Witness Name: Michael Williams
Statement No.: WITN5725001
Exhibits: WITN5725002 - 003
Dated: 14.03.22

INFECTED BLOOD INQUIRY

FIRST WRITTEN STATEMENT OF DR MICHAEL DAVID WILLIAMS

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 05 July 2021.

I, Michael Williams, will say as follows: -

Section 1: Introduction

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

1.1. Name : Michael David Williams.

1.2. Date of Birth: GRO-C 1953

1.3. Address: Known to the Inquiry

1.4. Qualifications: MB ChB (Liverpool) 1977; MD (Liverpool) 1987; FRCP 1997; FRCPath 1997; FRCPCH 2010

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. Employment History:

2.1.1. Pre-Registration House Officer, 1.9.77 - 31.8.78. Walton Hospital, Liverpool

2.1.2. SHO Medicine, 1.9.78 - 30.6.80. Walton Hospital, Liverpool and Royal Liverpool Hospital, Liverpool

2.1.3. Trainee General Practice, 1.7.80 – 9.4.81. Cheltenham

2.1.4. Registrar, General Medicine and Haematology, 13.4.81 – 25.2.84. Walsgrave Hospital, Coventry.

2.1.5. Research Fellow, Haematology, 27.2.84 –1.12.85, Birmingham Children's Hospital.

2.1.6. Senior Registrar, Haematology, 2.12.85 – 18.10.92, W Midlands Training Scheme

2.1.7. Research Fellow, Haematology, 1989-90. Royal Melbourne Hospital, Australia

2.1.8. Consultant Haematologist, Birmingham Children's Hospital and Birmingham Women's Hospital November 1992.

2.1.9. Full time Consultant Haematologist, Birmingham Children's Hospital 2002- December 2017

2.2. Roles and Responsibilities:

2.2.1. Following my medical registrar post, I spent 21 months as Research Fellow in the Department of Haematology, Birmingham Children's Hospital. This research post was based on the further clinical and laboratory investigation of previously reported immune dysfunction in haemophilic boys at BCH and resulted in several publications and an MD thesis, entitled "A Study of the Inter-Relationships between immunosuppression, treatment and infective complications in haemophilic boys".

2.2.2. I was appointed senior registrar in haematology, W Midlands Training Scheme, in 1985. During the next 6 years, I rotated to various teaching

and district general hospitals within the Region and gained training in a broad range of adult and paediatric clinical and laboratory haematology.

2.2.3. Following my completion of the RCPath examination I was able to spend a year off service as Research Fellow in the Department of Haematology, Royal Melbourne Hospital. During this year I gained experience in cell culture techniques and was responsible for establishing methodologies for the identification of gene mutations in Australian families with Protein C Deficiency.

2.2.4. I was appointed consultant in haematology at Birmingham Children's Hospital and Birmingham Maternity Hospital in November 1992 and worked as a full time paediatric haematologist at BCH from June 2002 to December 2017. I remain an honorary consultant at this hospital.

2.2.5. I was Director of the Regional Paediatric Haemophilia Centre from 2005-17, Head of Laboratory Haematology 2005-17, Head of Clinical Haematology 2008-2010, Director of the Regional Molecular Haemostasis Service 2007-2018, and have had a large clinical workload throughout my consultant post at BCH, encompassing a wide spectrum of malignant and non-malignant disorders. I have developed my subspecialty interest in disorders of haemostasis and thrombosis throughout my consultant career.

2.2.6. I was appointed Honorary Consultant Paediatrician, University Hospital of North Midlands 2010 and Honorary Senior Research Fellow, School of Clinical and Experimental Medicine, Birmingham University from 2009-2018.

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. I was Chairman of the British Society for Haematology working party for neonatal haemostasis and thrombosis 2001-17.

3.2. I was a member of the Advisory Committee of the UK Haemophilia Centre Doctors Organisation (UKHCDO) 1997-2017.

3.3. I was a member of the UKHCDO's working party on paediatric haemophilia from 1994 -2017 and was its Chairman from 2001- 2007.

3.4. I was a member of the UKHCDO rare bleeding disorders working party since its inception in 2003 up to 2009.

3.5. I was a member of the UKHCDO inhibitor working party 2006 - 17.

3.6. I was a member of the BSH working party for paediatric venous thrombosis 2008-17.

3.7. I was a member of the British Society of Haematology Paediatric Committee since 2006, being Scientific Secretary since 2007 up to May 2010 and Chair of this committee 2010- April 2013, responsible for representing paediatric haematology in various forums such as SAC, BSH, RCPath, RCPCH.

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 and copies of any statements or reports which you provided.**

4.1. I have not been involved in such activity.

Section 2: Decisions and actions of the Birmingham Children's Hospital

5. **Please:**

a. **Describe the roles, functions and responsibilities of the Department of Haematology and in particular the Haemophilia Centre at the Birmingham Children's Hospital ("the Centre") during the time that you worked there;**

5.1. The Department of Haematology at Birmingham Children's Hospital provides a comprehensive clinical and laboratory service to the hospital, a tertiary service to the West Midlands region and an extra-regional service for some aspects of paediatric haematology. It is the second largest paediatric haematology department in the country. Clinically it is responsible for the diagnosis and treatment of children with a wide range of malignant and non-malignant disorders, including leukaemia, bone marrow failure syndromes, inherited and acquired bleeding and thrombotic disorders and haemoglobinopathies.

5.2. The Haemophilia Centre is a UKHCDO comprehensive care centre, responsible for the care of children with inherited bleeding disorders from birth up to the age of 16 years, after which time their care is usually transferred to the adult comprehensive care centre at University Hospital, Birmingham. It is supported by an on-site haematology laboratory department which includes a comprehensive haemostasis laboratory.

5.3. During my time at BCH the Haemophilia Centre had multiple roles and responsibilities which have always included the diagnosis of inherited bleeding disorders, treatment of such disorders and their complications, education and counselling of patients and their families, genetic counselling, support and advice for schools, training of carers and individual children in the recognition of bleeds and in the administration of treatment including home treatment programmes and prophylaxis. Like all Haemophilia Centres, BCH was involved in the consequences of the transmission of HIV and HCV through factor concentrate in terms of the identification of affected patients and their ongoing care, and more recently was involved in the look back programme for vCJD. The Centre has also had the responsibility of introducing successive generations of viricidally-treated plasma- derived factor VIII and IX concentrates for haemophilic boys, and more recently, recombinant factor concentrates. It continues to maintain a surveillance programme to detect adverse effects of such treatments such as inhibitor formation. The Centre also has a significant number of patients with rare bleeding disorders involving other factor deficiencies or platelet defects as well as a large number of patients with VWD, and again provides a comprehensive service to those patients and families.

5.4. The Centre fulfilled a comprehensive care role for the Region and as such had close relationships with the Region's haemophilia centres (Stoke, Coventry, Shrewsbury) including shared care of patients.

5.5. Throughout my involvement with BCH Haemophilia Centre there continued to be strong interests in research and teaching in inherited and acquired bleeding disorders, with the early introduction into clinical practice of previous research such as the application of molecular genetics to the genetic diagnosis of bleeding and thrombotic disorders.

b. **Outline the facilities and staffing arrangements for the care of patients with bleeding disorders;**

5.6. The facilities and staffing arrangements for the care of patients with bleeding disorders have improved greatly during my various periods spent at BCH. When I was a research registrar there were only 2 consultants in haematology, one of whom had the responsibility for haemophilia, the other haemoglobinopathies. In addition, they were responsible for the diagnosis and treatment of all other haematology disorders, including most of the leukaemia patients, supported by haematology junior medical staff. The Haemophilia Unit consisted of a small treatment room on the haematology-oncology ward. The nursing staff consisted of one haemophilia sister. When I returned to BCH as a senior registrar there were 2 haemophilia sisters and a staff nurse, a social worker and a clinical psychologist; there were 6 dedicated beds for bleeding disorder patients. These increases were funded through additional monies made available to address HIV infection in the Centre's patients. When I was appointed consultant, nursing numbers had been maintained, there had been little change in physical space available but a block contract with the Region for haemophilia services had been agreed, which was to be of great benefit for the service in the years to come.

5.7. In 1998 the whole hospital moved to a new site (re-developed, pre-existing adult hospital) in the city centre. As far as the facilities for the Haemophilia Centre were concerned, this move was an improvement, resulting in a more spacious haemophilia unit (though still restricted and just about adequate), separate examination room, nursing office and interview room. Laboratory facilities had improved, and a molecular genetics laboratory was developed. Stronger links with physiotherapy and dentistry were developed, and with the other Regional haemophilia centres. The haematology consultant numbers increased to three (2.7) with my appointment and then slowly expanded over the next 20 years to the current seven. I probably had 5 sessions designated for bleeding disorders, though commonly this would be less because of other subspecialty pressures such as leukaemia and bone marrow transplantation. My senior colleague

Professor Hill probably had about the same number of sessions for haemophilia. On his retirement in 2008 he was succeeded by Dr J Motwanni, who took over the care of some of his patients and I was able to gradually increase my sessions for bleeding disorders. In addition, the haemophilia nurse specialist became an advanced nurse practitioner in haemophilia, with a haemophilia sister and junior sister making up the nursing team. A data manager and assistant were appointed during my last 5 years at BCH and the whole Unit moved to a new facility at BCH 4 years ago, at last giving patients a facility with appropriate examination and treatment areas. Unfortunately, over the last 10 – 15 years the Centre "lost" its dedicated social worker due to re-integration into the city's social services and clinical psychology sessions disappeared as a cost-saving exercise. The support from other services in the hospital however continued to be excellent, particularly from physiotherapy, dentistry and other relevant specialties.

c. **Identify senior colleagues at the Centre and their roles and responsibilities during the time that you have worked there, insofar as they were involved with the care of patients with bleeding disorders and/or patients infected with hepatitis and/or HIV in consequence of infected blood or blood products.**

5.8. When I was a research registrar and senior registrar at BCH, Professor Hill was solely responsible for the overall care of children with bleeding disorders, supported by a haemophilia sister Marion Gregory, then a second junior haemophilia sister (Angela Westoby) and staff nurse (Lynne Mathers). The second haematology consultant, Dr Phil Darbyshire and the junior medical staff were also involved in the emergency care of these patients or in Dr Hill's absence. I have described the changes in staffing levels with time.

5.9. Other senior colleagues were involved at various times, for example consultant microbiologists, respiratory physicians, intensivists, general paediatricians, infectious diseases consultants and in the case of patients with HCV, the BCH hepatology department headed by Professor Deidre Kelly.

6. **The Inquiry understands that you worked closely with Professor Hill at the Centre, including as Professor Hill's Research Registrar from at least 1981**

[MRCO0000022_082]. Please explain the nature of your working relationship with Professor Hill and how this developed over time.

6.1. This question is incorrect in terms of dates. I worked as Professor Hill's research registrar (i.e. he was my supervisor) from 1984-1985. The research project was discussed regularly, objectives set and the work reviewed. Likewise, if publications or presentations were to be a consequence of findings from the study, I worked closely with Professor Hill to achieve these. I was then appointed to the Regional training scheme in haematology and returned to BCH for 12 months for training in paediatric haematology (1988- 9 I think). Professor Hill was one of two consultants responsible for the training in laboratory and clinical haematology and had the major input into laboratory training and into the diagnosis and treatment of bleeding disorders. The working relationship was good and I gained a large amount of teaching and training from both consultants.

6.2. I was then appointed to BCH and BWH as consultant haematologist in 1992, so by definition as a colleague to the two existing consultants. I was obviously the junior consultant, and the next few years were spent learning the additional (non-clinical) roles required of the post in terms of managerial issues, budget control etc in addition to the clinical responsibilities at BCH and BWH. I had joint responsibility for the care of bleeding disorder patients, with patients split between myself and Professor Hill. My recollection is that most of the boys with HIV remained under his care (as they had been since diagnosis) until transfer to UHB although I think I did look after a small number of such patients. We worked to the same Unit protocols, with Professor Hill continuing to have responsibility for the majority of management/administration issues around the Centre. With the passage of time, I think our working relationship (which was always good) further developed, particularly as the work and interests of the Haemophilia Centre broadened and additional responsibilities were taken on. We continued to have research interests in haemostasis and worked together on these and in collaboration with other Centres. I took on the role of Centre Director on his retirement, as well as his additional responsibilities such as the laboratory and the haemostasis genetic service. I would add that I always found Professor Hill to be very supportive to me in each of these different roles I had at BCH, and fully believe that he was responsible for kindling my interest in paediatric haematology, and in haemostasis in particular.

7. **Please describe:**

a. **Your role and responsibilities at the Centre and how, if applicable, this changed over time;**

7.1. I think I have already answered this question.

b. **Your work at the Centre insofar as it involved the care of patients with bleeding disorders and/or patients infected with hepatitis and/or HIV in consequence of infected blood or blood products.**

7.2. As a senior registrar (and in the first few years of my consultant post) I would have been involved in the day to day care of these patients, this encompassing inpatient and outpatient care as well as emergency out of hours care. This would include contributing to the inpatient management of infective complications such as pneumocystis, the regular outpatient/Centre review of patients, monitoring and adjustment of treatment with antivirals (AZT). In terms of hepatitis, I recall this had a relatively low profile following the diagnosis of boys infected with HIV, but with the advent of HCV testing then I would have been involved with informing patients and families of the diagnosis and liaising with the Liver Unit about further management.

8. **Approximately how many patients with bleeding disorders were under the care of the Centre when you began your work there and over the years that followed? (If you are able to give exact rather than approximate figures, please do so).**

8.1. The exact numbers would be available from the annual returns to the UKHCDO from BCH Haemophilia Centre. When I started work as a research registrar then I think there were about 100 patients; my consultant job description from 1992 mentions 180 registered bleeding disorder patients at the Centre. In 2013 there were 350 patients registered (as detailed for a UKHCDO audit that year), and I think it has remained around the 400 number since then.

9. **To the best of your knowledge, what decisions and actions were taken, and what policies were formulated by the Centre and/or Professor Hill, regarding the selection, purchase and use of blood products (in particular factor concentrates) during the time that you worked there? In addressing this issue, please answer the following questions:**

a. **How, on what basis, and by whom, were decisions made about the selection and purchase of blood products?**
b. **What (if any) other bodies or organisations or individuals (e.g. other centres in the same region, or the Regional Health Authority) were involved in the arrangements for the selection, purchase or use of blood products?**
c. **What were the reasons or considerations that led to the choice of one product over another?**
d. **What role did commercial and/or financial considerations play?**
e. **What if any involvement did you have?**
f. **What products or treatments were generally used for treating (i) patients with severe haemophilia A; (ii) patients with moderate haemophilia A; (iii) patients with mild haemophilia A; (iv) patients with haemophilia B; (v) patients with von Willebrand's disease?**

9.1. As described previously, I worked at BCH at 3 different time periods. Up to my appointment as consultant the decisions about the selection and purchase of blood products were the responsibility of the Centre's Director, i.e. Professor Hill, given that there was no one else in post to share that responsibility. When I started my research post I became aware that BCH was in a relatively unusual position of restricting available factor VIII concentrate to NHS FVIII concentrate and, from 1976 onwards, a single commercial FVIII concentrate which was Armour Intermediate Purity FVIII (my understanding is that most centres used a number of different commercial FVIII concentrates at that time). Following the introduction of viricidally-treated FVIII concentrates the Centre moved to using UK plasma derived FVIII concentrate manufactured by Bio Products Laboratories, Elstree – this was firstly 8Y Intermediate Purity FVIII concentrate which was then succeeded by BPL high purity FVIII concentrate and by various commercial high purity FVIII concentrates. The use of plasma-derived FVIII concentrate was replaced by the introduction of recombinant FVIII concentrate, and this is likely to be replaced in the near future by newer agents such as FVIII

by-passing agents and by gene therapy. A similar progression of treatment has occurred for some but not all of the other congenital bleeding disorders.

9.2. The purpose of the above paragraph is to show that to a large extent product choice is dependent on availability of product, in terms of the state of medical knowledge at a particular time and how that has been applied to manufacturing particular blood products.

9.3. The reasons and considerations contributing to the choice of one product over another would depend on the time period relative to the development of these blood products (i.e. what sort of product was available at a particular time) but would include safety (plasma source, donor selection and screening, viricidal processes involved in manufacture of concentrate, results of product follow up data, risk of inhibitor formation), efficacy, availability of product and reliability of manufacturer, patient (and family) preference and ease of administration of product, and of course the cost of the product, particularly given the year on year increase in the amount of FVIII concentrate used in the UK over the last 3 decades.

9.4. Prior to the introduction of national tendering for factor concentrates, individual centres contracted with commercial manufacturers for products, cost often linked to volume of product contracted for. The policy of the BCH Centre during my time there as a consultant was to have a number of different suppliers of concentrate so that we were not dependent on a single supplier in case either the manufacturing process or supply chain were disrupted.

9.5. National contracting has been a huge success particularly in obtaining recombinant factor concentrate at some of the lowest prices in the world. The tendering process has included the considerations mentioned above, with concern about inhibitor formation becoming uppermost in terms of safety but cost of product has been extremely important for a cash-strapped NHS and a concentrate usage which increases annually. This is to say in answer to your question, commercial and financial considerations have always been important in the choice of product, but so have the other factors I have mentioned.

9.6. I have been involved with the decisions about factor purchase and usage at the Centre since my consultant appointment. In terms of other bodies/organisations etc involved in these arrangements (excluding the national tendering process),

haemophilia centres in the Region have tended to follow the lead of the 2 Comprehensive Care Centres. The use of blood products has followed guidelines by national bodies/committees during my time as a consultant.

9.7. In answer to the question about products and treatments, this again depends on the time period concerned as to the particular product, as described above. In general, severe haemophilia A patients received FVIII concentrate, severe haemophilia B patients FIX concentrate, patients with moderate haemophilia A usually FVIII concentrate but sometimes DDAVP +/- tranexamic acid depending on the nature of the bleed; patients with mild haemophilia A usually received DDAVP and/or tranexamic acid but would receive FVIII concentrate if treatment for the bleed required a FVIII level in excess of what DDAVP would be predicted to achieve. Patients with von Willebrand's Disease received cryoprecipitate and then 8Y FVIII concentrate when this became available. This was succeeded by commercial FVIII concentrates containing VWF, the one used mostly at BCH being Haemate P.

10. **What was the relationship between the Centre, Professor Hill and the pharmaceutical companies manufacturing/supplying blood products? What influence did that relationship have on the Centre's/Professor Hill's decisions and actions? In answering this question, please describe the kinds of interactions and communications (such as visits from sales representatives) you had with pharmaceutical companies which supplied factor concentrates.**

10.1. I am only in a position to answer the question about my own interactions with pharmaceutical companies. Throughout my consultant career I have had regular meetings with representatives from various companies involved in the production and selling of factor concentrates, meeting them about twice a year usually. These were opportunities to mention feedback with products, get latest information about new products in pre-production, be informed about publications on particular products and have a catch up with the company's plans for UK supply and costings etc. Company representatives were keen to support the Centre if possible, for example supplying educational material aimed at children and parents concerning the products, or teaching material for lectures etc. In addition, companies could be supportive of senior haemophilia staff such as myself attending international meetings in terms of meeting costs

of flights and accommodation – these meetings tended to occur 2-4 yearly. Meetings such as the ISTH, WFH, EAHAD were sponsored by various commercial companies and again gave the opportunity to meet with those companies and catch up with information about products. There was usually a good rapport established with most company reps, and again most were very supportive of the Centre during my time there, including ensuring timely and continuous supplies of concentrate.

10.2. Other interactions have included being involved in studies of particular products ranging from the use of 8Y FVIII to recombinant FXIII concentrate, all of which involved interaction with the companies involved. I have also received lecture fees from various companies and have been a member on a number of Advisory Committees for various pharmaceutical companies.

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. Responsibility lay with the Centre up to the introduction of national tendering for concentrates, a result of which was that particular concentrates were supplied to Regions in England on a fixed volume basis – it was up to Centres within that Region to have anticipated usage for that tendering period and monitor actual usage against these figures.

12. **Please describe your relationship/the Centre's relationship with the local Regional Transfusion Centre. Please explain whether the Regional Transfusion Centre supplied the Centre with cryoprecipitate and with NHS factor concentrates and whether (and if so to what extent and with what frequency) there were shortages or other difficulties in obtaining sufficient supplies.**

12.1. As a consultant haematologist there is always a professional relationship with the Regional Transfusion Centre, particularly for individuals like myself who were responsible for bleeding disorders (acquired as well as congenital) at BCH. The Regional Transfusion Centre supplied the Centre with cryoprecipitate, Fresh Frozen Plasma (and I would assume NHS factor VIII concentrate,

although this would have been before my time as a consultant at BCH). I cannot recall any shortage or difficulty in obtaining supplies for BCH.

13. **Please confirm whether the Regional Transfusion Centre had any involvement in supplying commercial factor concentrates or whether those were obtained from the pharmaceutical companies directly.**

13.1. Commercial factor concentrates were obtained directly from the pharmaceutical companies and delivered directly to the Haemophilia Unit at BCH.

14. **How were decisions taken as to which products to use for individual patients? What involvement did you have in such decisions? To what extent, if at all, were patients offered a choice as to which products to use?**

14.1. I can only answer this question from the time I became involved with such decisions, i.e. from the time I was appointed a consultant. Patients were informed about changes to products being purchased, for example from intermediate purity to high purity products, from BPL FVIII to other commercial factor concentrates, and then from plasma-derived to recombinant products, to extended half-life products from standard half-life products. This was done both on an individual basis and by a general letter sent out to families, and the reasons for change and the products involved were discussed. Sometimes individuals did not want to change product, e.g. from plasma-derived to recombinant, and these wishes were accommodated when possible and provided the product in question continued to be supplied.

15. **To your knowledge, what alternative treatments to factor concentrates were available in the 1970s and 1980s for people with bleeding disorders? What were, in your view, the advantages and disadvantages of those alternative treatments? What use did the Centre make of them? Do you consider that such alternatives should have been used in preference to factor concentrates so as to reduce the risk of infection? If not, why?**

15.1. To my knowledge, alternative treatments to factor concentrates in the 70s and 80s would include:

15.1.1. no treatment apart from rest of the affected bleed area/joint with ice packs, analgesia;

15.1.2. use of cryoprecipitate as a source of factor VIII, fibrinogen, von Willebrand Factor, FXIII.

15.1.3. Use of fresh frozen plasma as a source of factor IX, VII, XI, V,

15.2. The advantage of cryoprecipitate and FFP is that each unit is made from a single blood donor donation and that (up to the identification of vCJD) this would be plasma sourced from voluntary, non-paid donors in the UK. The disadvantages would include the variability of the amount of factor in a single unit of eg cryoprecipitate, the number of units required to raise the patient's factor level to that required depending on the nature of the bleed, the need to store both components frozen and to thaw when needed, the need to attend hospital for treatment, the need for cannulation to administer, the impracticability in the vast majority of cases for a home treatment programme to be rolled out.

15.3. From my experience of working at BCH, the Centre made use of cryoprecipitate and fresh frozen plasma when a factor concentrate was not available – which is still the case for such factor deficiencies as FV deficiency. Historically I think very young boys with haemophilia A were treated with cryoprecipitate beyond the introduction and availability of FVIII concentrate.

15.4. The advantages of factor concentrate compared to cryoprecipitate or FFP would include the use of a lyophilised concentrate made up in a small volume and easily/quickly injectable; the large amount of clotting factor present in such concentrate; the standardised amount of factor present in each vial; the ability to treat at home, to teach parents and children to administer.

15.5. In terms of do I consider cryoprecipitate or plasma should have been used in preference to factor concentrates so as to reduce the risk of infection, then probably not (up to the identification of the transmission of HIV through commercial factor VIII concentrate) unless it is assumed that a wholly different set up for the treatment of bleeding disorders would have been acceptable – i.e. treatment along the lines of what existed before the advent of factor

concentrates. Also, this would question the timing of the switch back from concentrate to cryoprecipitate/ FFP – presumably if this was to be done on the (pre-HIV) risk of infection it would have been done on the basis of the identification of non-A non-B hepatitis, which from my reading was considered a minor problem until percutaneous liver biopsies began to be carried out.

16. **What was the Centre's policy and approach as regards:**

a. The use of cryoprecipitate for the treatment of patients with bleeding disorders? Did that policy and approach change over time and if so how?

16.1. I have described the use of cryoprecipitate in the Centre since I worked there. Its use changed for example when factor concentrates containing von Willebrand Factor became available, which replaced cryoprecipitate in the majority of patients with von Willebrand Disease; likewise, fibrinogen concentrate replaced cryoprecipitate in the treatment of fibrinogen deficiency. Cryoprecipitate was (and continues) to be used in the treatment of acquired bleeding disorders such as massive blood loss or disseminated intravascular coagulation.

b. Home treatment? When was home treatment introduced?

16.2. Home treatment was in place for families when I first worked at BCH, so I assume in the late 70s and early 80s.

c. Prophylactic treatment? To what extent and when was treatment provided on a prophylactic basis? Did the policy and approach change over time and if so how?

16.3. Prophylaxis was provided to individuals with severe bleeding problems in the 1980s, though this tended to be relatively short term. Its use increased throughout the 1990s, reflected in an advisory document from UKHCDO in 1994 suggesting prophylactic regimens along the lines of those practised in Sweden and the Netherlands since the 1970s. Increasing numbers of boys were started on prophylaxis throughout the 1990s and the next decade (UKHCDO guideline published in 2010), with most boys started on secondary prophylaxis (after 2 joint bleeds). When and what regimen was dependent on discussions with families encompassing benefits and risks, use of indwelling central lines,

peripheral access, support for family etc. Over the last few years, the concept of primary prophylaxis (before second bleed/3 years old) was introduced, which some families were keen to implement. The introduction of prophylaxis had theoretically major cost implications and required some discussion with the commissioners for haemophilia. I recall that in many instances prophylaxis was started anyway on the basis that the reduction in bleeds and their treatment would more than compensate for the increased cost for prophylaxis.

17. **To what extent, and why, were people with mild or moderate bleeding disorders treated with factor concentrates?**

17.1. Boys with moderate and mild haemophilia A were treated with factor concentrate depending on their own factor VIII level, the nature of the bleed they were experiencing and the desired increase in factor VIII required to treat the bleed. For mildly and moderately affected haemophiliacs, the use of DDAVP coupled with tranexamic acid would be likely to increase the boy's factor VIII level 3-5 fold, depending on how the DDAVP was administered. If the bleed required a higher factor VIII level than this, for example pre-surgery, continued need for replacement treatment post-surgery or significant trauma, factor concentrate would be required. And factor concentrate may have been given by mistake in some infrequent instances rather than DDAVP, usually when the patient attended out of hours and was reviewed by an on-call doctor rather than his usual haemophilia team.

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

18.1. That is difficult to answer given that only these three viruses plus hepatitis A were routinely assessed. It would seem highly likely that cytomegalovirus and Ebstein Barr virus were transmitted, as seen with blood and blood products, and a study at BCH showed the transmission of human parvovirus by factor concentrate. The situation regarding vCJD will remain uncertain for some time.

Section 3: Knowledge of, and response to, risk

General

19. **What advisory and decision-making structures were in place, or were put in place at the Centre, to consider and assess the risks of infection associated with the use of blood and/or blood products**

19.1. In terms of the risks of infection associated with blood and blood products generally, there were regular updates and guidance from the National Blood Service and from the UKHCDO, SHOT and the Department of Health. I set up a Blood Transfusion Committee at BCH in 1995, which was multidisciplinary and included information about risks of transfusion, including TTI but excluding factor concentrates. In terms of the Haemophilia Centre, the availability and introduction of new products were regularly discussed at multidisciplinary meetings of the haemophilia staff, and microbiology colleagues were involved when appropriate.

20. **What was your understanding of the relative risks of infection from commercially supplied factor concentrates and NHS factor concentrates?**

20.1. My understanding of the relative risks of infection from these two sources of concentrate have only come about since patients were screened for exposure to hepatitis viruses and HIV, and from when such screening was introduced for donors. If considering the 1970s and early 1980s, the risk has been shown to be far greater when commercial concentrate from paid American donors has been used compared to the use of concentrate derived from UK donors – locally no patient treated exclusively with NHS concentrate was exposed to HIV though these were small numbers, and I can't recall details of HCV or HBV transmission. At BCH, HPV was shown to be frequently transmitted in commercial and NHS concentrate.

21. **How did you keep up-to-date with relevant scientific and medical developments in knowledge? What journals did you regularly read?**

21.1. Read relevant articles in medical journals, attended national and international haemostasis meetings, participated in various working parties and research

groups, discussed developments with haemostasis colleagues. In terms of journals, then before the availability of the internet – journals stocked at BCH and Birmingham Medical School Library. These included the Lancet and New England Journal of Medicine, Journal of Haemostasis and Thrombosis, Blood, British Journal of Haematology, Haemophilia. Access to other journals became available online over the years, especially with my honorary university access to the Medical School library facilities.

Hepatitis

22. **When you began work at the Centre, what was your knowledge and understanding of:**

a. **The risks of the transmission of hepatitis (including hepatitis B and NANB hepatitis/hepatitis C) from blood and blood products?**

22.1. When I began work at the Centre (by which I assume is meant when I took up the research registrar post), I would have known that Hepatitis B and non A non B Hepatitis could be transmitted through blood or blood products and that non-A non-B hepatitis was common in severe haemophiliacs who had received factor VIII concentrate.

b. **The nature and severity of the different forms of blood borne viral hepatitis?**

22.2. I would have known that Hepatitis B could result in a spectrum of problems, ranging from full immunity and minimal liver damage to liver failure. I was also aware that individuals could be carriers of Hepatitis B. Non- A non- B hepatitis was thought to be a mild inflammatory liver disorder, resulting in fluctuating, often low grade disturbances in liver function tests.

23. **What were the sources of your knowledge? How did that knowledge and understanding develop over time? What if any discussions did you have with Professor Hill or other clinicians at the Centre about the risks of hepatitis?**

23.1. Sources of knowledge would include Medical School teaching, exposure to patients through my medical rotations, preparation for MRCP exam, general medical reading. With time, gained understanding of hepatitis C and the non-benign nature of this disorder from the studies undertaken using percutaneous

liver biopsies and the increasing literature published on this infection in haemophiliacs. Patients with abnormal liver function tests were discussed in the Unit's weekly MDT meeting and advice from hepatologists and microbiologists would have been sought when appropriate.

24. **What, if any, actions did you and/or the Centre take to reduce the risk to patients of being infected with hepatitis (of any kind)?**

24.1. Regular testing of hepatitis B status, hepatitis B vaccination, regular review of liver function tests, limitation of brands of factor VIII concentrate and limitation of numbers of different batches of factor VIII given to individual patients. Introduction of viricidal-treated factor concentrates, high purity concentrates, recombinant factor concentrates.

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. I think I have answered this question previously.

HIV and AIDS

26. **What was your knowledge and understanding of HIV (HTLV-III) and AIDS and in particular of the risks of transmission from blood and blood products during your time working at the Centre? What were the sources of your knowledge? How did your knowledge and understanding develop over time? What if any discussions did you have with Professor Hill and/or other clinicians at the Centre about the risks of transmission of AIDS?**

26.1. My knowledge went from zero when I started my post as research registrar to becoming aware of HTLV- III during that post, sources of knowledge being through the various media reports, publications in the medical literature, presentations at scientific meetings and to my becoming involved in looking for evidence of HTLV-III in haemophilic boys as the research project developed. There was a huge amount of work published during from the mid-1980s

onwards with regard to HIV infection in this patient population, many presentations at scientific meetings and lots of discussion locally at the Centre and the Region and nationally through the UKHCDO and other bodies, which all contributed to my increasing knowledge over the years.

27. **How and when did you first become aware that there might be an association between AIDS and the use of blood products?**

27.1. I became aware of the possible association during my research post (see above) with the first descriptions of AIDS in haemophiliacs being published.

28. **What, if any, enquiries and/or investigations did you and/or Centre carry out or cause to be carried out in respect of the risks of transmission of HIV or AIDS? What information was obtained as a result?**

28.1. Stored serum samples from the boys taking part in the research project were tested for HIV (HTLV-III) when these tests became available – the study had been set up to look prospectively at immune abnormalities in haemophilic boys and to look at possible causes for these abnormalities, including treatment itself or agents transmitted through treatment. A number of boys were able to be identified who had been exposed to HIV. These were boys with haemophilia A who had received commercial factor VIII concentrate. Most of the infected boys were HIV antibody positive on samples taken in 1983 and 1984. Four boys seroconverted whilst receiving heat- treated Armour factorate in 1985-6. Stored samples of serum were also available for some boys from previous virology (Hepatitis B) tests, which showed that HIV was not present in available samples tested from 1979,1980 or 1981 but was found in a small number of stored samples from 1982. An extensive study of type of concentrate, specific batches of concentrate and amount of those batches infused implicated particular batches in seroconversion, though some boys who received the same batches remained HIV seronegative.

Response to risk

29. **What, if any, actions did you the Centre take to reduce the risk to the patients of being infected with HIV? What changes (if any) were made to the way in which patients were treated?**

29.1. My understanding is that BCH was one of the lowest users of FVIII concentrate in terms of units per patient in the country – this remained the case (as with the adult Birmingham centre) for many years. I don't know if any elective procedures were postponed prior to the introduction of heat-treated, donor- screened products, and don't recall any other changes in patient treatment, though I had left BCH by the end of 1985.

30. **Did the Centre continue to use factor concentrates to treat patients, after becoming aware of the possible risks of infection of HIV? If so, why?**

30.1. The Centre continued to use concentrate, primarily I would think because of the continuing need for treatment and the lack of other alternatives. I am probably not the best person to answer that question as I was not involved in those decisions.

31. **When did the Centre begin to use heat treated factor products and for which categories of patients?**

31.1. BCH began to use heat-treated factor VIII concentrate in December 1984 for haemophilic boys who required treatment with FVIII concentrate.

32. **Please set out what steps were taken to obtain heat treated products. Please also set out whether steps were taken to recall any stores of unheated products which patients had.**

32.1. I was not involved in this process so am unable to answer that question.

33. **Do you consider that heat treated products should have been made available earlier than they were? If not, why?**

33.1. I think it would have been difficult to have heat-treated products available earlier than they were in terms of prevention of HIV – the hitherto unknown virus had first to be identified, appropriate testing for the virus then developed, trials of concentrate using different viricidal processes undertaken and products licensed for use. If I were to use hindsight about events I was not involved with, perhaps the identification of non-A non-B hepatitis through transmission in blood products from the 1970s onwards could have been a stimulus to perhaps look at viricidal treatment of products, though again the causative agent had not been identified and the infection thought to be non-serious.

34. **Did you or your colleagues at the Centre revert to treatment with cryoprecipitate for some or all of the patients in response to the risk of infection? If so, how was it determined which patients would be offered a return to cryoprecipitate and which would not? If not, why not?**

34.1. I can't recall this happening when I was at BCH as a registrar.

35. **Do you consider that the decisions and actions of the Centre in response to any known or suspected risks of infection were adequate and appropriate? If so, why? If not, please explain what you accept could or should have been done differently.**

35.1. The response to the identification of HIV on serological testing was to move to alternative factor VIII concentrates when these became available. This was an appropriate thing to do. It was not my role to be involved in the decisions on how to do this and I don't know how decisions were made, and what alternative strategies were pursued - I have a vague recollection of attempts being made to procure significant amounts of NHS concentrate, but don't know how successful that was.

36. **Looking back now, what decisions or actions by the Centre could and/or should have avoided, or brought to an end earlier, the use of infected blood products?**

36.1. Looking back is of course with the benefit of hindsight and perhaps with inexact recall of events over time. I think the main thing would have been to try and procure NHS concentrate, though supplies of this were limited and I am not sure

how successful this would have been given that I would expect all other haemophilia centres in England and Wales would have this same response. Treating previously untreated patients with cryoprecipitate rather than factor VIII concentrate – not sure whether this was done anyway?

37. **What actions or decisions or policies of other clinicians or other organisations, within your knowledge, played a part in, or contributed to, the scale of infection in patients with bleeding disorders? What, if anything, do you consider could or should have been done differently by these others?**

37.1. There will be decisions before the identification of HIV and HCV and after the identification of these transfusion transmitted viruses. My understanding is that British governments from the 1970s onwards had talked about the need for the UK to be self-sufficient in the production of blood products, which would have meant the development of large-scale fractionation plants with the infrastructure to manufacture and deliver these products. Such self -sufficiency did not take place, which I think is the main reason why commercial concentrates were used so heavily in the UK in this period. I think the devastating effects of HIV (and HCV) infections in the recipients of blood products were not fully understood at the time, perhaps understandably given the new information that was accumulating, and the need to see if there was a difference in the course of infections in bleeding disorder patients compared with other at risk groups. Having said that, perhaps there could have been a greater degree of urgency in the clinical responses – reducing treatment as much as possible, use of cryoprecipitate and non-American commercial factor VIII concentrate as examples.

38. **Do you consider that greater efforts could and/or should have been made to inactivate viruses in blood or blood products prior to 1980? If so, who should have made or coordinated those efforts and what steps should have been taken and when? If not, why?**

38.1. Any effort to do this would have been based on the transmission of non-A, non-B hepatitis – anything other than that would have been speculative and based on the transmission of an as yet undiscovered pathogens (a similar argument

was put forward when discussions about funding rVIII were had 20 years later). So, there could have been a policy of producing the safest concentrate possible at that time – this would have involved trials of manufacturing processes and following the haemostatic efficacy of the product, its safety (inhibitor formation) and its lack of transmission of non-A non-B hepatitis, which would only have been followed at that time by liver function testing (not always a good marker). If such a decision was to have been made then in the UK I would assume would have been made by the Department of Health in conjunction with the National Blood Service, product regulators and other bodies such as the UKHCDO. In terms of commercial concentrates, I would think that the companies involved would respond to a clinical need/demand rather than altruistically introduce a process for an unproven benefit.

Section 4: Treatment of patients at Centre

Provision of information to patients

39. **What information did you provide or cause to be provided (or was, to your knowledge, provided by others) to patients at the Centre with a bleeding disorder about the risks of infection in consequence of treatment with blood products (in particular, factor concentrates) prior to their treatment commencing? Please detail whether, and if so, how this changed over time.**

39.1. I am not able to say definitively what information was provided to patients and their carers when I was a research registrar having not been involved in this process. When I was a senior registrar and a consultant, I know that families were provided with information about the factor concentrates being used, including source of plasma, viricidal treatment and risk of transmission of HIV and hepatitis viruses and risk of inhibitors as was known at that time. The information expanded as time progressed, with more products available, and again the risks of viral transmission and inhibitor formation were addressed, with more data having accumulated, The identification of HCV and the development of screening tests, plus the product surveillance schemes added to the information imparted. The introduction of recombinant factor concentrates was again discussed fully prior to commencement, including the risk of as yet

unknown agents: as knowledge grew about these products then inhibitor risk became far more pertinent than theoretical infection risks.

40. **What information did you provide or cause to be provided (or was, to your knowledge, provided by others) to patients about alternatives to treatment with factor concentrates? Please detail whether, and if so, how this changed over time.**

40.1. I have provided information about the use of DDAVP and tranexamic acid in non-severe haemophilia A as an alternative to factor VIII concentrate, and about the situations in which these treatments should and should not be used. The use of the contraceptive pill was introduced for menstrual problems in girls with various bleeding disorders, which helped reduce the use of factor concentrate (and other blood products) in these individuals. I don't recall discussing cryoprecipitate as an alternative to factor VIII concentrate. I think what changed over time was that information became more detailed and written as well as verbal information became the norm.

41. **What information did you provide or cause to be provided (or was, to your knowledge, provided by others) to patients before they began home treatment/home therapy?**

41.1. Patients and their carers would have been given information about the products prior to home treatment commencing. All carers went through a rigorous training programme undertaken by the haemophilia unit nurses covering the particular product, its storage requirements, making up the product, venepuncture and administration, disposal of used needles and syringes, recording of product and reason for administration, how to recognise a bleed, when to contact the Centre etc. To which was added training in use of indwelling central lines, electronic recording of usage of concentrate as these were introduced into the home treatment programmes (and a lot more in addition).

HIV

42. **When did you first discuss AIDS or HIV (HTLV-III) with any of your patients?**

42.1. I cannot recall having to impart and discuss the diagnosis of HIV with any of my patients as this had been done during my time away from BCH. I was involved in the care of a number of boys with HIV-related problems when I was a senior registrar at BCH and would have had discussions about their illness during that time.

43. **Please describe how and when you learned that patients under your care/the care of the Centre had been infected with HIV.**

43.1. I learned that patients at BCH had been infected with HIV after serological tests became available for this virus. These tests became available at BCH in 1984 through the PHLS at Colindale, and then through the Regional Virology Department at Birmingham Heartlands Hospital (formerly East Birmingham Hospital) in 1985 when testing became widely available.

44. **Please describe the arrangements that were made for the testing of the patients. Were they tested without their knowledge? What if any arrangements were made at the Centre for pre-test counselling?**

44.1. Testing of patients was done differently in different time periods.

44.2. The patients who were first tested for HIV formed part of the research study in which I was involved. The basis of this study had been explained to the carers, describing the outbreak of TB in haemophilic boys and the indication that their immune systems were somehow impaired. Possible causes of this were discussed, including the effects of treatment itself and/or the transmission of an agent through treatment which would account for such abnormalities. It was explained that patients recruited into the study would be reviewed prospectively, with clinical examination and blood tests forming part of that review. As well as immune tests, tests would be done to look at viral status, and in addition, samples of serum from these visits would be frozen and stored so that they would be available if any new investigations were indicated and became

available in the future. Consent was taken after these discussions, and also at each follow up visit (between 3-6 monthly). Looking for new agents which may have contributed to immune abnormalities was undertaken during the prospective study. It would be correct that patients were tested for HIV without their specific knowledge (or consent) that they were being tested for that specific virus at that particular time, i.e. the families were not gone back to and told that there was a novel test for HTLV-III which BCH might be able to access, and could samples stored from their child be tested – it was more an understanding that the consent taken for participation in the research study included the testing for as yet unknown agents which might cause immune abnormalities. The same could be said for testing for exposure to Human Parvovirus, which also was incorporated into the study.

44.3. When HIV testing became available Regionally, HIV testing became part of the routine testing of all patients at the Centre receiving blood products, along with their Hepatitis B status and then later their HCV status. This was explained to the patients and their families at the time.

45. **How and when and by whom were patients told that they had been, or might have been, infected with HIV? Were they told in person, by letter or by phone? Were they seen individually or in groups? What if any involvement did you have in this process?**

45.1. I don't think I had direct involvement in imparting this information. It would have been done by Professor Hill and the haemophilia unit nurses – when I returned to BCH as a senior registrar then all boys and families were well aware of their HIV status. I don't know the details of how the information was imparted.

46. **What information was given to them about the significance of a positive diagnosis? Were patients told to keep their infection a secret?**

46.1. Any answer I gave to this would be only be me assuming what information was given as I was not involved in the discussions.

47. **What was the Centre/your policy in relation to testing family members of people known or suspected to be infected with HIV? Under what circumstances were the tests carried out?**

47.1. Same answer as 46.

48. **What, if any, information or advice was provided by you or colleagues at the Centre to family members of people who were at risk of infection with HIV or were infected with HIV?**

48.1. I think it would have included discussing the ways in which HIV was transmitted and how to avoid this – safe needle disposal, hygiene at home etc. Not sure whether I was involved in such discussions.

49. **What if any arrangements were made at the Centre for post-test counselling?**

49.1. Post-test counselling would have initially been provided by Professor Hill and the haemophilia nursing staff, and by a clinical psychologist and social worker in due course (i.e. when funding had been obtained and appointments made for these posts).

50. **How many patients at the Centre were infected with HIV as a result of treatment with blood products? Of those infected,**

a. **How many had severe haemophilia A?**
b. **How many had moderate haemophilia A?**
c. **How many had mild haemophilia A?**
d. **How many had haemophilia B?**
e. **How many had von Willebrand's disease?**

50.1. As far as I am aware, 32 boys at the Centre had been infected with HIV by April 1984, (53% of all haemophilia A patients) and there were a further 4 seroconversions found in 1985-6 in boys who had previously tested negative for exposure to this virus.

50.1.1. 27/32 severe haemophilia A,

50.1.2. 3 moderate haemophilia A

50.1.3. 2 mild haemophilia A (one of whom was severe by way of inhibitor development).

50.1.4. 0

50.1.5. 0

50.1.6. In the late seroconversions, 3 boys had severe haemophilia A and one boy mild haemophilia A.

50.2. No patients with other congenital bleeding disorders were infected with HIV.

51. **Was work undertaken at the Centre to establish the time period during which patients seroconverted? If so, please describe what work was done and what if any conclusions were reached.**

51.1. This was an important branch of the research project with which I was involved. As mentioned previously, samples of serum were obtained from each review visit of children in the project and frozen so that further testing could be done in the future if new knowledge about potential causes of immune dysfunction came to light. In addition, historically if serum remained after virology testing of patients then samples of such serum were often frozen and stored in case the sample had to be re-investigated in the future. When HIV testing became available these stored samples were examined for serological evidence of exposure – in this way HIV sero-negative and sero-positive individuals could be identified and the date of their earliest positive sample identified. Sera was not available for all boys at all time periods, but the results of testing can be summarised as:

51.1.1. 1979: 0 of 17 boys tested seropositive

51.1.2. 1980: 0 of 17 boys tested seropositive

51.1.3. 1981: 0 of 12 boys tested seropositive

51.1.4. 1982: 5 of 15 boys tested seropositive

51.1.5. 1983: 25 of 28 boys tested seropositive

51.1.6. 1984: 32 of 32 boys tested seropositive

51.1.7. 1985: No further seroconversions took place between April 1984 and September 1985, but between September 1985 and October 1986, 4 previously seronegative boys became seropositive for HIV. No further seroconversions took place after this.

51.2. Further details of the results of HIV testing can be found in the referenced papers

51.2.1. Williams, M; Al-Rubei, K; Hill, FGH "A Prospective Study of HIV-Infected Haemophilic Boys and the Prognostic Significance of Immune and Haematological Abnormalities" *Thrombosis & Haemostasis.* 60(1):97-101, 1988 Aug 30 [WITN5725002]

51.2.2. Williams, M; Skidmore S; Hill FGH "HIV Seroconversion in Haemophilia Boys Receiving Heat-Treated Factor VIII Concentrate" Vox Sanguinis. 58(2):135-6, 1990 [HSOC0001628]

51.3. Regular surveillance blood tests were routine practice for all bleeding disorder patients but expanded to include HIV testing when this became available, as well as the existing blood counts, liver function tests, Hepatitis B status.

Hepatitis B

52. **Were patients infected with hepatitis B in consequence of their treatment with blood products informed of their infection and if so, how? What information was provided to patients infected with hepatitis B about the infection, its significance, prognosis, treatment options and management? What if any involvement did you have in this process?**

52.1. I'm sure they were but I have not been involved in this process.

53. **How many patients at the Centre were infected with hepatitis B?**

53.1. Most boys who had received large amounts of factor VIII concentrate had evidence of exposure to Hepatitis B, as did some who had received factor IX concentrate. I don't know how many patients at the Centre were infected with Hepatitis B but for the boys included in my research study, 28 of 58 boys with haemophilia A had been exposed to hepatitis B and 3 of 7 boys with haemophilia B when seen in 1984.

NANB Hepatitis/Hepatitis C

54. **Were patients infected with NANB hepatitis informed of their infection and if so, how and by whom?**

54.1. Discussion of liver function test abnormalities was part of patient review clinics and reviews on the haemophilia unit when I was a senior registrar and a consultant at BCH. These discussions would have been carried out by consultant haematologists, junior medical staff and haemophilia nurses.

55. **What information was provided to patients infected with NANB hepatitis about the infection, its significance, prognosis, treatment options and management? What if any involvement did you have in this process?**

55.1. My recollection is that the information given to patients and their carers at the time was based on the available knowledge of the infection in bleeding disorder patients at that time, in that it was regarded as relatively benign, resulting in occasional jaundice and fluctuations in liver function tests. Patients were told to present to the haemophilia unit for review if they became jaundiced.

56. **When did the Centre begin testing patients for hepatitis C and over what period of time were such tests first carried out? How, when and by whom were patients informed of their diagnosis of hepatitis C? Were they told in person, by letter or by phone? What if any involvement did you have in this process?**

56.1. I think this was in 1990 or 1991. My recollection is that the patient/carers were informed of the diagnosis in a clinic visit, and I would have been involved in a few conversations following my appointment as a consultant.

57. **What information was provided to patients infected with hepatitis C about their infection, its significance, prognosis, treatment options and management?**

57.1. This information changed with time and increasing knowledge. General discussion about the infection, carrier state, risk of progression over time would have been discussed. Treatment options in the early 1990s were limited, and patients were referred to the hepatology team at BCH for further investigation and treatment if appropriate. Additional sources of information became available through such bodies as the Department of Health, NBS, Haemophilia Society, UKHCDO etc.

58. **When the test for HCV became available, what if any steps were taken by the Centre and/or by you to ensure that all patients who had received blood products were traced and invited to be tested?**

58.1. HCV testing was undertaken on all Centre patients who had received blood products prior to 1991 (who were still patients registered at BCH), and the Centre was otherwise involved in the look-back exercises undertaken by the UKHCDO.

59. **Please consider documents NHBT0046122_010 and NHBT0046122_004 which concern an investigation conducted by you to rule out the possible infection of a patient with HCV. Please describe, as far as you are able, any other look back exercises you were involved in to trace recipients of blood products from donors that were later known to be infected with HIV, HBV, HCV or any other blood borne infection.**

59.1. I don't recall any other specific individual investigations. I was involved in the look back exercises for HCV and for vCJD as requested by UKHCDO when

patients at my Centre were identified as possible recipients of particular batches of concentrate.

60. **How many patients at the Centre were infected with hepatitis C as a consequence of their treatment with blood products?**

60.1. I don't know the numbers for BCH. However, given the general experience from all Centres in England, most of the boys receiving commercial non-viricidally treated concentrate up to the mid-1980s would have been exposed to the virus, and also to a lesser extent those who received NHS concentrate. There was a theoretical risk also of patients who had received single donor products (cryoprecipitate, FFP, platelet infusions, and units of blood) would also have been at risk of exposure but I don't recall any such patient being found to have HCV infection at BCH.

Delay/public health/other information

61. **Were the results of testing for HIV and hepatitis (of all kinds) notified to patients promptly, or were there delays in informing patients of their diagnosis? If there were delays in informing patients, explain why.**

61.1. I think there would have been a delay in notifying patients of their initial HIV tests. Firstly, the results needed to be confirmed and then there was then the uncertainty of what the result actually meant – did it mean that a person had been exposed to the virus and was therefore immune (as with measles, for example), or did it mean the antibodies were non-neutralising and that the virus was still active? Such uncertainties would have made conversations about prognosis very difficult. Knowledge at the time was limited but increasing month by month. I don't know when these results were first discussed with patients and carers. I don't think I was working at BCH at the time of these conversations but can't be sure. I don't recall delays in informing patients of their HCV status once these results were reported apart from the delay in organising times to discuss the results.

62. **To what extent, if at all, did you/your colleagues take into account the public health implications of HIV, AIDS, hepatitis B, NANB hepatitis and hepatitis C, when making decisions as to what information or advice to provide to patients or what treatment to offer patients?**

62.1. Public Health implications were taken into account for all such infections and the information changed as more information about the viruses became available over time.

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

63.1. I can remember talking to parents about risks of known and as yet unknown viruses or other infective agents when treatment was in the process of being changed, e.g. to viricidally-treated plasma products, and to recombinant factor concentrates.

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

64.1. Information was provided about the risks of infecting others with emphasis on sexual transmission of HIV, and to a lesser extent HCV, how these viruses were not transmitted and what to do in particular situations such as managing bleeds outside hospital.

Consent

65. **How often were blood samples taken from patients attending the Centre and for what purposes? What information was given to patients about the purposes for which blood samples were taken? Were patients asked to consent to the storage and use of the samples? Was their consent recorded and if so how and where?**

65.1. The frequency of blood tests being taken would depend on what time period is being discussed, for what condition and whether patients had been recruited to various research studies. Routine bloods were taken at least 6 monthly for

severe and moderate haemophilia A and B, annually for mild haemophilia. VWD 6-12 monthly usually and other bleeding disorders probably about once a year (more frequently if more severely affected). Routine blood tests included blood counts, liver function tests, Hepatitis B status, to which were added HIV and HCV status as these became available. The frequency of inhibitor testing varied as to patient – newly diagnosed patients were tested frequently, especially in the last decade or so, with tests done every 3-5 infusions of concentrate, whereas other boys who had received more than 30 infusions had inhibitor testing less frequently. If children were participating in research studies, including trials of new types of treatment, the frequency was determined by the trial protocol.

65.2. It was routine practice to store serum samples taken for virology tests if the residual sample was available (often not in young children because of the small sample taken). With regard to the prospective study of immune dysfunction in the early 1980s, patients and carers were aware that blood samples were being stored as part of the study, and that these samples would undergo future tests depending on what emerging knowledge/theories came to light during the study. The taking of consent was less formalised in the 1980s and early 90s, and I recall that consent was informed verbal consent rather than the written consent which has become standard practice since the 1990s.

66. **Did the Centre have a bank of stored samples? If so, was that storage undertaken with patients' knowledge and consent?**

66.1. See Q 65.

67. **Please consider the minutes of the third meeting of the UK Haemophilia Centre Directors Organisation Executive Committee which you attended where the issue of consent to treatment was raised, specifically whether formal consent forms or good note taking in patient records was the correct approach to recording consent [HCDO0000458_003, page 3]. Were patients under your care or under the care of your colleagues at the Centre treated with factor concentrates or other blood products without their express and informed consent? If so, how and why did this occur? What was your approach to**

obtaining consent to treatment? Was their consent recorded and if so how and where?

67.1. I can recall extremely few occasions where consent was not able to be taken and these would have been because of urgent clinical circumstances, such as a severe bleed in a previously undiagnosed haemophiliac where parental consent was not available at the time. (in the same way as a patient admitted to intensive care might need blood and blood products immediately without parental consent being available). Otherwise consent for treatment was always taken. My approach to taking consent for treatment was to include discussions about types of treatment in the first couple of meetings with the family and to ask if they were then happy to consent to their child being treated. A summary of the discussions would have been written in the hospital or haemophilia unit case notes and is likely to have been referred to in the first letter to the patient's GP. This gradually changed to more formalised ways of documenting consent as concepts of consent- taking changed over the years.

68. **Please consider the minutes of the tenth meeting of the UK Haemophilia Centre Doctors' Organisation Advisory Committee which you attended [HCDO0000254_104]. It is noted in the Chairman's report that Professor Hill had received communication from the DOH requesting information on Hepatitis C testing and how and when it was introduced, complaints having been received from patients by the GMC which were likely related to testing for Hepatitis C without patient consent (page 3). Were patients under your care ever tested for HIV or hepatitis or for any other purpose without their express and informed consent? If so, how and why did this occur? What was your approach to obtaining consent for testing? Was their consent recorded and if so how and where?**

68.1. As described above, there were times when patients were not informed specifically that they were in the process of being tested for HIV as it was understood that consent had been taken to look for any new agents/markers which were thought to be relevant (I am describing 1984 testing). I don't have a definite recollection of whether patient blood samples were tested for HCV before patients/families had been informed that testing was newly available, and whether specific consent for testing was obtained prior to testing.

Recombinant blood products

In answering the below questions, you may be assisted by consideration of DHSC0033758; BWCT0000065; BWCT0000066; BWCT0000067; DHSC0033752; BWCT0000057; BWCT0000055; BWCT0000036; HCDO0000133_015; HCDO0000133_013; HCDO0000014_396; HCDO0000109_008.

69. **Please describe your involvement in efforts to obtain recombinant blood products for patients with haemophilia. What, if any, difficulties did you encounter and why?**

69.1. My involvement consisted in making senior management at BCH, Regional commissioners for haemophilia, Public Health doctors and patients aware of the evolving situation regarding recombinant products, and in arguing the case for their introduction. The difficulties encountered were mainly around the reluctance to accept any potential, unproven benefits of introducing recombinant concentrates in place of plasma-derived concentrates, coupled with the significant cost of such a switch. Whereas I can understand the scientific basis of the arguments put forward to support not switching, I didn't think they took account of the patients' and families' perspective of treatment from the advent of HIV onwards, downplayed the potential for transmission of as yet unknown agents through plasma (including prions) and were being made by individuals with no clinical experience of haemophilia. BCH could not fund such a switch without additional resources, though as time progressed a unilateral decision was taken at BCH to start PUPs on recombinant factor concentrate, and also boys whose families who had been strongly pressing for such a change. This move was agreed with the strong support of the Medical Director at the time, who happened to be a microbiologist. The Trust was aware of the significant financial risk this policy entailed, and it was hoped that it would be a short-term risk as by that time most other Centres treating children had introduced recombinant concentrate - it was felt that the Department of Health would have to recognise this and agree to fund recombinant products for children, which is what happened.

70. **When were recombinant products first introduced for use at the Centre?**

70.1. I think in late 1997 or in 1998.

71. **Which category of patients at the Centre received recombinant treatment and how did this change over time?**

71.1. After a full discussion with carers and with their consent, previously untreated patients with severe haemophilia were the first group switched to recombinant factor VIII concentrate, together with boys whose carers had been very anxious about plasma derived FVIII and strongly pressing for recombinant concentrate. Discussions about change of treatment then took place with all families of severely and moderately affected boys – most families were happy to switch to recombinant products though a small number chose to remain on plasma-derived concentrates initially.

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

72.1. I think recombinant FVIII concentrate should have been available earlier, particularly to children and particularly to PUPs. There were delays centred around commissioners awaiting a review undertaken by Wessex Health Authority, although I remember that other reviews had already been carried out in other Regions of England which supported the use of recombinant concentrate, and the use was also strongly supported by the UKHCDO. A number of Centres had a different response from their Regional Health Authorities than the one we experienced and were allowed to purchase recombinant concentrate – some Trusts took the step of funding it from their existing budget. I think recombinant FVIII concentrate for children could have been introduced in 1996 – I'm not sure if this question implies that recombinant factor VIII concentrate should have been available to all haemophiliacs at the same time, which is clearly impractical. Rollout of recombinant FVIII was always going to be done in phases, but the concept of earlier availability applies to children and also to adults.

Research

73. **The Inquiry understands that you may have contributed to or provided data for the following:**

a. **An article published in 1996: "Importance of age at infection with HIV-1 for survival and development of AIDS in UK haemophilia population" [HSOC0002661];**
b. **An article published in November 1997:"Mortality from liver cancer and liver disease in haemophilic men and boys in UK given blood products contaminated with hepatitis C" [HCDO0000264_150];**
c. **An article published in 2001: "Treatment of haemophilia in the United Kingdom 1981-1996" [HSOC0023510];**
d. **A report from 2002 titled "HIV and Mortality in the UK Haemophilia Population: Demonstration of a Casual Relationship" [HCDO0000572];**
e. **A study from 1997 titled 'Immune status in HIV-1 infected males with haemophilia in the United Kingdom" [HCDO0000017_001];**
f. **A study from 1985: "Lymphocyte subset ratios and factor VIII usage in haemophilia" [RLIT0000670].**

Please explain the nature of your involvement, including the type of data you contributed and how this was collected and shared.

73.1. I would have contributed data to the UKHCDO by way of the required annual treatment returns from BCH, which would have been used in studies quoted in references a – e in this question. RLIT0000670 refers to the first study of T lymphocyte subsets carried out in haemophilic boys at BCH – I think I probably collected/checked some of the treatment data when I started my research post.

74. **Please consider document BPLL0005719 which describes a study in which you were involved, on 15 previously untreated patients (PUPs) recruited from the Centre who were being treated exclusively with intermediate purity dry heated factor VIII. Please explain the participant recruitment process for this study, including whether and how consent was obtained and recorded. Were you involved in other research concerning PUPs recruited from the Centre? If so, please provide details.**

74.1. I'm not sure whether I was involved in the recruitment process and think I had a more peripheral input into this paper. Some of the work would have been when I was a senior registrar at BCH, and I can recall being involved in the control group mentioned. In terms of other research involving PUPs, PUP data formed

part of the UKHCDO annual return data as previously discussed. I was involved through the UKHCDO paediatric working party in questionnaires sent to UK Centres asking about neonatal management of haemophilia (which would have included PUPs), and later in the production of Guidelines for neonatal management, inhibitors and treatment, which I think are outside the Inquiry's Terms of Reference (?).

75. **Document BPLL0005964 is a note dated April 1991 from J.K. Smith, which refers to a practice whereby the Protein Fractionation Laboratory provided certain products, mostly free of charge to a number of clinicians, on the understanding that clinical data would be provided in return. You are listed alongside Dr F.G.H Hill among the Factor XI users (page 8). Please explain your involvement with this arrangement and the type of clinical data that was provided from the Centre.**

75.1. I'm not sure why I was listed unless I had been involved in obtaining and using FXI concentrate when I was at BCH as a senior registrar. My recollection is that BPL became a commercial company and started charging for such "minor" products as FXI concentrate, having previously made them available free of charge, which I think is what the memo is referring to. Clinical data would include the indication for treatment, increase in FXI levels post infusion and rate of fall (half-life studies), together with efficacy of the concentrate in treating the bleed and its safety profile. Such information would have been included in submissions for product approval and licensing.

76. **Documents BPLL0005718 and RLIT0000670 concern two studies co-authored by you on a) lymphocyte subset ratios and factor VIII usage in haemophilia and b) transmission of human parvovirus B19. It is noted that you were supported by an Armour Research Fellowship. Please explain the nature of, duration and conditions attached to this Fellowship.**

76.1. I don't have my job description for this Fellowship but recall that it was funded for up to two years, and that there would be an annual meeting with Armour representatives to generally discuss the research to date. Otherwise, Armour would have no other input into the research being carried out or into any subsequent publications apart from the acknowledgement of their support.

77. **Please list all other research and epidemiological studies that you were involved with during your time as a consultant at the Centre insofar as relevant to the Inquiry's Terms of Reference, and please:**

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

77.1. Other research and epidemiological studies in addition to the studies already mentioned have included the following. I have assumed that case reports are included in the term "research study". I have not listed any nurse-led projects as I have no clear recollection or record of any.

77.2. The clinical observation that a higher-than-expected incidence of TB amongst haemophilic boys during a ward outbreak of TB at BCH (8 of 30 bleeding disorder patients) in 1981 prompted studies into immune dysfunction and a possible relationship to treatment. A prospective study was set up to study these abnormalities over a period of time, ethics approval having been obtained from the local ethics committee prior to my taking up the research post. Informed, verbal (I think) consent was taken from all participants and their carers. During the course of the study, HIV (HTLV-III) testing became available. HIV seropositivity and dates of seroconversion/positivity were established whenever possible. As well as the amount of treatment received by each boy in the study, relationships of abnormalities to specific batches were sought.

77.3. The introduction of viricidally-treated concentrate prompted an investigation as to the effectiveness of the method employed in reducing/eradicating parvovirus transmission through treatment, compared to the situation before heat-treatment of concentrate.

77.4. These studies can be listed as:

77.4.1. Beddall AC. Hill FG. George RH. Williams MD. Al-Rubei K. Unusually high incidence of tuberculosis among boys with haemophilia during an outbreak of the disease in hospital. Journal of Clinical Pathology. 38(10):1163-5, 1985 Oct [MACK0002038_001]

77.4.2. Beddall AC. Al-Rubei K. Williams MD. Hill FG. Lymphocyte subset ratios and factor VIII usage in haemophilia. Archives of Disease in Childhood. 60(6):530-6, 1985 Jun. [RLIT0000670]

77.4.3. Williams MD. al-Rubei K. Hill FG. A prospective study of HIV-infected haemophilic boys and the prognostic significance of immune and haematological abnormalities. Thrombosis & Haemostasis. 60(1):97-101, 1988 Aug 30. [WITN5725002]

77.4.4. Williams MD. Cohen BJ. Beddall AC. Pasi KJ. Mortimer PP. Hill FG. Transmission of human parvovirus B19 by coagulation factor concentrates. Vox Sanguinis. 58(3):177-81, 1990. [BPLL0005718]

77.5. An outbreak of Hepatitis B in 11 haemophilic boys occurred 1984-5 in which a single batch of commercial factor VIII concentrate was identified as the likely source of the outbreak. 9 of the 11 boys had a de novo infection but the remaining two showed a recurrence of previous infection, suggesting an impaired immune response to the virus. Details of this outbreak were published:

77.5.1. Williams MD. Boxall EH. Hill FG. Change in immune response to hepatitis B in boys with haemophilia. Journal of Medical Virology. 25(3):317-27, 1988 Jul. [WITN5725003]

77.6. Ongoing clinical and laboratory surveillance of boys post-introduction of heat treated commercial factor VIII concentrate identified 4 boys who seroconverted for HIV between late 1985 and October 1986. This was reported to national bodies and quickly led to that particular commercial concentrate being withdrawn from the UK market. The seroconversions were subsequently described in the publication:

77.6.1. Williams MD. Skidmore SJ. Hill FG. HIV seroconversion in haemophilic boys receiving heat-treated factor VIII concentrate. Vox Sanguinis. 58(2):135-6, 1990.[HSOC0001628]

77.7. Prospective surveillance of patients with bleeding disorders became routine clinical practice once HIV testing was available.

77.8. The clinical evaluation of viricidally-treated factor concentrates included regular assessments of viral transmission and inhibitor risk, as well as their clinical efficacy etc. With the availability of HCV antibody tests, a review of this data encouragingly showed evidence of prevention of transmission of Non-A Non-B Hepatitis (HCV) in the boys reported.

77.8.1. Skidmore SJ. Pasi KJ. Mawson SJ. Williams MD. Hill FG. Serological evidence that dry heating of clotting factor concentrates prevents transmission of non-A, non-B hepatitis. Journal of Medical Virology. 30(1):50-2, 1990 Jan.[BPLL0010891]

77.9. Intermediate purity 8Y FVIII concentrate contains von Willebrand factor as well as FVIII. The use of this concentrate in preference to cryoprecipitate was advocated by the UKHCDO as preferred treatment for VWD; this study looked at the clinical and laboratory effects of this treatment in 6 children with different types of VWD and showed 8Y concentrate to be safe and effective treatment. This was a change of treatment study, with at least two commercial FVIII-VWF concentrates having been shown previously to be effective. Informed consent was taken from the families as with any change in treatment.

77.9.1. Pasi KJ. Williams MD. Enayat MS. Hill FG. Clinical and laboratory evaluation of the treatment of von Willebrand's disease patients with heat-treated factor VIII concentrate (BPL 8Y). British Journal of Haematology. 75(2):228-33, 1990 Jun.[BPLL0005721]

77.10. With the introduction of 8Y FVIII concentrate, regular clinical and laboratory review became standard, and at BCH included the monitoring of T lymphocyte subsets. This study reported the results of 32 months follow up of boys treated solely with this concentrate, showing none of the T cell abnormalities previously described in frequently treated haemophiliacs.

77.10.1. Evans JA. Pasi KJ. Williams MD. Hill FG. Consistently normal CD4+, CD8+ levels in haemophilic boys only treated with a virally safe factor

VIII concentrate (BPL 8Y). British Journal of Haematology. 79(3):457-61, 1991 Nov.[BPLL0005719]

77.11. A study into treatment of HCV with interferon or a combination of interferon and ribavirin. This was a study undertaken with the Hepatology Department, in the form of a randomised trial using interferon or a combination of interferon and ribavirin. I cannot recall how many bleeding disorder patients were recruited and what the outcomes were.

77.12. My involvement in the above studies varied according to the particular study, and included patient recruitment, clinical and laboratory reviews, authorship of papers etc.

77.13. In terms of other bodies and organisations, then in the above studies other departments/organisations were involved at various times, such as the Regional Virology Department at Birmingham Heartlands Hospital and the Public Health Laboratories at Colindale.

77.14. Patient data was submitted to the UKHCDO as part of the annual returns. Additional information was sent as requested and as a part of the agreed UKHCDO response to particular issues, such as those concerned with transfusion transmitted infections.

77.15. In terms of funding, I have mentioned the Armour 2 year research grant. I don't know the source of funding (if any) for the other individuals mentioned in the above studies. A significant amount of the work was done in addition to the "normal" job plan and in an individual's own time. Departmental Trust funds did exist from Charity and personal donations, and these were used to fund such things as laboratory reagents, travel to scientific meetings etc.

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

78.1. I think a distinction should be made as to what is a research study, what is a case report and what is a report of continuing treatment. Also, as to what data is included in reports to the UKHCDO and whether that constitutes research – my understanding is that it did not. Local research studies were submitted to the local ethics committee for approval. Case studies did not require to go through

this process but informed consent from carers, and patients where appropriate, was taken when necessary. I have discussed consent being taken for the investigation of immune abnormalities in haemophilic boys and that families were not revisited to discuss consent for testing for specific viruses ahead of these tests being performed. The answer to the question is otherwise no, taking into account issues around the requirements for consent at that time.

79. **Was patient data (anonymised, de-identified or otherwise) ever 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?**

79.1. Anonymised patient data was presented in various lectures and also formed part of data collected by the UKHCDO. Not data specific to an individual patient but collective data for a patient group. As far as I am aware, specific consent was not required for this.

80. **Was patient data (anonymised, de-identified or otherwise) ever shared with third parties without their express consent? If so, how, and why did this occur, and what information was provided to whom?**

80.1. Lectures/talks to specific audiences, usually to haematologists and haemophilia nursing staff. See above.

81. **Please provide details of any articles or studies that you have published insofar as relevant to the Inquiry's Terms of Reference.**

81.1. See Q77.

Treatment of patients who had been infected with HIV and/or Hepatitis

82. **How was the care and treatment of patients with HIV/AIDS, Hepatitis B and Hepatitis C managed at the Centre? 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 to those infected?
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?

82.1. My recollection is that patients with HIV/AIDS were treated by their consultant haematologist and other haemophilia staff, with input from microbiology and other relevant specialties such as respiratory medicine, infectious diseases and immunology (Bham Heartlands Hospital). Boys were referred over to the adult haemophilia services from the age of 16 onwards.

82.2. Patients with Hepatitis B and /or Hepatitis C were referred to the Hepatology Department if further investigation or treatment was required, and the patient managed jointly with the haemophilia service.

82.3. Treatment options included the use of anti-retroviral drugs for HIV and the use of interferon, ribavirin for HCV.

82.4. I don't remember what specific written information was provided to patients about treatment but discussions about side effects, prognosis were regularly discussed.

82.5. My recollection is that boys with HIV infection were seen at variable intervals depending on their clinical condition and how frequently monitoring of therapy needed to place. This may have varied from weekly to monthly.

82.6. Boys with HBV or HCV were seen 3-6 monthly as were all children with severe or complicated bleeding disorders, and more frequently if required as part of hepatology follow up.

83. **What, if any, arrangements were made to provide patients infected through blood products with counselling, psychological support, social work support and/or other support?**

83.1. Counselling and support was provided by haemophilia centre staff, who would have included, haematologists, haemophilia nurses, clinical psychologists, a social worker and a play therapist. The Liver Unit offered similar support for children with HBV and HCV infections.

84. **Did the Centre receive funding from the Department of Health and Social Security or from any other source to help with the counselling of patients infected with HIV?**

84.1. Yes, by way of the appointment of a clinical psychologist and social worker.

85. **What (if any) difficulties did you/Centre encounter in obtaining sufficient funding for the treatment of people who had been infected with HIV and/or hepatitis C? You may find it helpful to consider BWCT0000018; BWCT0000019; BWCT0000015; BWCT0000065.**

85.1. There has always been a battle to obtain appropriate funding for the comprehensive care offered to patients with inherited bleeding disorders, whether relating to Centre space, staffing levels, support staff and treatments. Some of the historical funding was in part dependent on how supportive Regional commissioners of health were towards this specialty, which has always been seen as a very high cost, low volume specialty with significant financial risk involved to the Trust and to the Region. Some commissioners were more supportive than others over the years, and the same can be said of hospital chief executives and medical directors, some of whom saw haemophilia care as a low-profile specialty within the hospital. Professor Hill was able to negotiate a significant uplift to haemophilia services through funding available from the Department of Health for the care of HIV infected patients, which resulted in designated beds, additional nursing staff, psychology and social worker support. This was incorporated into the block contract for haemophilia services and as such was protected from the various cuts and cost savings,

changes to patient tariffs etc brought in over the years. I think Professor Hill or the relevant commissioners would be able to answer this in more detail.

85.2. The quoted letters refer to my responses to Service Managers, the Chief Executive and Clinical director concerning the lack of support from Regional purchasers of haemophilia care for the use of interferon and the use of recombinant FVIII concentrate. There would have been a number of other communications and discussions concerning lack of funding. Over recent years it has been instructive to see how limited a commissioner can be in terms of being able to increase funding to haemophilia care – there has been absolutely no extra money available from the DoH, and whereas a commissioner can agree that a particular part of the service needed development, they were totally unable to provide any funding for this.

86. **What if any involvement did you or your patients have with clinical trials in relation to treatments for HIV and/or hepatitis? Please provide full details.**

86.1. I am not aware of any HIV treatment trials dating from the times I was at BCH. A small number of my patients with HIV were recruited to a trial of interferon and ribavirin, led by Professor Deidre Kelly and the Liver Unit team, with haemophilia support undertaken by the haemophilia staff.

Records

87. **What was the Centre's policy with regards to recording information on death certificates when a patient had been infected with HIV or hepatitis? Were you involved with any inquests in relation to patients who had been infected with HIV or hepatitis as a result of their treatment? If so, please provide details.**

87.1. I cannot recall the Centre's policy as existed when I was a senior registrar at BCH. I can distinctly recall signing a very small number of death certificates where the individual had died of the complications of HIV and think that HIV or AIDS was included on the death certificate as a contributory cause. I've not been involved in any inquests as far as I can recall.

88. **What were the retention policies of the Centre in regards to medical records during the time you were practising there?**

88.1. Every patient of the Haemophilia Centre had a hospital set of clinical notes and also a separate haemophilia file kept on the Unit, which detailed diagnosis, specified treatment, attendances, treatments etc. The Haemophilia Unit files of transferred/deceased patients were originally kept in a locked facility on the Haemophilia Unit but had been moved to an off-site storage facility before I retired. Hospital notes are kept according to existing hospital policy.

89. **Did you:**

a. Maintain separate files for some or all patients? If so, why; where were those files located; and where are those files now?

89.1. When I undertook my research project in 1984, I constructed separate files for individual boys with details of all batches of concentrate received since 1980 onwards, the quantity of the batch and number of treatments. The files were expanded to include the results of immunology testing and virus status together with other laboratory parameters such as blood count and liver function tests as the project developed. Those files were destroyed once I had completed the writing up of my MD thesis and submitted papers for publication.

b. Keep records or information (e.g. information being used for the purpose of research) about any of your patients at your home or anywhere other than the Centre? If so, why, what information and where is that information held now?

89.2. See above. As most of the writing up was done in my own time some of these files would have been transferred between hospital and home. Patient identity on these files was by the initials of the first and second names.

90. **Do you still hold records or information about any of your patients from the 1980s and 1990s? If so, explain why and identify the records or information that you still hold.**

90.1. The only information I have is a single copy of my MD thesis, which contains details of the research project carried out 1984-6.

Section 5: UKHCDO

91. **Please describe your involvement with UKHCDO (including any of its working parties, committees or groups). Did you usually attend the annual general meetings?**

91.1. I was a member of the Advisory Committee of the UK Haemophilia Centre Doctors Organisation (UKHCDO) 1997-2017.This meant I represented the BCH Haemophilia Comprehensive Care Centre in this forum, received various communications from the UKHCDO Executive Committee, completed data requests including the annual returns prior to electronic recording of treatment details, participated in the triennial audits of comprehensive care centres and was a member of the following working parties:

91.2. I was a member of the UKHCDO's working party on paediatric haemophilia from 1994 -2017 and chaired the committee from 2001- 2007.

91.3. I was a member of the UKHCDO rare bleeding disorders working party since its inception in 2003 up to 2009.

91.4. I was a member of the UKHCDO inhibitor working party 2006 - 17.

91.5. I attended the annual general meetings when possible, probably on average about twice every three years.

92. **During the period that you belonged to UKHCDO, please outline any involvement which you had in the development of policies or advice by UKHCDO which are relevant to the Inquiry's Terms of Reference.**

92.1. I was involved in producing various guidelines through membership of the above working parties. These included management of rare bleeding disorders (2004), management of inherited platelet disorders (2006), the use of prophylactic FVIII concentrate for children and adults with haemophilia A (2010) and management of haemophilia in the fetus and neonate (2011). All these would have guidance on treatment of these conditions.

92.2. I don't think I have been otherwise involved in the development of policies or advice by the UKHCDO though would have had the opportunity to comment on various guidelines/advice before they were disseminated to haemophilia centres/published. I have never been a member of the UKHCDO Executive Committee.

Section 6: Pharmaceutical companies

93. **Have you ever:**

a. **Provided advice or consultancy services to any pharmaceutical company involved in the manufacture and/or sale of blood products?**
b. **Received any pecuniary gain in return for performing an advisory/consultancy role for a pharmaceutical company involved in the manufacture and sale of blood products?**
c. **Sat on any advisory panel, board, committee or similar body, of any pharmaceutical company involved in the manufacture or sale of blood products?**
d. **Received any financial incentives from pharmaceutical companies to use certain blood products?**
e. **Received any non-financial incentives from pharmaceutical companies to use certain blood products?**
f. **Received any funding to prescribe, supply, administer, recommend, buy or sell any blood product from a pharmaceutical company?**
g. **Undertaken medical research for or on behalf of a pharmaceutical company involved in the manufacture or sale of blood products?**
h. **Provided a pharmaceutical company with results from medical research studies that you have undertaken?**

If so, please provide details.

93.1. (a-c). I have participated in a few Advisory Boards for companies involved in the manufacture and sale of blood products and have received fees for doing so. Similarly, I have received speaker fees for lectures given at various sponsored meetings and have been in receipt of educational grants to enable me to attend international scientific meetings.

93.2. (d-f) I have never received financial incentives or non-financial incentives from pharmaceutical companies to use certain blood products nor received funding to prescribe, supply, administer, recommend, buy or sell any blood product from a pharmaceutical company.

93.3. (g) I have participated in medical trials of a new product which have been undertaken and run by a pharmaceutical company involved in the manufacture of blood products, for example trials of a recombinant form of FXIII concentrate which contributed to this product being licensed for sale in the UK.

93.4. (h) I have not unless involved in the sort of research trial outlined in (g).

94. **Please consider the enclosed letters from Dr A Kelly addressed to you regarding a protocol for treatment with interferon and Ribavirin of haemophiliac patients infected with Hepatitis C, where Dr Kelly refers to a proposal to seek funding from pharmaceutical companies [BWCT0000014 and BWCT0000013]. Please explain the details of this study, including what funding, if any, was provided by pharmaceutical companies.**

94.1. This followed discussions about a study to determine optimal treatment protocols for bleeding disorder patients with HCV by way of a trial looking at the use of interferon and a combination of interferon and ribavarin. Patients would be randomised by HCV genotype. Funding for the drugs and for study support was sought from the two manufacturers mentioned in Deidre Kelly's letter. I don't recall what funding was obtained or how many patients were recruited to the study.

95. **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?**

95.1. Yes. This would have been part of the research application to the ethics committee.

Section 7: vCJD

96. **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?**

96.1. I became aware of the identification of vCJD in the UK population following the publication of details of this occurrence in (I think) 1996. Although it had initially been assumed that infection with vCJD was dietary in origin, there was a theoretical risk of transmission of vCJD from asymptomatic blood donors into the donor plasma pool from which factor concentrates and other products such as albumin were manufactured. The first evidence of transmission through blood and blood products was described in 2004. The risks of vCJD were regularly discussed in UKHCDO meetings, and the UKHCDO worked with the Department of Health and other bodies to identify recipients of UK plasma-derived factor concentrates between 1980 and 2001 as well as giving guidance to haemophilia centres on Public Health measures, identification of potential recipients, information to patient and families etc.

97. **Please consider DHSC0034984, a notice sent to you and Professor Hill regarding a product recall initiated by Bio Products Laboratory following concerns about possible CJD contamination of donor blood. The notice states the Lothian Ethical committee had advised that recipients of the affected batches should not be informed that the product they had received had been recalled. Please explain what actions, if any, you took on receipt of this notice.**

97.1. I can't remember whether or not the recipients of the implicated batches were informed about the reason for the recall. I think they were but I can't be certain.

98. **Did you have any involvement in decisions as to what information to provide to patients about vCJD? If so please answer the following questions (you may be assisted by consideration of BWCT0000040):**

a. **What steps were taken to inform patients about possible exposure to vCJD and to provide information to them about vCJD?**
b. **What steps were taken to arrange for counselling, support and/or advice to be offered to patients who were being informed that they might have been exposed to vCJD?**

98.1. With the evolving information about vCJD, the uncertainty about risk of infection and the changing Public Health advice, all patients and carers at my Centre were sent written information about vCJD, including that infection with VCJD was a possible risk for those recipients of UK plasma derived concentrates between 1980 and 2001. All carers were asked to confirm or not whether they would wish to be informed if their child had been exposed to such concentrates, and whether they would want to know if they had received any implicated batches.

98.2. Appointments were made for those families who wanted to know of exposure to UK plasma-derived concentrate and /or to implicated batches, and discussions, counselling, advice and support offered by the Haemophilia Centre medical and nursing staff. The response from families was very variable, ranging from wanting as much information as possible and post discussion advice and counselling to a significant number not wishing to know whether implicated batches had been received, to some wanting a straight yes or no answer but no further discussion.

98.3. BWCT000040 refers to a meeting which was organised with the families of haemophiliacs at BCH to update/inform them of the UKHCDO recommendations for treatment products for haemophilia and the difficulties we were experiencing at BCH with the introduction and funding of recombinant FVIII.

99. **What measures were put in place at the Centre from a public health perspective, in relation to the care and treatment of patients? If patients at the Centre were identified as at risk for public health purposes, did that impact detrimentally upon them in terms of their ability to access treatment and care (whether at the Centre or elsewhere?).**

99.1. At risk patients were identified and an at-risk notice placed in their clinical notes. Recommended Public Health measures were introduced and co-ordinated with the departments of microbiology and histology, with other specialties such as surgery and ENT being fully informed about recommended measures on tissue collection for example. For the very infrequent at-risk patient who required endoscopy, again Public Health recommendations specific to endoscopy were followed and the endoscopy quarantined. There were issues about funding additional endoscopies which were resolved. I don't believe that the ability to access treatment and care at BCH was affected by these measures. Most patients with bleeding disorders had dental care carried out at BCH – I can't recall a specific problem with accessing routine care at a local dentist.

Section 8: The financial support schemes

100. **What if any involvement did you have with the different trusts or funds (the Macfarlane Trust, the Eileen Trust, the Macfarlane and Eileen Trust, the Caxton Foundation, the Skipton Fund, EIBSS) which were set up to provide financial support to people who had been infected?**

100.1. I had very little direct involvement following my appointment as a consultant at BCH. Most of the involvement came from my colleague Professor Hill, the Centre's senior nurses and the social worker attached to the Centre. I occasionally completed medical details on forms submitted to the Skipton Fund.

101. **To what extent, during your time at Centre, did staff (including you) inform patients about the different trusts or funds?**

101.1. Patients were both informed and advised by the Centre's staff. Many also had access to the information provided by the Haemophilia Society and the UKHCDO.

102. **Did the Centre have any policy or any guidance for staff members in relation to referring patients to the trusts and funds for support?**

102.1. I don't think there was an official, written policy but more of advising appropriate patients and families on the various Trusts and Funds and helping with applications – this would include providing clinical information to sitting down with the carer and helping to fill in the application forms. Also answering further queries from those bodies about the application when necessary.

103. **What kind of information did the Centre provide to the trusts and funds about, or on behalf of, patients who were seeking assistance from the trusts and funds?**

103.1. See Q102.

104. **Did the Centre provide practical assistance to patients in relation to making applications to the trusts and funds? If so please provide details.**

104.1. See Q102.

105. **Based on your own dealings with any of the trusts or funds and/or based on your knowledge of the experiences of your patients in relation to the trusts or funds, do you consider that the trusts and funds were well run? Do you consider that they achieved their purposes? Were there difficulties or shortcomings in the way in which they operated or in their dealings with beneficiaries and applicants for assistance?**

105.1. My own dealings were very limited, and I am not therefore able to answer that question in any depth.

Section 9: Other Issues

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

106.1. None made.

107. **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.**

107.1. The tragedy of HIV and HCV in haemophiliac boys and men has been profound and far-reaching. There has been a slowness to acknowledge the extent of this, and the financial support offered by various governments to affected individuals and families has been totally inadequate to date.

107.2. The life expectancy of a haemophiliac in the early 1980s was reported as near normal before the effects of HIV transmission in commercial FVIII concentrate became known. It is very likely that the transmission of HIV could have been greatly reduced if the UK had been self-sufficient in the production of factor VIII and IX concentrate from the 1970s onwards, (which also applies to HCV to a lesser extent).

107.3. The most problematic issues for me as a haemophilia treater have always revolved around funding issues for the haemophilia service, and how these funding decisions have been made nationally, regionally and within a particular hospital. My feeling is that the year on year increases in factor VIII usage, the move to prophylaxis and the use of more expensive concentrates have not incurred the expected financial penalties as the DoH seemed content to allow the overspends to continue, perhaps based on past responses by government to the various crisis in haemophilia care.

107.4. The implementation of a service specification for the comprehensive care of individuals with bleeding disorders was a big step forward in the 1990s, and this

has been improved upon over time. Audit of Comprehensive Care Centres has been part of this, and the recent changes in this process to make it more demanding of the Centres and more evidence-based will be helpful. The move to include haemophilia centres in this process is to be welcomed and may lead to the rationalisation of the number of small centres which have existed.

107.5. The DoH has worked much more closely with haemophilia organisations over the last 15 years, as exemplified by the national contracting process for the purchase of blood products for the treatment of congenital bleeding disorders, and this is to be commended and allowed to continue.

107.6. I have been retired 3 years and have already forgotten a lot of the haematology knowledge which I used on a day to day basis. I have found being asked to remember events, actions etc from almost 40 years ago prone to inaccuracy unless there are specific handles to prompt my memory, such as the publications mentioned. I am sure that is the case for most people involved. I am also aware that medicine has changed greatly during the time I worked, particularly in medicine itself becoming less paternalistic, patients becoming more involved in decision making, consent becoming more detailed and transparent. Many of the questions I have been sent refer to various aspects of practice, and I think it is important not to apply current concepts of practice to events 40 years ago.

Statement of Truth

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

Signed

GRO-C

Dated

14.03.22

Table of Exhibits

Date	Description	Exhibit Number
28/04/1988	WIlliams M.D., Al-Rubei K. & Hill F.G.H. (1988), "A prospective study of HIV-infected haemophilic boys and the prognostic significance of immune and haematological abnormalities", *Thrombosis and Haematosis*.	WITN5725002
21/12/1987	Williams M.D., Boxall E.H. & Hill F.G.H. (1988), "Change in immune response to Hepatitis B in boys with haemophilia", *Journal of Medical Virology*.	WITN5725003