Witness Name: Dr David Michael Keeling

Statement No.: **WITN4743001**

Exhibits: **WITN4743002 – WITN4743012**

Dated: 18 March 2021

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DR DAVID MICHAEL KEELING

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 27 January 2021.

I, **DR DAVID MICHAEL KEELING**, will say as follows: -

Section 1: Introduction

1. Please set out your name, address, date of birth and professional qualifications.

1.1 My name is David Michael Keeling.

1.2 My address is GRO-C

1.3 My date of birth is GRO-C 1958.

1.4 My qualifications are:

B.Sc.	University of London, August 1979.
M.B. B.S.	University of London, July 1982.
M.D.	University of London, March 1996.
F.R.C.P.	(M) July 1986, (F, London) May 2004.
F.R.C.Path.	(M) June 1994, (F) January 2002.

2. Please set out your employment history including the various roles and responsibilities that you have held throughout your career, as well as the dates.

2.1 My employment history is set out in some detail in my CV which is attached **[WITN4743002].** The haematology posts which I have held that are most relevant to this Inquiry are set out below for ease of reference.

2.2 01.07.95 to 28.02.18 - Consultant Haematologist, Oxford University Hospitals NHS Trust and Honorary Senior Clinical Lecturer in Haematology at the University of Oxford. Oxford Haemophilia & Thrombosis Centre, Churchill Hospital, Oxford. My roles and responsibilities at Oxford are set out under Question 7 below.

2.3 01.04.92 to 30.06.95 - Senior Registrar (Honorary Clinical Lecturer) to Professor R.W. Carrell, Dr. T.P. Baglin, Dr. R.E. Marcus and Dr. A.R. Green, Department of Haematology, Addenbrooke's Hospital, Cambridge. My role was that of a haematology senior registrar. I worked in all areas of haematology under consultant supervision and I supervised a registrar, an SHO and a house officer. Most of the work was in malignant haematology. I had very little involvement in haemophilia care before my consultant post in July 1995.

2.4 01.01.89 to 31.03.92 - Clinical Lecturer (Honorary Senior Registrar), Department of Haematology, University College London.

I was researching into the nature of antiphospholipid antibodies and possible mechanisms for their association with thrombosis. This work formed the basis of my MD thesis. I was supervised by Professor S.J. Machin and Professor D.A. Isenberg and supported by a grant from the Arthritis and Rheumatism Council.

2.5 07.12.87 to 31.12.88 - Registrar to Professor G.C. Jenkins, Dr. B.T. Colvin and Dr. A.C. Newland, Department of Haematology, The London Hospital, London. My role was that of a haematology registrar. I worked in all areas of haematology under supervision of consultants and senior registrars, mostly in malignant haematology.

2.6 01.02.87 to 06.12.87 - SHO to Professor A.V. Hoffbrand, Drs. H.G. Prentice, A.B. Mehta, M.K. Brenner and P.B.A. Kernoff. Department of Haematology, Royal Free

Hospital, London. I spent six months on the bone marrow transplant unit as the SHO and the rest of the time in the haematology laboratory.

3. Please set out your membership, past or present, of any committees, associations, parties, societies or groups relevant to the Inquiry's Terms of Reference, including the dates of your membership and the nature of your involvement.

3.1 These are set out in my CV **[WITN4743002]**.

3.2 Of most relevance to this Inquiry, I was a member of the United Kingdom Haemophilia Centre Doctors' Organisation ("UKHCDO") between 1995-2018. I was secretary to the UKHCDO from 2005 to 2011 and Vice-Chair from 2011 to 2016.

4. Please confirm whether you have provided evidence to, or have been involved in, any other inquiries, investigations, criminal or civil litigation in relation to human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Creutzfeldt-Jakob disease ("vCJD") in blood and/or blood products. Please provide details of your involvement. Please also provide copies of any statements or accounts that you provided to the inquiries etc., if you are still in possession of such statements.

4.1 I have not provided evidence to, or been involved in, any other inquiries, investigations or criminal litigation in relation to human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Creutzfeldt-Jakob disease ("vCJD") in blood and/or blood products.

4.2 I have been instructed to provide an expert report by solicitors acting for a claimant in a civil claim who alleges he was exposed to HCV due to unnecessary treatment with FVIII concentrate at West Kent Hospital in September 1978. The case is ongoing. I understand that the expert report I have prepared is not disclosable to the Inquiry as it is subject to legal professional privilege.

Section 2: Decisions and actions of those treating patients with haemophilia at the Oxford Haemophilia Centre

5. Please describe the roles, functions and responsibilities of the Oxford Haemophilia Centre ("the Centre") during the time that you have worked there and how they have changed over time.

5.1 When I first started at Oxford in 1995, the Centre was known as The Oxford Haemophilia Centre (OHC) and was based at the Churchill Hospital. Its primary function was as an outpatient service to adults and children with inherited bleeding disorders or acquired haemophilia.

5.2 An important aspect of my appointment was to establish a thrombotic side to the haematology service. This led to the Centre eventually becoming a haemostasis and thrombosis centre rather than just a haemophilia centre. A few years after I started, after a temporary name change to The Oxford Haemophilia and Thrombosis Unit, we settled on a the name of The Oxford Haemophilia and Thrombosis Centre (OHTC) to reflect this.

6. Please identify senior colleagues and the roles and responsibilities that they had during the time that you have worked at the Centre.

6.1 When I was appointed in July 1995, I joined Dr Paul Giangrande, the only other consultant haematologist. He had started working at the Trust in April 1991 and took over from Dr Charles Rizza as Centre Director in October 1993. I regarded him as the lead with respect to haemophilia and myself as the lead for thrombosis (DVT and anticoagulation) though we shared the large clinical haemophilia work load and consulted on major decisions. Dr Giangrande was the lead clinician (managerial/administrative lead) for the department until 2002 following which I took over until 2009 after which we alternated this role on a three-yearly basis. Dr Giangrande retired in May 2015.

6.2 In 2006, Dr Georgina Hall, a consultant paediatric haematologist based at the John Radcliffe Hospital, started running the paediatric haematology clinic in the OHTC.

6.3 In January 2013, we appointed a third consultant haematologist at OHTC, Dr Nicola Curry, who was part time (0.6 wte). I, Dr Giangrande and Dr Curry dealt with haemophilia and DVT patients. In 2007 the prevention of hospital acquired thrombosis (thromboprophylaxis) was becoming a major concern nationally and so I

had set up a hospital thromboprophylaxis committee. On her appointment Dr Curry took over the lead on this from me.

6.4 When Dr Giangrande retired in 2015, Dr Curry increased to 0.8 wte. and Dr Susie Shapiro (0.8 wte) was appointed in Dr Giangrande's place. From then until my retirement in 2018, I led on thrombosis, Dr Curry on haemophilia, and Dr Shapiro on thromboprophylaxis and anticoagulation.

6.5 In July 2015, paediatric haemophilia moved to the Children's Hospital on the John Radcliffe site with Dr Georgina Hall and Dr Neha Bhatnagar as the paediatric haemophilia consultants.

7. Please describe your role and responsibilities at the Centre and how those have changed over the years.

7.1 See 6.1, 6.3 and 6.4. I worked entirely in the field of haemostasis and thrombosis dealing with haemophilia and other bleeding disorders, thrombosis, thrombophilia, anticoagulation and general coagulation.

7.2 I set up an anticoagulation dosing service at the John Radcliffe Hospital and in 2001 introduced computer dosing with oversight by an anticoagulation clinical nurse specialist. I supervised the coagulation laboratory at the John Radcliffe from my appointment.

7.3 In 2001 I set up a DVT service based in the Centre. The anticoagulation service was then moved across to the Centre and integrated to some extent with the DVT service. Thrombophilia testing was also moved from the John Radcliffe into the coagulation laboratory in the Centre.

7.4 From its establishment until my retirement in February 2018, I was the lead for the DVT service. I was the lead for the anticoagulation service until Dr Shapiro's appointment in 2015 and lead for thromboprophylaxis from 2007 (when the role was created) until 2013 when this role was then taken over by Dr Curry.

8. Approximately how many individuals with bleeding disorders were under the care of the Centre when you first started working there and over the years that followed? Approximately what proportion were adults and what proportion

were children? (If you are able to give exact rather than approximate figures, please do so).

8.1 I don't believe the number of patients with bleeding disorders changed too much over the years I was at Oxford. Accurate data can be obtained from OHTC and the NHD (National Haemophilia Database). From memory, we had approximately 150-160 patients with severe haemophilia, about 40 children and 110-120 adults. There were many more patients with moderate/mild bleeding disorders. The total numbers of patients registered was in the order of 800 or so.

9. To the best of your knowledge, what responsibility did the Centre have for the selection and purchase of blood products (in particular factor concentrates)? What policies were formulated and what decisions were taken as to which products to purchase and use? In addressing these issues, please answer the following questions:

a. How, and on what basis, were decisions made about the selection and purchase of blood products?

9.1 From my appointment in 1995 until 2004, a consortium of PCTs (known as the Thames Valley Consortium and covering Oxfordshire, Northamptonshire, Buckinghamshire, Berkshire and Gloucestershire) worked with the Trust to purchase blood products through a tender process. The consortium reimbursed the Trust the cost of any factor purchased so this did not put the Trust at risk if volumes used fluctuated. Dr Giangrande, Kevin Clarke (Clinical Unit Manager) and I would estimate the volumes of each type of product (e.g. high purity FVIII) we needed. There would be a tender so we had a price for each individual product in each category. There was then a meeting to decide which products we should purchase and from which manufacturer. The people at these meetings were Dr Giangrande, myself, Kevin Clarke, and a public health doctor from the consortium, Dr Kendal Bird. There may have been others present but these were the key people.

9.2 From 2004 onwards factor concentrates were purchased under the national procurement schemes. These exercises were in 2004, 2007, 2010 and 2014.

b. What particular products were used for treating patients at the Centre, over what period of time and for which categories of patients?

9.3 Haemophilia A (if not desmopressin responsive) – factor VIII (FVIII), all plasma-derived FVIII used was virally inactivated (e.g. with heat treatment). When I started I think the FVIII used was the intermediate purity FVIII BPL 8Y. Over time we used high purity plasma derived FVIII (e.g. Replenate, Alphanate) and recombinant FVIII (first generation Kogenate, Recombinate, second generation Kogenate FS, Advate, Refacto). Extended half-life recombinant products were being introduced in my last year or so (Elocta).

9.4 Haemophilia A with inhibitors – Novoseven (recombinant VIIa) and FEIBA (a virally inactivated plasma product). Porcine factor VIII was still in use in the late 1990s but in general was more likely to be of use in acquired haemophilia. I don't recall ever using porcine factor VIII at the Centre.

9.5 Haemophilia B – Factor IX (FIX) all plasma-derived FIXI used was virally inactivated (e.g. with heat treatment). I can't remember whether BPL 9A was still in use when I arrived or whether patients were already on high purity FIX (e.g. Replenine, Alphanine). Later, and I cannot recall exactly when, recombinant FIX (Benefix) was used. Extended half-life recombinant products were being introduced in my last year or so (Idelvion, Alprolix).

9.6 VWD – desmopressin was the treatment of choice unless ineffective or contraindicated. If not desmopressin responsive our favoured treatment was Haemate P and later Voncento which are virally inactivated intermediate purity products which contain Von Willebrand Factor (VWF) of good quality. BPL 8Y may have been in use when I started.

c. What were the reasons or considerations that led to the choice of one product over another?

9.7 For haemophilia A there was an advance from intermediate purity, to high purity, to recombinant. When vCJD became a possible issue with British plasma, patients were offered plasma-derived concentrate from non-British plasma. The move to recombinant was due to a perceived safety advantage and took place mainly as part of a national scheme due to what at the time was a large increase in cost. The first generation recombinant products were regarded as equivalent, the second-generation recombinant products were regarded as a step forward but equivalent to

each other. When choosing between products which we regarded as equivalent, price would be an issue but also not "putting all our eggs in one basket" in case of supply issues.

9.8 For haemophilia B we moved from high purity plasma-derived concentrate to recombinant when we could, again because of a perceived benefit in safety.

9.9 For VWD, when desmopressin could not be used, we regarded Haemate P and later Voncento as having superior efficacy to other concentrates so we chose these.

d. Where were products used at the Centre sourced?

9.10 They were purchased by the Centre but the cost was reimbursed by the consortium described above.

e. What role did commercial and/or financial considerations play?

9.11 I think the only significant financial constraint was over the introduction of recombinant FVIII and FIX, otherwise, as stated above, financial considerations only came into play where we were comparing two products that were equivalent.

f. What was your involvement in this process?

9.12 See 9.1.

g. What involvement did other clinicians at the Centre have in making these decisions?

9.13 See 9.1.

10. What, if any, was the relationship between the Centre and the pharmaceutical companies manufacturing/supplying blood products? What influence did that relationship have on the Centre's decisions and actions?

10.1 Pharmaceutical companies did not influence our decisions.

11. If the responsibility for the selection and purchase of blood products lay with an organisation other than the Centre, please specify which organisation and provide as much information as you can about its decision-making.

11.1 Before 2004 the responsibility lay with the Centre but we would follow UKHCDO guidelines. After 2004 we took part in national procurement.

12. How were decisions taken as to which products to use for particular patients? What role did you have in such decisions? Were patients given any choice or involved in any discussions as to which products to receive?

12.1 We would use products for our patients according to the type of bleeding disorder they had and how effective the treatment was likely to be – see 9.3 to 9.6 above. If we had two or more products in one category which we regarded as equivalent (e.g. Kogenate FS and Advate) we didn't have criteria as to which individual patients got which product (other than say children in the same family having the same product). Patients were not asked to choose between them. If a patient preference had been expressed it would have been fulfilled but it wasn't to me.

13. What alternative treatments to factor concentrates were available for people with bleeding disorders?

13.1 I interpret 'factor concentrates' as including both plasma derived concentrates and recombinant concentrates. An alternative treatment was desmopressin (DDAVP, usually given with tranexamic acid) which was available to all in whom it was effective.

14. What were, in your view, the advantages and disadvantages of those alternative treatments? What use was made of them at the Centre? Do you consider that they should have been used in preference to factor concentrates so as to reduce the risk of infection? If not, why?

14.1 If desmopressin was effective, and not contraindicated, its use avoided exposing patients to plasma products when that was the alternative. Desmopressin was used at the Centre for patients with mild haemophilia or VWD wherever possible. When using desmopressin, excessive fluid retention needs to avoided by limiting fluid intake to 1 litre in the subsequent 24 hours and plasma sodium should be monitored if

desmopressin is used in children <2 years old or whenever repeated doses are given. Desmopressin use has rarely been followed by occlusive arterial events and should not be used in patients who are likely to have atherosclerosis.

15. What was the Centre's policy and approach in relation to prophylactic treatment? Did that policy and approach change over time and if so how?

15.1 Prophylaxis in children with severe haemophilia was in place when I started in 1995. This was then extended to all patients with severe haemophilia. I cannot remember when prophylaxis for adults with severe haemophilia became standard treatment. Over time there has been a tendency to intensify prophylaxis.

16. What was the Centre's policy and approach in relation to home treatment? Did that policy and approach change over time and if so how?

16.1 Home treatment was in place when I started for patients who needed regular treatment or who were on prophylaxis. Home delivery was introduced in 2005.

17. If children were treated at the Centre, what was the Centre's policy and approach in relation to the use of factor concentrates for children? Did that policy and approach change over time and if so how?

17.1 There was no difference with regard to children other than as mentioned above they got recombinant factor earlier and began prophylaxis earlier than adults.

18. To what extent, and why, were people with mild or moderate bleeding disorders treated at the Centre with factor concentrates?

18.1 People with mild and moderate bleeding disorders were treated with factor concentrates only if it was necessary and they could not be treated with desmopressin (e.g. type 2A VWD patient with angiodysplasia and GI bleeding unresponsive to desmopressin, major surgery in moderate haemophilia).

19. What if any viruses or infections, other than HIV, HCV and HBV, were transmitted to patients at the Centre in consequence of the use of blood products?

19.1 In my time at the Centre no patients were infected with HIV, HCV or HBV through use of blood products. There were multiple patients infected with HIV and HCV before 1985. Patients were exposed to UK plasma-derived concentrate at the time of vCJD. One of our patients who had no neurological symptoms and no clinical evidence of vCJD had prion protein in his spleen at post-mortem examination **[HCDO0000799]**.

Section 3: Knowledge of, and response to, risk

General

20. When you began working in haematology, what did you know and understand about the risks of infection associated with blood and/or blood products? What were the sources of your knowledge? How did that knowledge and understanding develop over time?

20.1 I began working in haematology as an SHO in February 1987 at the Royal Free Hospital in London. I was not involved with haemophilia care at the Royal Free other than as an on call SHO. I knew at that time that hepatitis B (HBV), non-A non-B hepatitis and HIV could potentially be transmitted by blood and blood products. Although the fact that non-A non-B hepatitis could cause chronic hepatitis was not appreciated at first I believe this was known when I started in haematology in 1987 though it was not until PCR testing for HCV in 1990 that persistent viral infection was demonstrated.

20.2 I was aware of AIDS in 1983 when I worked in a sexually transmitted diseases clinic for three months. The cause was not then known. HIV was identified in 1984 and HCV in 1988 and I believe I would have been aware of those discoveries shortly afterwards.

20.3 In terms of sources of knowledge, after qualifying, during my medical (physician) jobs, I scanned the general medical journals (BMJ, Lancet, New England Journal of Medicine (NEJM)) for important papers and revised for the MRCP.

20.4 After starting haematology I added the general haematology journals (British Journal of Haematology and Blood) to the journals I scanned. In my Senior Registrar job in

haematology at Addenbrooke's (April 1992 to June 1995) I revised for the MRCPath and attended some courses for this.

20.5 When I took up my consultant post in Oxford I added the journal "Thrombosis and Haemostasis" to my regular reading and also the "Journal of Thrombosis and Haemostasis" from its inception in 2003. The recently started journal "Haemophilia" was available in the department. As a consultant I attended frequent scientific meetings as part of my professional development.

21. What advisory and decision-making structures were in place, or were put in place, at the Centre and/or within the area covered by the Centre, to consider and assess the risks of infection associated with the use of blood and/or blood products?

21.1 When I started in Oxford in July 1995, desmopressin was used when indicated and all the plasma derived concentrates (other than porcine FVIII) were virally inactivated. I don't remember using porcine FVIII. There was then a move to recombinant products. I think some children started these as or just before I arrived but adults not until "recombinant for all" in 2003-2006. I know of no case of blood product borne viral transmission in Oxford during my time there.

22. What was your understanding of the relative risks of infection from (i) the use of commercially supplied blood products, and (ii) the use of NHS blood products? How did this understanding change over time? How, if at all, did this inform or influence the Centre's decisions as to which blood products to use in treating patients?

22.1 When I started in Oxford in 1995 the risk of viral infection from commercially supplied blood products and NHS blood products were both considered to be very low and neither product was felt to be superior to the other in this regard. I cannot comment on how this changed over time before then as I had not been involved in discussions or safety evaluations. When vCJD became an issue it was regarded as preferable to avoid UK plasma products (see 23.1).

23. What decisions and actions were taken by the Centre and/or by you to minimise or reduce exposure to infection?

23.1 After the 1997 recall of some BPL products due to vCJD it was felt preferable to use plasma-derived products which were not made from UK plasma. Patients on plasma-derived products were offered the option of switching from those made from UK plasma to those made from non-UK plasma. There also followed an increased desire to introduce recombinant products.

Hepatitis

24. When you began working in haematology, what was your knowledge and understanding of the risks of the transmission of hepatitis (including HBV/HCV) from blood and blood products? What were the sources of your knowledge? How did that knowledge and understanding develop over time?

24.1 See 20.1 and 20.2.

25. What was your understanding of the nature and severity of the different forms of blood borne viral hepatitis and how did that understanding develop over time?

25.1 See 20.1 and 20.2.

Section 4: Treatment of patients at the Centre

Provision of information to patients

26. What information did you provide or cause to be provided to patients with a bleeding disorder:

a. about the risks of infection in consequence of treatment with blood products (in particular factor concentrates) prior to such treatment commencing?

26.1 I would discuss with a patient (or parent of a patient) with newly diagnosed haemophilia the history of haemophilia and how treatment had evolved over time. Patients/parents often perceived it as an invariably crippling condition which with modern prophylaxis is not the case. They would often be aware of past blood borne infections particularly HIV. When plasma products were being used I would discuss

that viral inactivation procedures were now used and that the risk of viral transmission was regarded as very low though could not be guaranteed to be zero. The possibility of unknown pathogens would be acknowledged. After 1997, vCJD and the use of non-UK plasma would be discussed. Otherwise I would explain that we now used recombinant (synthetic products). Vaccination against HBV and HAV was still recommended because of the risk of blood transfusion being required.

b. about alternatives to treatment with factor concentrates?

26.2 Desmopressin (and tranexamic acid) would be discussed if appropriate. In VWD patients (other than types 2B and type 3) a trial of desmopressin would be organised.

27. How (if at all) did this change over time?

27.1 This changed over time only is so much that plasma products were phased out where possible.

Hepatitis C

28. When did the Centre, or the other hospitals you worked at, begin testing patients for HCV? Over what period of time was testing for HCV carried out after a test became available? How and when were patients told of their diagnosis of HCV? Were they told in person, by letter or by phone?

28.1 All those who attended the Centre had already been tested for HCV when I started in Oxford in 1995 and all had been told of the result.

28.2 I do not know what had been done to trace those who had been treated in the past but who no longer attended, though a search was made for these in the "look-back" exercise of 2011. I remember that this generated a large amount of work and that we had to complete forms which were sent to UKHCDO but cannot recall the identification of any previously unknown HCV cases. NHD should have the details.

28.3 I do not know when testing began in my training grade hospitals.

29. What information was provided to patients who had tested positive for HCV about the infection, its significance, prognosis, treatment options and management?

29.1 This was before my appointment but I know that the HCV positive patients were under the care of a consultant hepatologist who did a clinic in the Centre once a week. When I arrived this was Dr Joan Trowell. It was later Dr Jane Collier who later moved the patients to her hepatology clinic at the John Radcliffe. I did not look after patients with hepatitis.

30. Were the results of testing for HCV notified to patients promptly or were there delays in informing patients of their diagnosis? If there were delays in informing patients, please explain why.

30.1 I do not know. All had been informed by the time I was appointed.

31. How many patients at the Centre, or the other hospitals you worked at, were infected with HCV?

31.1 I haven't got the figures for the number of infected patients but this will be available from OHTC or the NHD.

Other information

32. What information was provided to patients about the risks of other infections?

32.1 Patients who might be treated with plasma-derived products were told about HAV and HBV and offered vaccination against them. vCJD and the use of non-UK plasma was discussed.

33. What information was provided to patients about the risks of infecting others?

33.1 The possibility of transmission of HCV to a partner was thought to be low but patients were told of the possibility of sexual transmission by the hepatologists. Sexual transmission of HIV would have been discussed by the infectious diseases team.

Consent

34. How often were blood samples obtained from patients attending the Centre, or the other hospitals you worked at, and for what purposes? What information was given to patients about the purposes for which blood samples were taken? Were samples stored for prolonged periods and if so why? Did the Centre, or the other hospitals you worked at, obtain patients' informed consent to the storage and use of those samples?

34.1 At the Centre, bloods were usually taken at each clinic visit. The patients/parents would be aware of what tests were being done e.g. FVIII, inhibitors screen, LFTs.

34.2 In the coagulation laboratory left over plasma was stored. This enabled an assay to be repeated if the result seemed strange. If a patient had a new positive inhibitor screen a sample from the previous visit could be tested to see if a weak inhibitor had been missed.

34.3 Informed consent for plasma storage was not taken.

34.4 I do not know what the practice was at other hospitals I worked at in relation to storage of samples.

35. Were patients under your care and/or at the Centre, or the other hospitals you worked at, treated with factor concentrates or other blood products without their express and informed consent? If so, how and why did this occur? What was the approach to obtaining consent to treatment?

35.1 Patients at Oxford were not treated without their informed consent (or consent of their parents). Patients with bleeding disorders would have had their treatment agreed in advance. The exception might be a severe bleed in an undiagnosed neonate or infant. This would present as an emergency to the paediatricians and rapid treatment might be necessary before the normal full discussion could take place.

36. Were patients under your care and/or at the Centre, or the other hospitals you worked at, tested for HIV and/or for HCV and/or for any other purpose without their express and informed consent? If so, how and why did this occur? What was the approach to obtaining consent to testing?

36.1 In my time at Oxford (1995 onwards) patients were not tested for HIV or HCV without discussing testing with them. I do not know about the other hospitals I worked at.

Recombinant

37. Please set out what you can recall about the introduction of recombinant products in the UK. In answering this question, you may find it useful to consider the enclosed minutes of UKHCDO meetings attended by you on 9 October 2003 [HCDO0000502] and 13 October 2005 [HCDO0000504] and a letter from Charles Hay dated 12 February 2003 about the Department of Health funding for recombinant products [HCDO0000109_038].

37.1 In Oxford I think children were put onto recombinant just before or around the time I started in 1995. This should be recorded with the NHD. I believe recombinant for children was national policy in 1998.

37.2 In England recombinant for adults ("recombinant for all") was rolled out over three years from 2003 to 2006. This required a large increase in funding which came via PCTs and was the stimulus for the first round of national procurement. As far as I remember adults in Oxford were switched as part of this national scheme. As we purchased plasma-derived concentrate at lower prices than most centres the increase in cost to purchase recombinant products at national prices was greater than average for our consortium of PCTs.

38. Please explain your involvement, and that of UKHCDO, with efforts to obtain recombinant blood products for patients with haemophilia. What difficulties were encountered and why? You may find it useful to consider the email communication from yourself to Frank Hill on 25 May 2001 [HCDO0000013_037].

38.1 The efforts made to obtain recombinant blood products are well documented in the minutes of the UKHCDO meetings. The main issues with obtaining recombinant blood products were supply and finance.

38.2 In 2001 there had been a world-wide shortage of recombinant due to the FDA halting production at a Bayer plant in the USA. Some patients had to be taken off

recombinant. I remember some children reducing, and perhaps even temporarily stopping, prophylaxis.

38.3 By 2003 supply was not an issue but switching adults to recombinant came at a significant cost (at 2003 prices) and this required the Department of Health to channel extra funding through the PCTs to pay for the switch over. This was phased over 3-4 years. I believe patients were largely swapped by age bands.

38.4 UKHCDO had favoured a move to recombinant FVIII in 1997. If cost was not an issue, I believe adults would have received recombinant products from the late 1990s, albeit there would have been much more severe product shortages for a period in 2001. However there was (at the time) a significant increase in cost so it was a political and health economic decision for the DoH as to where to prioritise health spending and so when recombinant could be introduced.

39. In your view, should recombinant blood products have been made available to all haemophiliacs earlier than they were? If so, when?

39.1 See 38.4. It is a political and heath economic decision for the DoH as to where to prioritise health spending. I am not in a position to judge where health spending is best directed.

40. When were recombinant products available to patients (and which categories of patients) treated at the Centre?

40.1 See 37.1 and 37.2.

Research

41. Other than is set out in response to earlier questions, please list all the research studies that you have been involved with during your time working at the Centre, or the other hospitals you worked at, (insofar as relevant to the Inquiry's Terms of Reference) and:

a. Describe the purpose of the research;
b. Explain the steps that were taken to obtain approval for the research;
c. Explain what your involvement was;

d. Identify what other organisations or bodies were involved in the research;

e. State how the research was funded and from whom the funds came;

f. State the number of patients involved;

g. Provide details of steps taken to inform patients of their involvement and to seek their informed consent; and

h. Provide details of any publications relating to the research.

41.1 I do not have a list of research studies I was involved with during my time working at the Centre. Oxford University Hospital NHS Trust (OUH) has a department through which clinical studies must go. They should be able to provide a list of all studies done at OHTC along with the chief investigator and other investigators.

41.2 I was involved in the study identified in the Rule 9 request. "*Variant CDJ infection in the spleen of a neurologically asymptomatic UK adult patient with haemophilia*" **[HCDO00000799].** The responses to questions a-h above will be evident from the publication. My role was to provide the clinical case history from the patient's records.

41.3 Over the years there were several trials of new recombinant factor concentrates in Oxford. I think Dr Giangrande was chief investigator on all of them but I would have been an investigator.

41.4 I entered a patient into the International Immune Tolerance Study, principle investigator Prof. Charles Hay, Manchester. This resulted in a publication entitled "*The principle results of the International Immune Tolerance Study: a randomized dose comparison*" Blood. 2012;119(6):1335-1344 **[WITN4743003]**. The purpose of the study was to compare "low dose" immune tolerance with "high dose" immune tolerance in patients with inhibitors. The responses to questions a-h above will be evident from the publication. I would have consented the patient and followed the study protocol.

41.5 In my last few years at Oxford, I was chief investigator for a study of emicizumab in haemophilia A patients with inhibitors. I entered two patients. I would have consented them and followed the protocol.

41.6 I also recruited and followed up a patient with haemophilia B who went into a gene therapy trial at the Royal Free in my last year.

41.7 The purpose of the studies on new unlicensed products (e.g. recombinant concentrates, emicizumab) was to gain a licence. Patients who agreed to take part could access these products before they were commercially available, for example it allowed some to access recombinant factors earlier than they otherwise could.

41.8 All studies would have gone through the correct approval process e.g. Central Office for Research Ethics Committees (COREC) and all conformed to Good Clinical Practice guidelines. The ethics committee would have to assess that the potential benefits and risks were reasonable.

41.9 The companies involved funded the trials, they paid money to the Trust in lieu of doctors and nurses time, for any assays, etc. and the products used in these trials were provided by the company at no cost so there was a considerable saving to the consortium of PCTs who funded concentrate at the Centre as they did not need to purchase commercial concentrate for these patients.

41.10 In all the above studies any patient data was anonymised/de-identified.

41.11 Patients would have the study fully explained to them, be provided with information leaflets and have to freely give informed consent. Data collection would respect patient confidentiality. Researchers would have to be competent to carry out the study and behave with honesty and integrity and declare any conflicts of interest.

42. What do you understand to be the ethical principles that should guide research? Did you apply those principles to the research studies referred to above and if so, how? If not, why?

42.1 The ethical principles that should guide research are set out in Good Clinical Practice and GMC guidance.

42.2. See 41.8, 41.10 and 41.11. Ethical principles were followed at all times.

43. Were patients involved in research studies without their express consent? If so, how and why did this occur?

43.1 No, but see 44.1 regarding epidemiological studies using the NHD.

44. Was patient data (anonymised, de-identified or otherwise) used for the purpose of research or for any other purpose without their express consent? If so, what data was used and how and why did this occur?

44.1 See 41.10 regarding patient data used for the purpose of research.

44.2 Patient data sent to the NHD was not anonymised. How to consent for this was the subject of discussion in UKHCDO. My practice when seeing a new patient was to discuss the NHD. I would say it was a useful resource for examining the epidemiology of bleeding disorders in the UK and so of help in procuring factor concentrate and that it might be useful if they were taken unwell outside Oxford and basic information about them was needed. I also said I would issue them with a NHD bleeding disorders card which would have basic information about their condition which they could keep on their person (it is credit card size). Their agreement was taken as consent. Later NHD produced a leaflet about the database which was also given to new patients (and also provided at follow-up clinics). This said they could withdraw from the database if they wanted to though none did to my knowledge. Whether patients should also give written consent was debated but was not requested by NHD and not done in Oxford at the time of my retirement.

45. Was patient data (anonymised, de-identified or otherwise) shared with third parties (e.g. UKHCDO) without their express consent? If so how and why did this occur, and what information was provided to whom? You may find it useful to refer to correspondence to Frank Hill regarding use of UKHCDO database for research from Frank Hill on 27 November 2003 [HCDO0000254_033] and from Simon Brown on 10 February 2004 [HCDO0000254_035].

45.1 See 44.2. To my knowledge the NHD would not pass on patient identifiable information outside the UKHCDO.

45.2 In 2003, when discussing inhibitor risk with colleagues, we realised that some of us who used BPL 8Y seemed to have a low inhibitor rate. It certainly seemed so in Oxford as we had only one such patient. Simon Brown from the Royal Free proposed a few of us look into this. The possibility instead became a possible project for the inhibitor working party. The proposal would have been to compare inhibitor rates in

patients in the NHD who use 8Y with matched controls who used other products (**[HCDO0000254_033]**, **[HCDO0000254_035]**). This proposed epidemiological study did not proceed but I cannot remember why. It could have been a quick crude look at the data showed no effect or it may have been subsumed into a larger inhibitor working party study. I note the inhibitor working party published a study, "*Factor VIII brand and the incidence of factor VIII inhibitors in previously untreated UK children with severe haemophilia A, 2000-2011*" though this was many years later (Blood. 2014;124:3389-3397).

46. Please provide details of any articles or studies that you have published (other than those already referred to) insofar as relevant to the Inquiry's Terms of Reference.

46.1 Other than those already referred to in the Rule 9 request, articles in which I am an author that may be relevant to the Inquiry's Terms of Reference:

46.1.1 Collins, P., Chalmers, E., Chowdary, P., Keeling, D., Mathias, M., O'Donnell, J., Pasi, K.J., Rangarajan, S. & Thomas, A. *The use of enhanced half-life coagulation factor concentrates in routine clinical practice: guidance from UKHCDO*. Haemophilia 2016;22:487–498 **[WITN4743004].**

46.1.2 Maclean PS, Richards M, Williams M, Collins P, Liesner R, Keeling DM, Yee T, Will AM, Young D, Chalmers EA. *Treatment related factors and inhibitor development in children with severe haemophilia A. Haemophilia*. 2011;17:282-287. **[WITN4743005].**

46.1.3 Chalmers EA, Brown SA, Keeling D, Liesner R, Richards M, Stirling D, Thomas A, Vidler V, Williams MD & Young D. *Early factor VIII exposure and subsequent inhibitor development in children with severe haemophilia A.* Haemophilia 2007;13:149-155. **[WITN4743006].**

46.1.4 Collins PW, Hirsch S, Baglin TP, Dolan G, Hanley J, Makris M, Keeling DM, Liesner R, Brown SA & Hay CR. *Acquired haemophilia A in the UK: a two year national surveillance study by UK Haemophilia Centre Doctors' Organisation*. Blood 2007;109:1870-7. **[WITN4743007].**

46.1.5 Hay CR, Brown S, Collins PW, Keeling DM & Liesner R. *The diagnosis and management of factor VIII and IX inhibitors: a guideline from the United Kingdom*

Haemophilia Centre Doctors Organisation. Br J Haematol 2006;133:591-605. **[WITN4743008].**

46.1.6 Laffan M, Brown SA, Collins PW, Cumming AM, Hill FG, Keeling D, Peake IR & Pasi KJ. *The diagnosis of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organization*. Haemophilia, 2004;10:199-217. **[WITN4743009].**

46.1.7 Hay CR, Baglin TP, Collins PW, Hill FG, Keeling DM. *The diagnosis and management of factor VIII and IX inhibitors: a guideline from the UK Haemophilia Centre Doctors' Organization (UKHCDO)*. Br J Haematol. 2000;111:78-90 **[WITN4743010].**

46.1.8 Sukhu K, Keeling DM, Giangrande PL. *Variation in inhibitor reactivity in acquired haemophilia A with different concentrates*. Clin Lab Haematol. 2000;22:287-290 **[WITN4743011].**

Previously untreated patients

47. Detail all decisions and actions taken at the Centre, or the other hospitals you worked at, by you or with your involvement with regard to a category of people referred to as 'previously untreated patients' (PUPS).

47.1 Previously untreated patients are generally new-born children, neonates or infants or patients with mild disease. They were treated in the same way as previously treated patients but when recombinant was in short supply they were prioritised. This was sensible as they had never been exposed to plasma-derived products and the doses required were much smaller than in a severely affected adult.

Treatment of patients at the Centre

48. How was the care and treatment of patients with HBV managed at the Centre, or the other hospitals you worked at? In particular:

a. What steps were taken to arrange for, or refer patients for, specialist care?

b. What treatment options were offered over the years?

c. What information was provided to patients about the risks and benefits of specific treatments and about side effects?

d. What follow-up and/or ongoing monitoring was arranged in respect of patients who were infected with HBV?

48.1 I am only aware of coming across one patient with past HBV at Oxford who was under the hepatologists. I don't remember patients with HBV any at other hospitals.

49. How was the care and treatment of patients once they were diagnosed with HCV managed at the Centre, or the other hospitals you worked at? In particular:

a. What steps were taken to arrange for, or refer patients for, specialist care?

49.1 At the Centre, HCV antibody positive patients had PCR analysis to confirm active hepatitis infection, genotyping and HCV viral load. Patients with active infection were then referred to a consultant hepatologist (initially this was Dr Joan Trowell and later Dr Jane Collier) who managed their hepatitis.

b. What treatment options were offered over the years?

49.2 I know in the early days some patients were treated with interferon and ribavirin. More recently many underwent eradication therapy with protease inhibitors.

c. What information was provided to patients about the risks and benefits of specific treatments and about side effects?

49.3 I do not know, this was done by the hepatologists.

d. What follow-up and/or ongoing monitoring was arranged in respect of patients who had been diagnosed with HCV?

49.4 Those patients who successfully eradicated HCV and had no evidence of cirrhosis on fibroscan, had normal LFTs and were not diabetic were no longer followed in the hepatology clinic and at haemophilia follow up they had annual hepatitis HCV PCR tests. Otherwise regular hepatology follow-up continued.

49.5 I do not know how patients with HCV were managed at other hospitals I worked at.

50. How was the care and treatment of patients with HIV/AIDS managed at the Centre, or the other hospitals you worked at? In particular:

a. What steps were taken to arrange for, or refer patients for, specialist care?
b. What treatment options were offered over the years?
c. What information was provided to patients about the risks and benefits of specific treatments and about side effects?
d. What follow-up and/or ongoing monitoring was arranged in respect of patients who had been diagnosed with HIV?

50.1 Patients who had contracted HIV were followed up by Professor Chris Conlon (and later also Professor John Fratt) and their team at the infectious disease outpatient clinic. All issues related to HIV were managed by the infectious diseases team. As I understand it patients were offered up-to-date drug regimens as they became available.

50.2 I do not know how patients with HIV/AIDS were managed at other hospitals.

51. What if any involvement did you and/or colleagues at the Centre, or the other hospitals you worked at, have with clinical trials in relation to treatments for HIV and HCV? Please provide details.

51.1 I had no involvement with any clinical trials in relation to treatments for HIV or HCV.

52. What arrangements were made for the care and treatment of children infected with HIV and/or hepatitis? How did those arrangements differ (if at all) from the arrangements made for adults?

52.1 I don't remember any HCV or HIV positive children when I started in 1995.

53. What if any arrangements were made at or through the Centre, or the other hospitals you worked at, to provide patients infected through blood products

with counselling, psychological support, social work support and/or other support?

53.1 To my recollection we had no bespoke counselling, psychological support or social support services at the Centre though our nurses did provide much support to patients. I don't know what was available to patients from hepatology or infectious diseases.

54. Was the Centre, or the other hospitals you worked at, allocated (whether by the DHSS/it's successors or another source) any funding to help with the counselling of patients infected with HIV?

54.1 I am not aware of any funding provided to help with the counselling of patients infected with HIV.

55. What if any difficulties did you/the Centre, or the other hospitals you worked at, encounter in obtaining sufficient funding for the treatment of people who had been infected with HIV and/or HCV?

55.1 I am not aware of how the infectious diseases team or the hepatology team obtained funding to treat patients with HIV and/or HCV.

Records

56. What was the Centre's policy or practice, or that of the other hospitals you worked at, as regards recording information on death certificates when a patient had been infected with HIV or hepatitis?

56.1 At Oxford, death certificates would be completed as accurately as possible by the admitting clinical team but not by the Centre as we provided an outpatient service.

56.2 I do not know what the practice was at other hospitals I worked at.

57. What were the retention policies of the Centre, or the other hospitals you worked at, in relation to medical records during the time you have worked there?

57.1 At the Centre, the haemophilia case records were retained indefinitely and even after a patient's death.

57.2 I do not know what the practice was in relation to retention of records at other hospitals.

58. Did you maintain separate files for some or all patients? If so, why; where were those files located; and where are those files now?

58.1 Patients with haemophilia had separate paper clinical notes which were kept in the Centre. This was for rapid access if a patient presented with a bleed and needed urgent attention. It was also extremely helpful if they telephoned for advice. I have not worked at the Centre since 2018 and cannot therefore confirm where those files are now kept.

59. Did you keep records or information (e.g. information being used for the purpose of research) about any of your patients at your home? If so, why, what information and where is that information held now?

59.1 When I started at Oxford in 1995 the Centre had a list of patients who required regular treatment on a spreadsheet. This was prepared and regularly updated by Dr Giangrande's secretary and recorded name, date of birth, diagnosis, factor level, inhibitor status and the product they were usually treated with. I kept a paper copy of this spreadsheet at home in my study for several years after I started in case phoned at home by a registrar called upon to treat an emergency bleed out of hours who could not access the information rapidly. The practice of keeping a paper copy at home was stopped when the registrars could be given rapid electronic access to this data through secure internal hospital servers.

60. Do you still hold records or information about any of your patients? If so, explain why and identify the records or information that you still hold.

60.1 I hold no records or information about any of my previous patients.

61. What system was followed for keeping records of the blood or blood products used in the Centre, or the other hospitals you worked at, (both in relation to source and use)?

61.1 When I started at Oxford all factor concentrates given to patients were recorded along with their batch numbers in hand written "black books" kept in the Centre, separate from the clinical notes. This was soon abandoned in favour of recording the information on a local electronic database. The batch numbers of all products given to patients were always recorded so patients treated with a specific batch of factor concentrate could be traced.

61.2 For home treatment we only had a record of total volumes given out or sent by home delivery. Patients were however encouraged to use "Haemtrack" (a secure therapy recording system, developed by the NHD, using phone apps and a website) to record individual doses they gave themselves at home.

61.3 I do not know what record keeping system for blood products was followed at other hospitals I worked at.

Section 5: Blood services

62. Please set out any interactions and dealings you had in relation to the blood services in your role at the Centre, or the other hospitals you worked at, insofar as relevant to the Inquiry's Terms of Reference.

62.1 Factor concentrate was purchased through the Centre and the bulk of stock was kept at the Centre. A small satellite stock (under our control) was kept in fridges at the blood bank at the John Radcliffe for emergency use at that site.

62.2 Solvent detergent treated fresh frozen plasma (SD-FFP) and platelets were held and provided by the blood bank.

62.3 I did not have any dealings in relation to blood services at other hospitals I worked at that are relevant to the Terms of Reference.

63. Please set out any interactions and dealings you had in relation to BPL in your role at the Centre, or the other hospitals you worked at, insofar as relevant to the Inquiry's Terms of Reference.

63.1 I had no dealings with BPL.

Section 6: UKHCDO

64. Please describe your involvement with UKHCDO (including any of its working parties, committees or groups).[1]

64.1 I attended many UKHCDO advisory meetings as the representative for Oxford from 1995 until my retirement. I was secretary of UKHCDO from 2005 to 2011 and vice-chair of UKHCDO from 2011 to 2016.

64.2 I was on the Inhibitor Working Party (IWP) and on the VWD Working Party (VWDWP). I do not have the dates as to when I was a member but this information should be available to the Inquiry from the documents available.

64.3 Whilst on the IWP I contributed to the 2000 and 2006 inhibitors guidelines:

- Hay CR, Brown S, Collins PW, Keeling DM & Liesner R. *The diagnosis and management of factor VIII and IX inhibitors: a guideline from the United Kingdom Haemophilia Centre Doctors Organisation*. Br J Haematol 2006;133:591-605.
- Hay CR, Baglin TP, Collins PW, Hill FG, Keeling DM. *The diagnosis and management of factor VIII and IX inhibitors: a guideline from the UK Haemophilia Centre Doctors' Organization (UKHCDO)*. Br J Haematol. 2000;111:78-90

64.4 Whilst on the VWD WP I contributed to the 2004 and 2014 guidelines:

- Laffan, M.A., Lester, W., O'Donnell, J.S., Will, A., Tait, R.C., Goodeve, A., Millar, C.M. & Keeling, D.M. (2014) *The diagnosis and management of von Willebrand disease: a United Kingdom Haemophilia Centre Doctors Organization guideline approved by the British Committee for Standards in Haematology*. Br J Haematol. 2014;167:453-65. **[ABHB0000006]**
- Laffan M, Brown SA, Collins PW, Cumming AM, Hill FG, Keeling D, Peake IR & Pasi KJ. *The diagnosis of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organization*. Haemophilia, 2004;10:199-217. **[WITN4743009]**
- Pasi KJ, Collins PW, Keeling DM, Brown SA, Cumming AM, Dolan GC, Hay CR, Hill FG, Laffan M & Peake IR. *Management of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organizatio*n. Haemophilia, 2004;10:218-231. **[HCDO0000113_010]**

[1] **In answering this question, you may be assisted by the listed publications at item 1 and the bundle of minutes of UKHCDO meetings at item 2 of this request.**

64.5 I was also on three UKHCDO Task Forces. A task force (TF), unlike a working party (WP), is temporary and formed for a specific task, usually writing a guideline. The TFs I was on were the 2003 Therapeutics TF, the 2008 Therapeutics TF and the 2016 Extended Half-Life (EHL) products TF.

64.6 The 2003 Therapeutics Task Force produced:

- Christopher Ludlam, David Keeling, Trevor Barrowcliffe, Elizabeth Chalmers, Paul Giangrande, Christine Harrington, Frank Hill, Christopher Hodgson, Christine Lee, Mike Makris and Henry Watson. *Guidelines on the selection and use of therapeutic products to treat haemophilia and other hereditary bleeding disorders*. Haemophilia, 2003;9:1-23 **[HCDO0000244_125]**

64.7 The 2008 Therapeutics TF produced:

- Keeling D, Tait C. & Makris M. *Guideline on the selection and use of therapeutic products to treat haemophilia and other hereditary bleeding disorders. A United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) guideline approved by the British Committee for Standards in Haematology*. Haemophilia 2008;14:671-684. **[ABMU0000010_010]**

64.8 The 2016 EHL products TF produced:

- Collins, P., Chalmers, E., Chowdary, P., Keeling, D., Mathias, M., O'Donnell, J., Pasi, K.J., Rangarajan, S. & Thomas, A. *The use of enhanced half-life coagulation factor concentrates in routine clinical practice: guidance from UKHCDO*. Haemophilia 2016;22:487–498 **[WITN4743004]**

65. During the period that you were involved with UKHCDO, please outline:

a. The purpose, functions and responsibilities of UKHCDO, as you understood them;

65.1 UKHCDO is a charity, from the constitution its purpose is:

- to preserve, protect and relieve persons suffering from haemophilia and other inherited bleeding disorders;

- to advance the education of the medical profession, the nursing profession, professions allied to medicine and the general public in the knowledge of haemophilia and other inherited bleeding disorders and their treatment;
- to promote or assist in the promotion of audit and research into the causes, prevention, alleviation and management of haemophilia and other inherited bleeding disorders and to disseminate the useful results of such research.

b. The structure, composition and role of its various committees or working groups;

65.2 The Executive Committee comprised the Chairman, Vice-Chairman, Treasurer and Secretary. However all important decisions were made through the Advisory Committee which as well as the above included a representative from each Comprehensive Care Centre (CCC), a representative from a haemophilia centre (non-CCC), and the chair of each working party (WP). The WPs were set up to cover specific areas (e.g. inhibitors, VWD, genetics). WPs would produce guidance in the area they covered.

65.3 UKHCDO also maintains a national haemophilia database (NHD) which is a registry of patients in the UK with inherited bleeding disorders or acquired haemophilia. This guides health care planning and procurement of concentrate and supports audit and research in this area. UKHCDO owns a registered company (UKHCDL Limited) that employs staff to work on the NHD.

c. The relationships between UKHCDO and pharmaceutical companies;

65.4 Pharmaceutical companies sponsor the AGM and accompanying scientific meetings of UKHCDO and have promotional stands. They also fund post marketing surveillance studies.

d. How decisions were taken by UKHCDO;

65.5 All significant decisions were taken by the Advisory Committee.

e. How information or advice was disseminated by UKHCDO and to whom;

65.6 During the time of my involvement, information, advice and minutes of the Advisory Committee have been sent either to all members of UKHCDO or to all the Advisory Committee members. The year was reviewed at the AGM and in the annual report. Guidelines were submitted to peer reviewed journals and published.

f. Any policies, guidance, actions or decisions of UKHCDO in which you were involved and which relate to:

i. the importation, purchase and selection of blood products;

65.7 I was not a member of UKHCDO at the time plasma-derived blood products were transmitting HCV and HIV. I was involved with the 2003 **[HDCO0000244_125]** and 2008 therapeutic guidelines **[ABMU0000010_010]** which both recommended recombinant products.

ii. alternative treatments to factor products for patients with bleeding disorders;

65.8 The 2003 and 2008 therapeutic guidelines both recommended using desmopressin and tranexamic acid if possible to avoid blood products as did the 2004 and 2014 VWD guidelines **[ABHB0000006]**.

iii. the risks of infection associated with the use of blood products;

65.9 The 2003 and 2008 guidelines both discussed the risk of infection and how to minimise this risk.

iv. the sharing of information about such risks with patients and/or their families;

65.10 The 2003 and 2008 guidelines had a section on Patient information and Consent which said *"Good practice dictates that the necessity for treatment is appropriately explained to the patient and/or parent. This should include the advantages and risks of different therapies to allow an informed decision to be made."*

v. obtaining consent from patients for the testing and storage of their blood, for treatment and for research;

65.11 I was not involved in any policies, guidance, or decisions of UKHCDO with regard to obtaining consent from patients for the testing and storage of their blood for treatment and for research.

vi. measures to reduce risk;

65.12 The 2003 and 2008 guidelines discuss minimising risk from infections.

vii. vCJD exposure;

65.13 The 2003 guideline said, "*The description of vCJD and its association with BSE has resulted in a change in policy regarding the use of plasma for fractionation in the UK. As a result, all plasma-derived concentrates produced in the UK since 1998 have been manufactured from the plasma of European and USA donors*". A discussion of the risk from vCJD was also in the 2008 guideline.

vii. treatments for HIV and HCV.

65.14 I was not involved in any policies, guidance, or decisions of UKHCDO with regard to treatments for HIV and HCV.

Section 7: Pharmaceutical companies/medical research/clinical trials

66. Have you ever provided advice or consultancy services to any pharmaceutical company involved in the manufacture and/or sale of blood products? If so, please list the names of the companies and give details (including dates) of the advisory or consultancy services that you provided.

66.1 I have been through my electronic calendar and financial records from 2013-2018 which covers the last five years up to my retirement. These show that I attended advisory boards for CSL-Behring and Octopharma which are both pharmaceutical companies involved in the manufacture and sale of blood products.

67. Have you ever received any pecuniary gain in return for performing an advisory/consultancy role for a pharmaceutical company involved in the manufacture or sale of blood products? If so, please provide details.

67.1 I have identified attendance at the following advisory meetings for pharmaceutical companies involved in the manufacture or sale of blood products, with remunerations received in brackets, three for CSL-Behring on 25.03.14 (£600), 23.06.16 (£1,800) and 28.02.18 (£1,500), and one for Octapharma on 16.12.14 (£1,000). I have no details of the meeting I attended with CSL-Behring on 25.03.14. The other three meetings on 23.06.16, 28.02.18 and 16.12.14 were to discuss synthetic recombinant products (not blood products).

67.2 In my time as a consultant I have also attended advisories for NovoNordisk, SOBI, Bayer, Wyeth/Pfizer and Baxter to discuss synthetic recombinant factors (not blood products) and a Chugai advisory to discuss the synthetic antibody emicizumab.

68. Have you ever sat on any advisory panel, board, committee or similar body, of any pharmaceutical company involved in the manufacture or sale of blood products? If so, please provide details of your involvement (including dates) and of any financial or other remuneration you received.

68.1 See 67.1.

69. Have you ever received any financial incentives from pharmaceutical companies to use certain blood products? If so, please provide details.

69.1 I have never received any financial incentives from pharmaceutical companies to use certain blood products.

70. Have you ever received any non-financial incentives from pharmaceutical companies to use certain blood products? If so, please provide details.

70.1 I have never received any non-financial incentives from pharmaceutical companies to use certain blood products.

71. Have you ever received any funding to prescribe, supply, administer, recommend, buy or sell any blood product from a pharmaceutical company? If so, please provide details.

71.1 I have never received any funding to prescribe, supply, administer, recommend, buy or sell any blood product from a pharmaceutical company.

72. What regulations or requirements or guidelines were in place concerning declaratory procedures for involvement with a pharmaceutical company? If you were so involved, did you follow these regulations, requirements and guidelines and what steps did you take?

72.1 Attendance at advisories has been in my own time (e.g. by taking annual leave) and declared to my Trust and to UKHCDO.

73. Have you ever undertaken medical research for or on behalf of a pharmaceutical company involved in the manufacture or sale of blood products? If so, please provide details.

73.1 Over the years there were several trials of new recombinant factor concentrates in Oxford but I do not recall any trial involving blood products.

74. Have you ever provided a pharmaceutical company with results from medical research studies that you have undertaken? If so, please provide details.

74.1 I have never provided a pharmaceutical company with results from medical research studies that I have undertaken.

75. If you did receive funding from pharmaceutical companies for medical research, did you declare the fact that you were receiving funding and the source of the funding to your employing organisation?

75.1 None received.

76. In the enclosed February 2003 email chain between yourself and a number of colleagues [HCDO0000109_031], you discussed the possibility of a pharmaceutical company sponsoring new guidelines on the treatment of von Willebrand's disease. Please provide some context for those discussions. Were the guidelines sponsored? Are you aware of a pharmaceutical company sponsoring any other guidelines, whether issued by UKHCDO or any other

organisation? If so, what (if any) effect did the sponsorship have on the contents of the guidelines?

76.1 With regard to **[HCDO0000109_031]**, in 2003 the VWD working party was writing guidelines for the diagnosis and management of VWD. It was originally hoped to submit both to the British Journal of haematology (BJH). An initial approach to BJH had drawn a tentative negative response that they were too long and even if accepted, there could not be a guarantee that they could be published in the same edition. Someone suggested we could consider pharmaceutical company sponsorship for the guidelines to be produced together as a supplement. I and most others were against such sponsorship. I suggested we submit to the journal, Haemophilia, for peer review in the normal way and ask them to consider publishing them back to back if they were both accepted. This is what happened. There was no sponsorship, they were both accepted and published back to back in Haemophilia in 2014.

76.2 I am not aware of a pharmaceutical company sponsoring any guidelines by UKHCHO or any other organisation involved in haemostasis and thrombosis.

Section 8: vCJD

77. In answering these questions, you may be helped by considering letters that you and Dr Giangrande sent to a patient concerning the risk of vCJD in December 1997 [WITN3063002] and January 2001 [WITN3063004] and also an email from you to Frank Hill on 21 September 2004 [HCDO0000254_666]. When and in what circumstances did you become aware of the risks of transmission of vCJD associated with the use of blood and blood products?

77.1 I believe I would only have become aware of the risk of transmission of vCJD associated with the use of blood and blood products in November 1997 just before the letter was sent out in December 1997.

77.3 The letter dated 3 December 1997 **[WITN3063002]** is, I believe, a standard template letter that was sent out to all patients that were possibly affected by vCJD. It stated that three weeks previously BPL withdrew a batch of 8Y and a batch of Replenate because donors had subsequently developed vCJD. I do not believe anyone in Oxford received either of these batches, nevertheless we offered our patients

products made from non-UK plasma as an alternative to products made from UK plasma in order to reduce the risk.

78. What was your understanding of how decisions were taken (either nationally or locally or both) as to the information that should be provided to patients about vCJD and as to the steps which should be taken in relation to patients and their care and treatment? Who made these decisions?

78.1 My understanding is that in 1997 the government were advised to filter white cells from whole blood to reduce the possibility of spreading vCJD, I presume by the CJD surveillance unit or the Health Protection Agency (HPA). This raised the possibility of vCJD contaminating factor concentrate.

78.2 The decision from UKHCDO was that the risk would be reduced by using concentrates prepared from non-UK plasma. I was not involved in these discussions and I do not know what role the CJD surveillance unit or the Committee on Safety of Medicines or HPA played, if any.

79. What was the process at the Centre for informing patients about possible exposure to vCJD?

79.1 Patients registered with the Centre were initially informed by letter about the possible risk of exposure to vCJD. We first wrote to our patients in December 1997 and we offered alternatives to UK plasma-derived concentrates.

80. How and when were patients told of possible exposure to vCJD?

80.1 See 79.1 above.

81. What information was provided to patients about the risks of vCJD?

81.1 The information that was provided is set out in the template letter from the Centre.

82. What counselling, support and/or advice was offered to patients who were informed that they might have been exposed to vCJD?

82.1 Oxford patients were given the opportunity to switch to products made from non-UK plasma and any changes to treatment were discussed with them in clinic or over the telephone. I don't believe any formal counselling or support was offered.

82.2 The letter of 3 December 1997 **[WITN3063002]** indicates that we also offered our patients to attend a meeting at the John Radcliffe Hospital on 15 December 1997 to present the evidence and discuss the matter. I have memories that this meeting attracted a low attendance.

83. What measures were put in place, from a public health perspective, in relation to the care and treatment of patients who had or might have been exposed to vCJD?

83.1 None until 2004, see 85.4.

84. What steps were taken at the Centre following notification from BPL in 2001 that a plasma donor had been diagnosed with vCJD? (In answering this question, you may find it helpful to refer to the letter from you and Dr Giangrande on 22 January 2001 [HSOC0004273].)

84.1 In 2001 there was a further notification from BPL **[WITN3063004]** which indicated that a blood donor who donated plasma in 1996 had developed vCJD. Plasma from the donor had been used to manufacture a number of BPL products. Oxford did have patients who had received these products. These patients were written to, the letter stated, "*Whilst we recognise that this news may generate anxiety, we feel that our patients are entitled to be informed of all the facts about their treatment. However, we also sincerely hope that you will be reassured by the fact that there is no evidence of transmissibility of new variant CJD through plasma products*". Patients who did not receive the batches were also written to **[HSOC0004273]**, they were informed what had happened and told they had not received the implicated batches.

84.2 All patients were asked to contact the Centre if they wished to discuss matters further and of course this is a subject that would have been discussed at all follow-up clinic appointments.

85. Why was the view of the UKHCDO not to introduce a risk score to patients to inform the approach to patient counselling and did you agree with it? (See,

Minutes of the Thirteenth Meeting of UK Haemophilia Centre Doctors' Organisation Advisory Committee, 16 February 2004, [BART0000930]).

85.1 The minutes of a UKHCDO meeting on 16 February 2004 **[BART00000930]** indicate that there was growing concern about vCJD and blood products. Discussions had taken place within and presumably between the CJD incidents panel and the Communicable Disease Surveillance Centre (CDSC) and a statement had been made in parliament by the Secretary of State for Health.

85.2 There were two main issues discussed at this meeting. Firstly, the possible development of a risk score presumably so an individual risk could be attached to each patient. If such a score could be shown to be accurate it might have been helpful for patient counselling though of course no test for CJD and no treatment for CJD was available at the time. It is difficult to see how an unvalidated or inaccurate risk score would be more useful than a general discussion of risk. I believe the consensus was that an unvalidated or inaccurate risk score might cause unnecessary anxiety when there was still a lot of unknown information.

85.3 Secondly, the possibility was raised that patients with bleeding disorders who had received treatment containing plasma contributed by a donor who subsequently developed vCJD (an implicated batch) might constitute a risk of ongoing transmission to others.

85.4 In September 2004, haemophilia treaters received a "Tool Kit" to be used to inform patients about UK plasma sourced products and vCJD. I am not certain but I think this was developed by the Health Protection Agency (HPA). This indicated that patients who received FVIII or FIX concentrates made from UK plasma between 1980 and 2001 were deemed to be "at risk for public health purposes" i.e. might constitute a risk of ongoing transmission to others. Precautions were advised for operations involving lymphoid or nerve tissue and endoscopes used were quarantined.

85.5 Patients were also given the choice as to whether to be informed or not about whether they had received a batch containing plasma contributed by a donor who subsequently developed vCJD (an implicated batch).

85.6 My email to Frank Hill on 21 September 2004 **[HCDO0000254_666]** is about an inconsistency I spotted in the "Tool Kit". I do not have the "Tool Kit", let alone any drafts, and cannot be certain which way the correction had to be made, but I think it may have been a correction was made to the text because the batches in Table 3 were not to be regarded as implicated batches.

85.7 In 2013 the exposure period considered to put patients "at risk for public health purposes" was reduced from 1980-2001 to 1990-2001. So some patients were told they were no longer regarded as "at risk for public health purposes".

Section 9: Financial Support Schemes

86. What if any involvement did you have with any of the trusts or funds (the Macfarlane Trust, the Eileen Trust, the Macfarlane and Eileen Trust, the Caxton Foundation, the Skipton Fund, the English Infected Blood Support Scheme 'EIBSS') set up to provide financial assistance to people who had been infected. If you have been involved with one or more of the trusts or funds, please address the following matters:

a. How you came to be involved in the trusts or funds, whether you held any formal position and, if so, for how long you held that position.

b. What if any involvement you had in the development of any criteria or policies relating to eligibility for financial assistance.

c. Any advice you provided to any of the trusts or funds.

d. Whether you were involved in the assessment of any applications to the trusts or funds by people who had been infected.

86.1 I did not have any involvement with any of the trusts or funds (the Macfarlane Trust, the Eileen Trust, the Macfarlane and Eileen Trust, the Caxton Foundation, the Skipton Fund, the English Infected Blood Support Scheme 'EIBSS') set up to provide financial assistance to people who had been infected save that I completed forms on behalf of patients applying for financial assistance.

87. To what extent did the Centre, or that of the other hospitals you worked at, and staff, including you, inform patients about these different trusts and funds?

87.1 At the Centre, it was the clinical nurse specialist who informed patients about these different trusts and funds. This was done at routine follow-up clinics.

87.2 I do not know what information was provided by other hospitals.

88. Did the Centre, or that of the other hospitals you worked at, have any policy or guidance for staff members in relation to referring patients to the trusts and/or schemes for support?

88.1 There was no written departmental guidance at the Centre. I do not know about other hospitals.

89. What kind of information did the Centre, or that of the other hospitals you worked at, (whether through you or otherwise) provide to the trusts and funds about or on behalf of patients who were seeking assistance from them?

89.1 At the Centre, we completed application forms for patients. I do not know about other hospitals.

90. Did the Centre, or that of the other hospitals you worked at, or any staff, including you, act as a gateway for determining whether a particular patient met the eligibility criteria for the receipt of assistance from any of the trusts and funds?

90.1 The only "gateway" was we completed the forms as accurately as we could.

91. Was the Centre, or that of the other hospitals you worked at, or any staff, including you, involved in assessing or determining applications made by patients for assistance from the trusts and funds? If so please describe that involvement.

91.1 I was not, and I do not think anyone at Oxford was, involved in assessing or determining applications made by patients for assistance from the trusts and funds. I do not know about other hospitals.

92. Based on your own dealings with any of the trusts and funds and/or based on your knowledge of the experiences of the Centre's patients, or that of the other hospitals you worked at, in relation to them, do you consider that the trusts and funds were well run? Do you consider that they achieved their purpose? Were there difficulties or shortcomings in the way in which they operated or in their dealings with beneficiaries and applicants for assistance?

92.1 I cannot judge whether the trusts and funds were well run, or whether they achieved their purpose. I have no evidence that they did not, and I did not come across difficulties or shortcomings in the way in which they operated or in their dealings with beneficiaries and applicants for assistance.

Section 10: Current haemophilia care and treatment

(Please note that the questions in this section are aimed at enabling the Inquiry to understand how haemophilia care is currently provided and how the provision of care and treatment and the approach to patients may have changed over the years. Please base your answers on the current state of haemophilia care at the Centre at the time of your retirement in February 2018).

93. Please describe how the provision of care and treatment for bleeding disorders was organised at the Centre at the time of your retirement.

93.1 On my retirement, the Oxford Haemophilia and Thrombosis Centre (OHTC) provided haemostasis and thrombosis care locally and regionally. The adult haemophilia team were based at the Churchill Hospital, and retained close supportive links with the paediatric haematology team on the John Radcliffe site, with a strong transition programme.

94. Please outline the treatments provided to patients with bleeding disorders at the Centre at the time of your retirement.

94.1 I attach the Centre's protocol for haemophilia patients dated July 2017 which was valid at the time of my retirement in 2018 **[WITN4743012]**. To summarise:

94.1.1 Prophylaxis was the treatment of choice for severely affected patients and almost universal amongst children.

94.1.2 Patients with haemophilia A and haemophilia B had access to recombinant products and many were on or in the process of switching to recombinant products with extended half-lives.

94.1.3 Inhibitors were managed with NovoSeven and/or FEIBA but emicizumab was in trial at the Centre and is now likely a treatment of choice.

94.1.4 VWD patients were treated with desmopressin or if they needed factor concentrate they received Voncento.

95. Please describe how you typically obtained your patients' consent to treatment. In particular:

a. What information did you give patients about the risks of the treatment?

95.1 Patients with haemophilia were on recombinant products and the main risk to treatment they were informed of was the risk of developing inhibitors. They were told they had a greater than average risk of exposure to blood products and were offered vaccination against HAV and HBV. The risk of breakthrough bleeds on prophylaxis was discussed. Patients on plasma products (e.g. certain patients with VWD) were informed of the source of plasma, the viral inactivation procedures and the theoretical residual risk of infection.

b. What information did you give patients about the side-effects of the treatment?

95.2 See 95.1

c. What information did you give patients about the risks of not having the treatment?

95.3 The risk of not having the treatment was bleeding. The risk of long term joint damage with only a few joint bleeds would have been discussed. It would have been

explained that prophylaxis would likely reduce the risk of intracranial bleeding, for example following a head injury.

d. What information did you give patients about the benefits of having the treatment?

95.4 The benefits of having treatment was to stop or prevent bleeding.

96. Please describe how you typically recorded your patients' consent to treatment.

96.1 I would make brief written notes whilst talking with a patient and afterwards dictate a comprehensive letter covering the consultation which was sent to the GP and copied to the patient. Written consent to treatment was not taken.

97. Are blood samples routinely taken from patients attending the Centre? If so, what information would you expect to be provided to patients about the purposes for which the samples are being taken? Does the Centre obtain patients' consent to the storage and use of the samples and, if so, how and in what way is that recorded?

97.1 Blood samples were routinely taken in clinic. Patients would be informed of what tests were being done though for routine tests this may have been simply "we'll check your blood count, kidney function and liver function". Patients were not necessarily told that any leftover blood would be stored in case needed in the future.

98. Please describe how you typically (a) obtained and (b) recorded your patients' consent to testing (of any kind).

98.1 See 97.1. Written consent was not obtained. Results were added to the GP letter which was copied to the patient.

99. How many current patients at the Centre (a) were infected with HIV through blood products; (b) were infected with HCV through blood products; (c) were infected with HBV through blood products; (d) were co-infected with HIV and HCV through blood products?

99.1 I do not have the number of patients who were infected with HIV and/or HCV through blood products. I can only recall one patient with HBV. This data should be available from OHTC and/or the NHD.

100. What if any involvement did you have/does the Centre have in the treatment of the Centre's patients for HIV and/or HCV and/or HBV? Are there multidisciplinary clinics (e.g. haematology and hepatology), and if not would such arrangements be feasible and beneficial?

100.1 HCV antibody positive patients had PCR analysis to confirm active hepatitis infection, genotyping and HCV viral load. Patients with active infection were then referred to a consultant hepatologist (Dr Jane Collier) who managed their hepatitis.

100.2 Those patients who successfully eradicated hepatitis C and had no evidence of cirrhosis on fibroscan, had normal LFT's and were not diabetic were no longer followed in the hepatology follow up but at haemophilia follow up they had annual hepatitis HCV PCR tests. Otherwise regular hepatology follow-up continued.

100.3 Patients who had contracted HIV were managed by the infectious diseases team (Professor Chris Conlon and Professor John Fratt).

101. What, if any, psychological services are available at the Centre? Did you have a psychologist as part of the staff team? Is there psychological support specifically for those infected with HIV and/or hepatitis in consequence of infected blood products?

102. What if any other support services are available at the Centre?

102.1 There were no dedicated psychological services or other dedicated support services available at the Centre.

103. What has been the impact of the infection of patients with HIV and/or hepatitis through blood products:

a. upon patients at the Centre (without identifying any individual patient);
b. the ways in which decisions about treatment and care are taken, and treatment and care are provided, at the Centre?

104. Has the infection of patients with HIV and/or HBV and/or HCV through blood products:

a. Changed or influenced your professional practice and approach and if so how?

b. Changed or influenced the practice and approach of your colleagues and if so how?

c. Changed or influenced the way in which haemophilia care is now provided and if so how?

104.1 No patient was infected with HIV or hepatitis whilst I worked at the Centre from 1995 to2018, the last infections would have been in the first half of the 1980s. I am sure this had a dramatic effect on staff who worked there forty years ago. Many patients have died, many are still having treatment for HIV and many have undergone HCV treatment or developed the complications of HCV. The Inquiry will be fully aware of the devastating effect on the haemophilia community. The main effect in the following years was to drive the move away from plasma products where possible. For those of us who started our consultant careers a decade after the last infections it is difficult to know what, if any, influence this has had on current practice, medicine in general has changed a lot in over almost half a century.

Section 11: Other issues

105. Please provide details of any complaints made about you (insofar as relevant to the Inquiry's Terms of Reference) to your employer, the General Medical Council, the Health Service Ombudsman or any other body or organisation which has a responsibility to investigate complaints.

105.1 I know of no complaints made about me to my employer, the General Medical Council, the Health Service Ombudsman or any other body or organisation which has a responsibility to investigate complaints.

106. Please explain, in as much detail as you are able to, any other matters that you believe may be of relevance to the Infected Blood Inquiry, having regard to its Terms of Reference and to the current List of Issues.

106.1 I do not think I have knowledge of any other matters that may be of relevance to the Infected Blood Inquiry.

Statement of Truth

I believe that the facts stated in this witness statement are true. I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

Signed

GRO-C

Dated 18 March 2021

Table of exhibits:

Date	Notes/ Description	Exhibit number
Undated	CV of Dr Keeling	WITN4743002
09.02.2012	*The principle results of the International Immune Tolerance Study: a randomized dose comparison*	WITN4743003
2016	Collins et al - *The use of enhanced half-life coagulation factor concentrates in routine clinical practice: guidance from UKHCDO*. Haemophilia 2016;22:487–498	WITN4743004
2011	Maclean et al - *Treatment related factors and inhibitor development in children with severe haemophilia A. Haemophilia*. 2011;17:282-287.	WITN4743005
2007	Chalmers et al - *Early factor VIII exposure and subsequent inhibitor development in children with severe haemophilia A.* Haemophilia 2007;13:149-155.	WITN4743006
2007	Collins et al - *Acquired haemophilia A in the UK: a two year national surveillance study by UK Haemophilia Centre Doctors' Organisation*. Blood 2007;109:1870-7	WITN4743007

Date	Notes/ Description	Exhibit number
2006	Hay et al - *The diagnosis and management of factor VIII and IX inhibitors: a guideline from the United Kingdom Haemophilia Centre Doctors Organisation*. Br J Haematol 2006;133:591-605.	WITN4743008
2004	Laffan et al - *The diagnosis of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organization*. Haemophilia, 2004;10:199-217	WITN4743009
2000	Hay et al - *The diagnosis and management of factor VIII and IX inhibitors: a guideline from the UK Haemophilia Centre Doctors' Organization (UKHCDO)*. Br J Haematol. 2000;111:78-90	WITN4743010
2000	Sukhu et al - *Variation in inhibitor reactivity in acquired haemophilia A with different concentrates*. Clin Lab Haematol. 2000;22:287-290	WITN4743011
July 2017	Oxford Haemophilia Centre protocol	WITN4743012