shows that other Centres were paying 12p per iu for this product. Possibly Cutter were regulating their price, another memo states that all centres were paying 12p.

12. No external organisation was involved.

13. The main alternatives were desmopressin (DDAVP) and tranexamic acid.

14. Both these products were used whenever possible in Leicester to avoid the use of blood products. I had been involved in an early study of the use of DDAVP in haemophilia and was familiar with its use before my arrival in Leicester (Factor V111 response to intravenous DDAVP. Proc. XV11th Con Int Soc Haem Paris 1978). In patients with mild haemophilia A and von Willebrand's disease, DDAVP can increase endogenous factor V111 levels by 2 _ 5 fold, the response varying from patient to patient. The response wanes with repeated doses but can be sufficient to cover procedures such as dental extractions often in combination with tranexamic acid. DDAVP can cause fluid retention and is not recommended in very young children. Tranexamic acid is an antifibrinolytic agent which stabilises clots and is often used to treat mucosal bleeding from the mouth, nose or in combination with DDAVP for dental extractions when we used it as a mouthwash. Unlike DDAVP it can also be used in Haemophilia B. My only experience with porcine factor V111 is in the treatment of patients with an inhibitor to human factor V111. This product is no longer available. Recombinant porcine factor V111 is used in the treatment of acquired haemophilia.

15.

- We used cryoprecipitate to treat patients with von Willebrand's disease and mild to moderate haemophilia A where DDAVP was not appropriate or sufficient. We also used it to treat children with severe haemophilia A before they went on to home treatment. From the BMJ letter [PRSE0001555] it can be seen that we continued with this policy after the reference directors argued that cryoprecipitate should no longer be used.

- The policy will, of course, have changed as safer products became available but I no longer have the details.

- I will have been informed about new developments and policies by attending scientific meetings such as the UKHCDO AGM and reading the literature.

16. Young children with severe haemophilia were treated in the centre. At an age which depended on the parents' wishes, the frequency of bleeds and ease of venous access, the haemophilia sister would begin teaching the parents which could take some months.

17. As far as I remember prophylactic treatment was at first of short duration to treat a target joint or allow physiotherapy and mobilisation post-op. One adult patient who had athetosis following a cerebral haemorrhage as a child and could not self-treat was started on permanent prophylaxis soon after my arrival. Prophylaxis was used more in later years.

18. We did not use factor V111 concentrate for children until they went on to home treatment when we used NHS product. We used NHS factor 1X concentrate for children with haemophilia B. The policy will have changed when safer products became available.

19. Whenever possible we used alternatives to factor V111 concentrate when treating patients with mild haemophilia. Sometimes it was necessary as in the example of the patient who had open heart surgery (the B J Haem letter [IPSN0000156_089]). We could cover his cardiac catheterisation with DDAVP but not the surgery. Moderate haemophilia is usually considered to be a baseline factor V111 level between 1-5%. DDAVP is less likely to be

adequate to achieve haemostasis and treatment with factor V111 required. We would have used cryoprecipitate by preference or NHS BPL concentrate if necessary.

20.

- Parvovirus B19 is the only other viral infection we observed. The laboratory evidence in our patients that it had been transmitted by a heat-treated concentrate was very suggestive but not conclusive. However, its occurrence in three patients treated with the same product we felt should be recorded. It is a common viral infection of childhood and most adults show evidence in their blood of past infection. It can be very mild or asymptomatic so it might not be recognised when it occurs post transfusion.
- We did not see such a trend.

Section 3: Knowledge of, and response to, risk

21. I was aware of chronic liver disease in patients with haemophilia because I was as a senior registrar involved with the Sheffield study, "Percutaneous Liver Biopsy and Chronic Liver Disease in Haemophiliacs" F E Preston, J C E Underwood, V E Mitchell, D R Triger et al The Lancet 1978 ii 592-4. Some of the biopsies were interpreted as showing non-progressive changes but this was not true of others including those of two patients with mild haemophilia. Although not proved to be viral hepatitis the abnormalities were significant and seemed to be probably related to factor concentrate therapy. Other groups produced results indicating lack of progression in haemophilia patients with chronic liver disease and it was generally believed that this was the case. The Sheffield study had convinced me that for some at least haemophilia patients treated with factor concentrates chronic liver disease could be progressive. Further studies by that group reinforced that view.

22. As a single consultant in haemostasis I had to formulate my own policy. I was aware of the debate being carried on nationally and internationally.

23. I understood NHS products to be safer.

24. We had a strict treatment policy to try to reduce risk. DDAVP and tranexamic acid were used wherever appropriate, if not cryoprecipitate was used in the treatment of patients with von Willebrand's disease and mild to moderate haemophilia. Cryoprecipitate was also used in the treatment of children with severe haemophilia. NHS concentrate was preferred over commercial concentrate of which we reserved as much as possible of a single batch to try to reduce the number of donors to which patients were exposed.

25. Routine testing of blood donations for hepatitis B in the UK began in the early 1970s. In 1979 there was confusion about NANB viral hepatitis eg was there one or more viruses and with some believing that the abnormal liver function tests in haemophilia patients were not due to viral hepatitis. I was aware of the risk of chronic liver disease from my time in Sheffield and that at least in some patients it could be progressive. My sources of information would have been publications and scientific meetings. It became clearer in the mid-1980s that the risk of viral transmission by multi-donor concentrates was very high and the development of an antibody test for hepatitis C in 1990 underlined this.

26. I have recorded the Sheffield study I was part of above. This group in later years produced follow up studies in which I was not personally involved emphasising the seriousness of the problem although other respected international authorities at that time regarded hepatitis in haemophilia as non-progressive.

27.

- As detailed above we had a strict treatment policy to restrict the use of large donor pool concentrates as much as possible to try to reduce the risk of hepatitis. My concern arose from the Sheffield study referred to above in 21. Whatever the pathogenesis of chronic liver disease in haemophilia might be, and this was not clear in 1980, reducing exposure to multi-donor concentrates seemed likely to be beneficial.
- I hoped that by reserving as much as possible of one batch of a product from a single supplier to reduce the exposure of my patients and reduce the risk of chronic liver disease. In my view it had to be better than having multiple batches of several products in use in the centre. I believe this policy was adopted soon after my taking up the Leicester post. I believe the policy helped to reduce the number of patients infected with HIV, I am less sure about HCV, HBV I do not remember occurring in our patients at that time.
- I am sure both I and the haemophilia sister will have mentioned at least aspects of our treatment policy with colleagues.
- I am not sure that I did think Leicester was out of step, colleagues from other centres were using DDAVP to avoid blood products and using cryoprecipitate for the treatment of children.

28. A full blood count and basic biochemistry screen would have routinely been carried out at each haemophilia review clinic. This would have included bilirubin and liver enzyme assays.

    Deterioration in these might indicate the onset of more serious liver disease. Monitoring and treatment were later carried out by the Infectious Diseases Dept and hepatologist.

29. As detailed above my concern about chronic liver disease in haemophilia arose from the 1978 Sheffield study. This showed that at least in some patients, liver disease was significant and progressive. It became clear with time that progression was not uncommon. In the early 1980s there was debate over the cause of abnormal liver function tests in haemophilia patients and its significance, but I am sure Leicester was not alone.

30. I am not sure when I became certain of the risk of HIV transmission by blood products possibly 1983. In 1983 some reports were reassuring but testing became available suggesting a widespread problem in late 1984.

31. I am not certain, possibly late in 1983.

32. Until testing was available, I was dependent on published information and the UKHCDO.

33.

- The policy we had in place to try to reduce the risk of liver disease was equally applicable to HIV and was continued.

- I believe that the policy of using as much as possible of a single batch from one supplier did help to reduce the risk of HIV infection.
- I do not remember many problems with asking the supplier to reserve a single batch for the Leicester Centre.
- The haemophilia sister and I will have mentioned aspects of our treatment policy with colleagues at meetings. I do not remember specific responses.
- Other centres used DDAVP and cryoprecipitate in similar ways, but I am not aware of their insisting on a single batch of a single product being reserved for their centre's use.

34. Factor V111 concentrates used from 1985 onwards were heat treated which was effective in preventing HIV transmission. At the time of the BMJ letter [PRSE0001555] and the 1986 returns we were using heat treated products. I was frequently reminded of the effects of inadequate treatment of severe haemophilia from seeing the effects on Leicester patients to whom this had applied in the 1960s and 19705. The commonest cause of death in haemophilia patients in the 1980s was cerebral haemorrhage. I had two patients who had suffered from this in their childhood with significant life-long disabilities.

35. I and the haemophilia sister will have had individual discussions with patients about hepatitis and HIV including trying to counter the misrepresentation and misinformation in the press.

36.

- We used heat treated commercial factor V111 from early 1985, we used NHS heat treated product the same year and NHS heat treated factor 1X became available I believe in the autumn of 1985.

  Our heat-treated products were from the NHS (BPL) and Cutter. We had to obtain permission to increase the spending on commercial factor V111 before the pharmacy could order it. The delay was not major.
- From the 1983 and 1986 returns we did in fact use much more NHS heat-treated product. NHS factor V111 used in Leicester in 1983 was 210305iu and in 1986, 512375iu, an increase of 143%. The increase may in part have arisen from my discussion with Dr Wagstaff, Director of the Trent Regional NBTS and from my letter to Dr Snape indicating our needs. Commercial factor V111 usage rose by 17% over the same period. We used BPL heat treated product in preference because it came from volunteer donors and underwent a more vigorous virucidal treatment.
- Clearly from the evidence you provide, there were difficulties for commercial suppliers in reserving a batch for a single centre as a change to heat-treated material took place. It seems that these difficulties were overcome.

37. We did find the solubility problem to be an issue with 8Y. As my answer to 36b shows we used it on a large scale. In 1989 a safety trial from Birmingham Children's Hospital presented evidence that 8Y did not transmit hepatitis viruses confirmed by later studies. (Pasi KJ, Hill FG, Arch Dis Child 198964(10) 1463-1467 [PRSE0000949].)

38.

. I have no memory of this but believe that our patients did transfer as a group.

. I believe and expect that we would have been credited for returned material. We did have to wait for pharmacy to be given permission to purchase the more expensive heat-treated concentrate.

c. Yes.

39.

. I have no memory of this pressure from regional colleagues or of a suggestion by Professor Preston that Sheffield should purchase all commercial concentrate for the region.

. In common with many centres we did continue to use Koate HT at that time. This did change when newer safer products became available.

. I do not remember a clear preference for Profilate HT. This seems to have been based on a claim of greater safety than other products which was rather undermined by the occurrence of markers of hepatitis in Derby and St Thomas's patients stated in another memo.

40. We did not have problems with the efficacy of Koate HT in terms of treatment. Like other heat-treated factor commercial concentrates at the time it did not transmit HIV but it transpired that it was not completely safe from hepatitis transmission. In this it did not differ from the other available products other than BPL 8Y which proved to be safer.

41. NHS heat-treated factor 1 X (9A) was available later than 8Y.

. Until then we used non heat-treated NHS factor 1X for most patients.

. I did not consider the commercial products to be safer. My patients had been receiving NHS factor 1X for some time and none had tested positive for HIV antibody. The one patient who did receive commercial heat-treated factor 1X developed hepatitis B.

. The circumstances were unusual. The parents of a GRO-D year old boy with severe haemophilia B were extremely anxious about the risk of HIV infection despite discussions with me and the haemophilia sister. GRO-D GRO-D I was asked to change him to heat treated factor 1X concentrate immediately. As pharmacy were dealing with Cutter already and I was not aware of any disadvantage with Konyne that was provided.

42. I very much believe that treated factor concentrates should have been available sooner.

43. I did not revert to treatment with cryoprecipitate over and above the categories of patients who were already receiving that therapy (mild and moderate haemophilia A patients, children with severe Haemophilia A and von Willebrand's disease.) However, a Cutter memo [BAYP0000007 _045] states that we had 6 patients to transfer from cryoprecipitate to heat treated concentrate. For a centre like Leicester in 1985 to have so many patients at that stage indicates we must had been keeping patients on cryoprecipitate longer.

44. I felt that a ban on the use of cryoprecipitate was inappropriate. As explained its use was an important part of our treatment policy.

. Professor Bloom told me "it was a good letter". One or two colleagues from other centres felt our policy would be difficult if not impossible to maintain because mistakes would be made out of hours. I do not remember any response from other sources.

45.

a.b.1 do not remember this discussion. Although we at Leicester used cryoprecipitate to treat patients with moderate to mild haemophilia A and von Willebrand's disease as well as children with severe haemophilia A, in common with the vast majority of haematologists I would not have regarded it as suitable for the home treatment of severe haemophilia A. It requires storage in a deep freezer which should be alarmed and which few patients owned at the time, the factor V111 level which varied from bag to bag averaged only about 70iu per bag so that an adult severe haemophilia patient would have to draw up and administer many bags, reconstitution and administration were much more difficult and prolonged and there was a risk of allergic reactions.

. In 1983 haematologists were very aware of the dangers of inadequate treatment and that severe haemophilia was a life long painful life shortening illness. Haemorrhage was still the commonest cause of death.

. We used a significant amount of cryoprecipitate and I do not remember problems with its supply or that of commercial concentrate. We were also using an increasing amount of NHS concentrate. I do not believe that the Trent Regional BTS centre could have supplied sufficient cryoprecipitate to replace commercial factor concentrate in the five sizable haemophilia centres in the region. An attempt to do so would have had a very serious impact on the production of other essential blood products such as fresh frozen plasma and platelet rich plasma. It would also have made it impossible for the Trent centre to continue to supply plasma to BPL for the manufacture of NHS factor V111 and 1 X concentrates.

46. I was trying to do as much as I could to reduce risk and protect patients. Although I believe our policy was appropriate and did reduce risk, I am very sorry we were not always successful.

47. I am not sure what we could have done differently. We always tried to be aware of the risks.

48. If the UK had obtained self-sufficiency in plasma products pre 1980 then it seems likely that the numbers of patients infected with HIV could have been greatly reduced.

49. There were indications that clotting factor concentrates were not free of risk in the late 1970s with reports of liver disease in some patients with haemophilia. This should have led to a much greater efforts to make safer products. It seems that it took the HIV epidemic to motivate governments and plasma fractionators into doing so.

Section 4: Treatment of patients

50. This was not a common situation in Leicester where most patients were already on treatment when I took up post. This was also true of patients transferring from other centres. If with increasing availability, we transferred a patient from commercial to NHS concentrate we would have explained why we believed it to be safer. When children transferred to NHS concentrate to allow home treatment then the haemophilia sister,

GRO-A would fully inform the parents of what we knew at the time.

51. We will have had discussions about liver disease with patients in haemophilia review clinics. The information given will have varied with particular circumstances. Further discussions will have taken place with the haemophilia sister.

52. Only some patients could be treated with alternatives to factor concentrates. When we could we used them and would explain to the patient. For adult patients with severe haemophilia perhaps treating themselves three times a week there was no practical alternative.

53. Training of parents to undertake home treatment for their child was carried out by the haemophilia sister GRO-A. The training would take weeks if not months and gave the opportunity for a series of discussions about the product.

54. Presumably 1983 - 4.

55. A national programme of HIV testing of haemophilia patients was carried out by the PHLS Virus Reference Laboratory in 1985.

56. Patients were contacted by the haemophilia sister and invited to attend the centre for the test. She would explain the nature and significance of the test. Witness W1620 [WITN1620001] describes the process and records that he gave informed consent.

57. I saw the patients individually often with the haemophilia sister.

58. They were told what we knew about this new virus and the significance of the test. They were not told to keep the diagnosis a secret.

59. We did not routinely test partners or family members.

60. We would meet with family members with the patient's agreement and in his presence. We would have given the advice detailed in 76.

61. We did not have access to professional counsellors or clinical psychologists. Further counselling would be carried out by myself or the sister.

62.

Severe haemophilia A	8
Moderate haemophilia A	0
Mild Haemophilia A	0
Haemophilia B	0
Von Willebrand's disease	0
Children	0

These figures are the same as in the BMJ letter PRSE0001555] with the addition of one positive case who having initially tested negative, tested positive later in 1985. No further positives occurred in the Leicester patients. The figures do not include some adult patients known to have been HIV antibody positive before transferring to Leicester.

63.

No.

64.1.

65. Our two patients as described in the B J Haem [IPSN0000156_089] were informed by me. In the case of the child his parents were informed and I had discussions with his father particularly about the significance and prognosis, initially hoping for spontaneous clearance. The other patient was referred from elsewhere and his hepatitis managed there.

66.2

67.

. I have explained the circumstances in which the first patient received Konyne in 41 c. There are some errors in the internal Cutter memos. He was the only patient in Leicester receiving heat treated factor 1 X, the other 5 on the same batch must have been in other UK centres. He had not been treated with "national product" at almost the same time but 11 months before he became HBsAg positive.

. The other patient had mild haemophilia A and DDAVP was sufficient for his cardiac catheterisation but for open heart surgery he required factor V111 concentrate. He had previously been treated at his own centre with cryoprecipitate and non heat-treated commercial factor V111. The first two doses of Hepatitis B vaccine were given but his clinical condition deteriorated and the cardiac surgeons decided they must operate before the third dose. Following successful surgery he was given the final dose but subsequently found to be HBsAg positive. The BTS tested the 8 donors whose blood and platelets he had received with negative results. I do not know why vaccination failed, unfortunately he had to have his operation after only two of the three doses.

. I concluded that from this evidence that Hepatitis B had been transmitted by these heat treated concentrates. Although Cutter did not accept this they did not challenge our letter to the British Journal of Haematology [IPSN0000156_089]. I know of no mechanism to resolve such disputes.

68. NANB hepatitis was the name given to raised liver enzymes found in, amongst others, patients who had been treated with coagulation factor concentrates. The name assumes the cause to be an unknown virus which proved to be correct but at the time was doubted by some doctors. Patients may have been told they had often mildly abnormal liver function tests but they were asymptomatic and there was no clear information on prognosis and no treatment.

69. I believe about 1990. The patients were told individually by me either alone or with the sister.

70. Much of this information was not available in the early 1990s and only emerged over the years. The antibody test for HCV did not distinguish between those who had cleared the virus and those who were still infected for example and treatment was not available. Counselling patients therefore could only be done in general terms which would be amplified later either in the centre or by the infectious diseases consultants or hepatologist.

71. I do not have access to this information.

72. Patients who might have been infected were contacted and asked to attend the centre for testing.

73. Patients were always seen individually and informed promptly.

74. I am not sure what public health considerations are being queried. These patients would not be blood or tissue donors and were not a danger to the public. Advice listed in 76 was given to safeguard others.

75. My patients with HIV antibody were a" we" at the time of testing and none had symptoms. I cannot remember if they were immediately counselled about the risks of other infections. They would have contacted us about any such event. Later such advice would have been given.

76. Patients were told about not sharing razors or toothbrushes, care with needles and clinical waste and unprotected sex, although this latter was more important in HIV infection than hepatitis C. They were advised to cover cuts and grazes with dressings and to clean up any blood from surfaces with household bleach.

77. I do not remember this particular discussion. From the minutes it seems to be a recommendation from a Transfusion Transmitted Infections Working Party presumably to monitor the continued safety of products. Other attendees may have more knowledge.

78. Routine blood counts and baseline biochemistry were taken at haemophilia review clinics to monitor general health. Pre and post factor levels might be required to monitor the response to treatment. Samples were not stored. When tests for HIV or hepatitis viruses were carried out this was always done with fully informed consent as Witness W1620 records [WITN1620001].

79. Patients with severe haemophilia were usually on regular treatment with the same product. If a change was required, they would be fully consulted. Other patients less frequently treated would of course have the procedure of for example DDAVP infusion explained to them. It was not then normal practice to record written consent.

80. We did not test patients without their consent. As stated above Witness W1620 [WITN1620001] confirms that he gave informed consent to HIV testing in 1985 and subsequently hepatitis C antibody testing in 1990. I do not know if these consents were recorded.

81. I did not take part in PUPS trials.

82.

. Patients who were HIV antibody positive were referred to the Infectious Diseases Department for management.

b.c.d. I have no information on these points.

83. Only one patient with chronic hepatitis B was being followed up in Leicester Haemophilia Centre. The other patient infected during treatment for open heart surgery returned to his own haemophilia centre and we did not hear if the virus cleared.

Our patient was treated with interferon and ribavirin when this treatment became available. The initial course was unsuccessful and he was referred to the Infectious Diseases

Department for further management and would later be reviewed by the consultant hepatologist.

I was not involved in the evolution of further treatment options in hepatitis treatment nor its monitoring.

84. NANB hepatitis was the name given to often mildly abnormal liver function tests in treated haemophilia patients and others. Most turned out to be infected with hepatitis C. There was no treatment available at that stage. Most patients were monitored for their general health and liver function tests.

85. Initially some patients were treated with interferon and ribavirin when this became available in the centre. They were reviewed by doctors in infectious diseases and this aspect of their care transferred to that department. I was not involved with further developments in treatment or monitoring.

86. None of our children were infected with HIV. I cannot specifically recall children with hepatitis, they would have been referred to Infectious diseases or a paediatric consultant.

87. The haemophilia centre was not involved with HIV or HCV treatment trials.

88. I greatly regret that we did not have access to independent counselling or to a clinical psychologist. I did counsel patients in clinics and other times. The haemophilia sister did a lot of counselling GRO-A GRO-A who was prominent in the local Haemophilia Society as well as being a highly professional clinical specialist she was well placed to do so.

89. We received no funding. I had some difficulty obtaining permission to prescribe interferon and ribavirin because of the cost implications. Eventually the medical director gave his authorisation.

90. I know that the UKHCDO did campaign to obtain recombinant products in part because it was felt that risks were still attached to conventional therapy. Letters to the government and meetings with ministers were part of this campaign.

91. I would like to have seen recombinant products available as soon as possible. I cannot now remember the timescale of availability internationally.

92. I do not remember exactly when we received recombinant products ?1998 for factor V111 and a year later for factor1X. I believe we gave priority to children under 16 - in fact this was government policy at that time.

93. This was a major shortage affecting the whole of the UK in 2001. Very large centres such as St Thomas held more stock and were in a much better position. A relatively small centre like Leicester was more severely and immediately affected. In common with many other centres we did not treat adults with recombinant products during the shortage and also had to take some older children off recombinant products. I do not remember how long the situation lasted or if it was helped by the UKHCDO's plan to redistribute available recombinant product to centres with the most acute shortages. The replacement material would have been the current high purity plasma derived factor. We will have explained to the affected patients the situation and what we hoped would happen. All would have received plasma derived product in the past since the youngest children who had not

continued on recombinant. I do not remember adverse effects although the affected patients will have been disappointed.

94. Because of lack of time and resources we were not able unlike large centres to do basic research in haemophilia. My published work from Leicester is mainly in the fields of thrombosis/thrombophilia and haemato-oncology.

Familial exudative vitreoretinopathy associated with familial thrombocytopathy. B. J. Ophthal1983 291 213

Severe homozygous factor X deficiency in a family with independent expression of MPSI mucopolysaccharidosis of unusual type. La Ricerca 1986291 213

Loss of the Philadelphia chromosome in chronic myeloid leukaemia associated with coeliac disease and splenic atrophy. BMJ 1988296 1574-5

Transmission of hepatitis B by dry heat-treated factor V111 and 1 X concentrates. B J Haem 198869421

Effects of dry heating of coagulation concentrates at 80C for 72 hours on transmission of non A non B hepatitis Study Group of UK Haemophilia Directors Lancet 1988 ii 814-816 [PRSE0000044]. This was a study co-ordinated by the NHS Blood Products Laboratory to confirm the effectiveness of their anti-viral treatment of prolonged high temperature heat treatment of clotting factor concentrates. There were 33 patients from 12 haemophilia centres, many much larger than Leicester so our contribution is likely to have been one or two patients. All patients needed treatment and gave informed consent. I presume that BPL funded the study.

Chronic urticaria with angio-oedema controlled by warfarin. BMJ 1988 297 1382-3

Discoid lupus erythematosus associated with anticardiolipin syndrome. B J Derm 1989 120469-470

Symptomatic parvovirus B12 infection and heat-treated factor 1X concentrate. Lancet 19891 1085

The use of D-dimer assay by enzyme immune assay and latex agglutination techniques in the diagnosis of deep vein thrombosis. Clin Lab Haemat 1990 12 37-42

Free protein Sand C4b binding protein. Am J Clin Path 1991 96434-5

Multilobulated multinucleated multiple myeloma. B J Haem. 199281 622-624

Measurement of HbA 1 using patient collected finger prick specimens. Practical Diabetes 1993 10 182-184

Unique presentation of a clonal T cell disorder B J Haem 1993 62 84

Haemophilia B caused by a missense mutation in the prepeptide sequence of factor 1 X. Human Mutation 19932103-7

Multiple fungal infection in acute lymphoblastic leukaemia. Clin Lab Haem 1993 15(2) 149-150

Therapeutic efficacy of ambisome. Am J Haem 1995 48(3) 208-209

Plasma D-dimers as a marker for post-operative deep vein thrombosis Thromb & Haemostasis 1994 72(5) 663-5

Acute lymphoblastic transformation of essential thrombocythaemia. B J Haem 89 (4) 921-922

Specific markers of bone formation in total protein S deficient patients. Thromb. Res. 1996 84 (3) 482

POEMS syndrome and Waldenstrom's Macroglobulinaemia J Clin Pathol199618(3) 221-223

Cyclical thrombocytopenia as a rare manifestation of myelodysplastic syndrome. Clin Lab Haem 1996 18(3) 221-223

Clinical features and molecular analysis of a family with multiple colon tumours and reduced plasminogen activator activity. Int J Colorectal Dis.1997 i 12 1-3

Cutaneous vascular infarcts secondary to spontaneous platelet aggregation. B J Derm 1998138(6) 1061-3

95. No.

96. No.

97. No.

98. Apart from the 3 articles known to the inquiry (the BMJ letter, the B J Haem letter and the Lancet letter) the only relevant article is one I wrote by invitation for The Prescribers' Journal on Coagulation Factor Concentrates. Prescribers' Journal 1992 32 56-62.(WITN3174004).

99.

. I was involved in treating patients with haematological disorders other than haemophilia until 1995. The patients who were transfused had bone marrow failure due to acute leukaemia or other haematological malignancy. I did not treat patients with thalassaemia or other haemoglobinopathies or children other than those with a bleeding disorder. The purpose of the transfusions was to keep the patient alive until treatment could bring about a remission so that the bone marrow once more produced blood cells. The patient was often very ill with sepsis, severely anaemic, bleeding and intensely anxious.

b.c.d. It was not current practice to discuss the risks of single donor blood components in the face of much more immediate dangers. I do not believe that the protocols produced by the Medical Research Council which were normally followed in these cases recommended this. The Handbook of Transfusion Medicine (HMSO 1989) issued by the United Kingdom Health Departments is highly detailed but does not mention consent or counselling.

. The haematologists did have discussions with colleagues in other specialties such as surgery and anaesthetics about transfusion. We discouraged transfusion when anaemia could be treated by other means, top ups before discharge and arranged for

single unit transfusion requests to be challenged by blood bank. Medical students were also taught about transfusion.

. The treating clinician.

100. I do not remember this arising or issuing a death certificate.

101. The notes were signed by me to indicate they should be retained indefinitely.

102. No.

103. No.

Section 5:UKHCDO

104. I was a member of the UKHCDO from 1980. Ordinary members met only at the AGM when a number of presentations were made by Reference Centre Directors and invited experts. The committee of Reference Directors evolved and enlarged in the 1990s with the concept of Comprehensive Care Centres. I became a member of the new larger committee of Comprehensive Care Centre Directors in 1995. I was a member of a working party developing guidelines for the diagnosis and treatment of von Willebrand's disease.

105.

. The UKHCDO exists to improve the care of patients with bleeding disorders by ensuring the maintenance of high standards of care through regular audit of haemophilia centres, education of doctors, nurses and others, provision of guidelines on diagnosis and treatment of bleeding disorders and liaison with other interested groups such as the haemophilia nurses association, the Haemophilia Society but also the Department of Health.

. At that time there was an executive committee of Comprehensive Care Haemophilia Centre Directors, a secretariat based in Oxford overseeing the national returns and a number of working parties.

. I am not aware that the UKHCDO as an organisation dealt directly with pharmaceutical companies.

. We paid an annual subscription, I believe. There may have been contributions from the Department of Health towards such costs as the National Data Base.

. Publication of guidelines, annual reports, patient information including lists of treatment centres.

. I am afraid I do not remember these discussions. I left 17 years ago and I do not have minutes or other documents.

Section 6: Pharmaceutical companies/medical research/clinical trials

106. No.

107. No.

108. No

109. No

110. I believe I was already planning to attend the 1986 World Federation of Haemophilia meeting in Milan presenting a paper at a poster session. Cutter it seems offered assistance with travel and accommodation costs. This was regarded as acceptable then, in fact the overseas study leave form had a space to declare support from other sources. The committee could then award study leave only without expenses. The Royal College of Pathologists July 2002 publication on Good Medical Practice states "You may accept personal travel grants and hospitality from companies for conferences or educational meetings as long as the main purpose of the event is educational. "

111. No.

112. I was not involved in a consultancy or advisory role with a pharmaceutical company.

113.

. I do not believe that Leicester took part in this trial. From the returns we were not using Feiba at this time. Neither the 1983 or 1986 annual returns show any use of Feiba and in fact in 1986 we used over 30,000 units of porcine factor V111 to treat a haemophilia A patient with an inhibitor rather than Feiba.

. I do not remember this discussion or correspondence. This would have been at a time when we were looking to transfer all our patients on non heat-treated concentrates to heat treated concentrates. The only result of this offer would have been to let a single patient transfer a little earlier, that would not have constituted a study and I do not believe it happened.

. I do not remember this study and cannot find anything about it on searching on-line. If it took place it does not seem to have been published. It is not included in Professor Mannucci's list of Koate HS safety studies in his article "Clinical evaluation of viral safety of coagulation Factor V111 and 1 X concentrates" Vox Sang 1993 64 197-203.

. Leicester with a number of other haemophilia centres took part in a BPL study in 1999. The study "Replenine Virus Filtered Pharmacokinetic Study" was carried out with patients with haemophilia B who had received at least 20 previous exposures with factor 1 X concentrate. The purpose was to measure the recovery and half - life of BPL's high purity factor 1X concentrate. The study had Multi-Centre Research Ethics Committee approval and local ethics committee (LREC) approval. All patients gave informed consent. BPL funded the study. The medical director and finance department of Leicester Royal Infirmary were fully informed by BPL. The study does not appear to have been published and I do not know the number of patients involved.

A previous BPL study is described in section 94.

114. Not outside the studies described in 113d.

115. We did receive funding for research in thrombosis/thrombophilia. The funding was held within the LRI Charitable Funds, the sources were known and formal application and approval required to access the funds.

Section 7: vCJD

116. I presume 1997 when the UKHCDO wrote to the government and published a letter in the medical press about the risk and urging the adoption of recombinant products. The following year BPL stopped using British plasma instead importing from I believe the USA and elsewhere.

117. Most of the subsequent events took place after my retirement in 2003 when in 2009 a haemophilia patient was found to have abnormal prion protein in his spleen although he had died of an unrelated illness. I do not have useful information on the other points.

Section 8: The financial support schemes

118. I had no involvement with the Eileen Trust and believe the Caxton Foundation and Skipton Fund were set up after my retirement.

119. We would have told relevant patients of the Macfarlane Trust and did have literature about it. Patients would also have learnt about the Trust from other sources such as the Haemophilia Society.

120. Not in the time I was in post.

121. Not in the time I was in post.

122. As far as I am aware information about the Macfarlane Trust, the haemophilia sister and my successors may have done more with the later trusts.

123. Not up to 2003.

124. Not up to 2003.

125. I am not in a position to judge.

Section 9: Other Issues

126. I am not aware of any such complaints.

127. There any no other issues.

Statement of Truth

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

Signed GRO-C

Dated 9th October 2020

Table of exhibits:

Date	Notes/ Description	Exhibit number
9th October	Coagulation Factor Concentrates	WITN3174004
2020	Prescribers' Journal 1992 vol 32	