Witness Name: Dr David Bevan
Statement No: WITN4106001

Dated: 9 November 2020

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DR DAVID BEVAN

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

I, Dr David Bevan, will say as follows: -

Section 1: Introduction

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

My name is David Huw Bevan, my address is known to the inquiry. My date of birth was GRO-C GRO-C 1949. My qualifications are MB.BS. FRCP FRCPath.

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.

After qualification (MB.BS. Newcastle 1973) I completed pre-registration posts at Darlington Memorial Hospital (House Surgeon 01/08/1973 – 31/01/1974) and Royal Victoria Infirmary, Newcastle-on-Tyne (House Physician 01/02/1974 – 31/07/1974).

I was Senior House Officer in General Medicine at Shotley Bridge General Hospital, County Durham, from 02/08/1974 until 31/07/1975.

I was Registrar in General Medicine at Darlington Memorial Hospital from 12/08/1975 until 31/10/1976. I was the sole registrar covering all acute inpatient medical care at this general hospital, including in the emergency department, the general ITU, and the coronary care unit as well as extensive outpatient duties.

After obtaining MRCP I took up the post of Senior House Officer in Medical Oncology at The Royal Marsden Hospital, Sutton, from 01/11/1976 to 07/05/1977. This post included the frontline care of individuals with leukaemia on the Bud Flanagan isolation ward, including some of the UK's earliest bone marrow transplant recipients, as well as rotation through the Lymphoma, Breast cancer, and Testicular cancer Units.

During the brief interim (June-July 1977) before my next NHS post commenced, I worked as Resident Medical Officer at The Harley Street Clinic in London and St Anthony's Hospital in Cheam.

I was Registrar in Haematology at St George's Hospital, London SW1 and SW17 from 01/07/1977 until 06/12/1978. This was a rapid introductory period for the novel cohort of trainees who had no prior experience of laboratory work and who were recruited for their acute

medical experience and MRCP in order to care for patients with blood diseases. The first six months were spent learning microscopy and other basic bench-work at the Hyde Park Corner branch, where there was no haemophilia contact. During the second part, at Tooting, I was first introduced to the haemophilia laboratory, the laboratory diagnosis of haemostatic disorders, and to people with haemophilia. I was also informed that the lab was a 'haemophilia centre', although the clinical facilities consisted of a single bed, housed in one of the warren of wooden outbuildings comprising the laboratory, and shared by the venepuncture team. During my time doing lab on-call as a formally untrained technician, I would often answer the outside door at night when haemophilia patients needing cryoprecipitate sought access to their centre.

I was then appointed as Lecturer and Honorary Senior Registrar in Haematology at St George's Hospital Medical School from 07/12/1978 until 1984. Despite its title this involved little academic or teaching work. It was part of the South West Thames Senior Registrar Training rotation, during which trainees accumulate enough knowledge in the branches of the subject to pass the MRCPath examination (the training exit exam) and to decide whether to sub-specialise in teaching hospital practice or become a general haematologist at a (then) District Hospital. Like nearly all MRCP-holding Haematologists, I originally planned to specialise in leukaemia (haemato-oncology). Early in the specialist registrar rotation, I was posted to St James's Hospital Balham for a year, working in all branches of the subject (except haemophilia), and then at the Royal Marsden Hospital, Sutton, to gain experience in the laboratory diagnostic and blood banking aspects of leukaemia and lymphoma. During these attachments I published papers on leukaemia and presented data on leukaemia treatment at International conferences in Montreal, Rome and Assisi. I also undertook formal training in blood transfusion during attachment to the South London Blood Transfusion Service at Tooting. I learnt more about haemophilia and other bleeding disorders: at that time this was mainly in respect of the forthcoming MRCPath examination, the two parts of which most frequently failed were the practical exams in Coagulation and Blood Transfusion. Fortunately, I passed.

I was then appointed Senior Lecturer and Honorary Consultant in Haematology at St George's Hospital Medical School from 1984 until 30/09/2004. Although the responsibility for teaching medical undergraduates increased, this role was still essentially that of a consultant clinician. Prior to the summer of 1985, I had a clinical role in haemostasis but no specific responsibilities in haemophilia because the title and role of centre director was still held by Professor Peter Flute, who remained head of department. My memory of the series of events and their dates is not clear; but I do recall that the first year or so of my time in this job was spent dealing with major organizational issues. St James's Hospital Balham, our sister hospital was closing, so its substantial haematology practice and laboratory work had to be seamlessly transferred to St George's in Tooting, and our Senior Lecturer / consultant colleague at St James's, Dr Michael Rose, had left his post. This increased workload was already challenging for three substantive consultants (Professor Flute, Dr John Parker-Williams, and myself). Peter Flute then took early retirement to become South West Thames Postgraduate Dean.

John Parker-Williams and I had to divide up all the consultant functions of the department between us. He took on the roles of undergraduate and postgraduate teaching and training; the entire laboratory service including its developing quality control agenda; all of blood transfusion; and retained clinical outpatient roles. I took on haemato-oncology, including leukaemia, lymphoma and myeloma; the care of all inpatients, including a rapidly expanding sickle cell service; and all of haemostasis, including anticoagulation and haemophilia. I was also

responsible for the care of children with blood diseases, including haemophilia, in concert with the professorial paediatric unit at SGH (Prof Neil Mckintosh). The title of Haemophilia Centre Director passed to me in the summer of 1985. Hitherto it would have been a small part of my practice, but I had already realized that this was not going to be the case anymore.

We were also granted funding for a haemophilia counsellor and were able to appoint a skilled and well-informed individual to this role. A major transformation took place due to the appointment of a new Professor of Haematology at SGH in 1987. Professor Edward Gordon-Smith was able to bring substantial investment to the department in the form of new members, doctors, nurses, scientists, and also released funding for the first haemophilia nurse roles at the Centre. New colleagues were able to gradually take on haemato-oncology, thereby releasing me to devote more time to the organisational requirements of the haemophilia Director role. However, I remained responsible for an increasing haemoglobinopathy / Sickle Cell practice, the increasing field of haemostasis/thrombosis, and the apheresis service (from 1991).

Due to Medical School re-organisation in the light of the Research Assessment Exercise, which made it highly counterproductive for universities to employ academics who were busy clinicians, my contract was changed to Consultant Haematologist and Honorary Senior Lecturer, an NHS post I held from 01/10/2004 until 20/04/2008.

To the best of my recollection, in 2003 I became Lead in Laboratory Haematology, and in 2005 left that role to become Lead Clinician in Clinical Haematology. By this time the Pan-Thames Haemophilia Consortium had transformed the purchasing of coagulation factors in London and subsequently the National Tendering process was put in place.

Haemostasis and haemophilia had become my major area of interest and the possibility of moving to lead a true Comprehensive Care Unit became a major motivation.

From 20/04/2008 until April 2016 I was Consultant Haematologist and Haemophilia Centre Director at Guy's & St Thomas' NHS Foundation Trust (GSTT). As far as I can recall, in early 2016, I relinquished the Director role, which passed to the current post holder, Dr Gerard Dolan. I continued as a consultant in the Haemophilia Centre until January 2017, then as (part-time) consultant in Haemostasis (Thrombosis) at GSTT until March 2018. I then retired from NHS practice, but was asked to return to GSTT for a further year as Locum Consultant in the Haemophilia Centre after the unexpected death of a senior colleague there: this post lasted until March 2019.

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. Please include an outline of your involvement with the British Committee for Standards in Haematology and British Society for Haematology.**

I was an ordinary member of the United Kingdom Haemophilia Centre Directors (later amended to Doctors) Organisation from 1985 until my retirement in 2019. Any of my attendances at UKHCDO meetings / conferences prior to 1985 were mandated by Professor Flute, in his absence, simply as a physical representative of St George's Hospital. I was never a member of any of its formal subcommittees or working groups*, until in 2008, due to my move to GSTT, I became a member of both its Musculoskeletal Working Party and its Comprehensive Care Centre Directors Committee.

As far as I can recollect, I was an ordinary member of the British Society for Haematology from 1978 until my retirement. Apart from writing papers and annotations for the British Journal of Haematology and attending some of its annual conferences, I performed no other role for the organisation. Some of the UKHCDO meetings indicated above took place at the BSH conference room in Islington.

As far as I can recollect, I have had no involvement with the British Committee for Standards in Haematology. As will be seen from the above, I make no pretence of being an expert in laboratory practice or standardisation. In general, I have avoided writing national guidelines, and only written local guidelines when absolutely unavoidable. When I review my career, it becomes clear that the same goes for committees in general.

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.

To the best of my recollection and knowledge, I have not provided evidence to, nor have been involved in, any other inquiries, investigations, criminal or civil litigation (insofar as I understand those terms) in relation to HIV, HBV, HCV or vCJD.

5. Did you provide evidence in any cases involving patients with bleeding disorders? Please provide details and any relevant documents if so.

I have not provided evidence in any cases relating to HIV, HBV, HCV or vCJD in patients with bleeding disorders. In the context of question 4.

6. The questions below focus predominantly on your work at St George's Hospital Haemophilia Centre ("the Centre"). It is the inquiry's understanding that you began working at the Centre in 1974 and became its Director. The Inquiry also understands that you moved to become Director of the Guy's and St Thomas's Haemophilia Centre ("St Thomas's") around 2007-2008, and that you continued working there until at least 2014. If you have information concerning St Thomas's which is not covered by the questions below, but which is relevant to the questions posed in relation to the Centre and/or to the broader issues being investigated by the Inquiry, please include that information in your response.

I have provided my correct starting dates at St Georges under 2 above. I have no other information concerning St Thomas's not covered by the questions below.

Section 2: Decisions and actions of those treating patients with bleeding disorders at St George's Hospital Haemophilia Centre ("the Centre") and your decisions and actions

7. Please describe the facilities, organisation, roles, functions and responsibilities of the Centre during the time that you worked there, and how they changed over time.

During my early trainee period as a registrar the facilities of the St George's Haemophilia Centre (HC) were extremely limited, consisting of a laboratory able to diagnose haemophilia and related bleeding disorders by assaying coagulation factor levels in blood samples, to detect and assay FVIII inhibitors, a freezer to store frozen blood products (plasma, cryoprecipitate) and a refrigerator for lyophilized coagulation factors (FVIII, FIX). The laboratory manned a 24-hr

telephone line available for patients with registered bleeding disorders to ring in the case of bleeds or other issues. Attached to the laboratory in Knightsbridge Wing were outbuildings containing patient areas for anticoagulation clinics, the outpatient phlebotomy service, and other procedures such as bone marrow aspirates and biopsies. One room in this area was allocated to the haemophilia centre, containing an infusion chair and a hospital bed, but was also used for other groups of patients.

The organization at this time consisted of a senior laboratory technician and their small team, with the Director (Professor P T Flute) taking all managerial responsibility, including maintaining the stock and composition of the therapeutic materials held in the laboratory. He was also responsible for deciding which therapeutic agent each patient was given to treat bleeds. These agents were administered to patients by duty trainee medical staff under his consultant supervision, although some patients preferred to self-inject. There were no departmental written guidelines or Standard Operating Procedures (SOPs). Therapeutic decisions were made on the basis of the patients' written medical notes, which contained a record of their current treatment product and dose, as well as their responses to previous treatment episodes. No haemophilia nurse, secretary or administrator was employed at the Centre at this time. There was no haemophilia office. Paediatric patients were seen in a joint pediatric/haematology clinic led by a senior consultant paediatrician, and treated on paediatric wards by junior medical staff. I cannot recall any policy decisions being discussed at any formal internal meetings where minutes were taken; any discussion took place ad hoc in the context of individual patients.

The centre looked after about 25 severely affected individuals with Haemophilia A and B, of whom about 8 were children. I cannot be sure of these numbers after such a long time. Accordingly, in National terms, HC was a small centre, albeit larger than many in that category. In the light of its size, the role and function of the centre was seen as, firstly, to provide a reliable laboratory diagnosis of haemophilia and other bleeding disorders, as well as to detect inhibitors developing in treated individuals, and thereby to register individuals found to have haemophilia and issue them with valid 'green cards' that indicated a diagnosis. Secondly, to maintain adequate stocks of therapeutic products (plasma, cryoprecipitate and clotting factor concentrates) to treat patients registered at the centre, and to administer the relevant product to the correct patient when required (or issue the product to patients able to self-inject), and to make a 24-hr telephone line available for patients to contact the centre. Treatment was strictly 'on-demand': little or no prophylactic treatment was carried out. As a junior trainee I was not privy to how or whether formal categorical patient consent to receive the products used in their treatment had been obtained at Centre level.

The responsibilities of the Centre were seen, at that time, to be to treat, monitor and support the patient group registered at the Centre according to the standards set out by the United Kingdom Haemophilia Centre Directors' Organisation; to maintain accurate records of the type and amount of treatment given to each patient, and the response to treatment in terms of efficacy; to monitor complications, including the development of inhibitors, and to submit that data yearly in the form of 'Haemophilia Returns' to the Oxford database.

In July 1985, when the role of Haemophilia Centre Director was added to those I was already carrying as Senior Lecturer/ Honorary Consultant, the lab had relocated to modern laboratory space in Hunter Wing in the Medical School [1980] but there were still no appropriate Centre facilities and no Haemophilia Nurses.

I cannot remember when, but the impact of HTLVIII seropositivity and AIDS in the haemophilia population resulted in our being given funding for the appointment of a specific counsellor for affected haemophilia patients. I cannot remember the name of the person appointed to this role. Paediatric patients were seen jointly by me and Professor Neil Macintosh and treated on the paediatric ward. Our patients with HIV / AIDS were jointly cared for by the Infectious Diseases Unit at St George's Hospital (Professor G Griffin and Dr Mark Wansborough-Jones). Our pediatric patients with HIV/AIDS were cared for by Dr Graham Davies in the paediatric department.

In 1988, after the appointment of Professor Gordon-Smith as overall head of haematology, additional consultant staff members were appointed, specialising in haemato-oncology, bone marrow failure and transplantation, and paediatric haematology. My paediatric colleague, Dr Sarah Ball, began to participate in the care of children with haemophilia. It became possible to invest in the service, and we were able to appoint a first haemophilia nurse, Ms Katy (I cannot now recall her surname) in 2000.

The number of individuals with bleeding disorders registered at the centre continued to increase over the next few years but never reached the number threshold required for recognition as a Comprehensive Care Centre (40 or more severely-affected individuals treated with concentrate per year). As far as I can recall, we looked after about 35 individuals with severe haemophilia at this stage, of whom about 12 were children.

Despite this brake on investment, additional haemophilia nurses, and a centre business administrator were appointed and a haemophilia office assigned to the team. Haemophilia by now was a much greater part of my work – I had left haemato-oncology practice at this time. A prolonged struggle to obtain a dedicated clinical space, restricted to haemophilia care, that would fulfill the requirements of a Comprehensive Care Haemophilia Centre ended in disappointment when the space we identified as ideal in Knightsbridge Wing was designated as a laundry sewing room. Adult patients with haemophilia were still treated on the haematology day unit and out of hours on the Ruth Myles Ward, and paediatric patients on paediatric wards: however, throughout this period an increasing proportion of treatment has been carried out at home in both groups now.

8. Please identify senior colleagues at the Centre and their roles and responsibilities during the time that you worked there.

<u>During my time as a trainee (1978 – 1985):</u>

- P T Flute, Professor of Haematology, head of Haematology Department and Haemophilia Centre Director. Responsible for the haemophilia service, including the Haemostasis Laboratory, the stock of therapeutic products, and the clinical care of adults with haemophilia and related disorders.
- Dr John Parker-Williams, General Haematology Laboratory and Blood Transfusion Head. Responsible for blood transfusion.
- During my tenure as Consultant Haematologist and Haemophilia Centre Director (1985-2008).
- Dr Sarah Ball, Consultant Paediatric Haematologist (from 1989 – 2005 [retd.?). Responsible for the clinical care of children with bleeding disorders.
- Dr John Parker-Williams, as above.

10. Approximately how many patients with bleeding disorders were under the care of the Centre when you first started working there and over the years that followed? Approximately what proportion were adults and what proportion were children? (If you are able to give exact rather than approximate figures,please do so).

The centre looked after about 25 severely affected individuals with Haemophilia A and B, of whom about 8 were children. I cannot be sure of these numbers after such a long time. These numbers gradually increased over time, so that at the end of my tenure we looked after about 35 individuals with severe haemophilia, of whom about 10 were children.

11. What decisions and actions were taken, and what policies were formulated, at the Centre 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, and on what basis, were decisions made about the selection and purchase of blood products and how did those decisions change over time?

Under Professor Flute's tenure as Haemophilia Director until the summer of 1985, he made all such decisions. I am only aware of the basis for his decisions insofar as he explained them to his junior staff at the time. He treated the handful of severe FIX deficient individuals with the concentrate made by Dr Bidwell's laboratory in Oxford. He treated the minority of adults with Haemophilia A (perhaps two or three individuals, I cannot remember the exact number) who agreed to it, with cryoprecipitate. The logic behind this was financial, since it cost less than concentrate. As far as possible he treated children and younger adults with UK-sourced FVIII concentrate from Elstree (initially via the Lister Institute) because he considered it less likely to transmit NANB hepatitis (even though, at that time, he evidently considered NANB less harmful than bleeding). Because there was never enough BPL FVIII, adults were usually given commercial FVIII concentrate from the USA in the form of Armour Factorate. This US concentrate was also given to the younger patients in the regular event that Centre stock of the BPL product ran out. At all times and in all clinical situations the absolute priority was that treatment for bleeding was never withheld. By far the leading cause of death in severe haemophilia at that time was untreated or inadequately treated bleeding.

From early 1985 Professor Flute tried, as far as possible, to convert the Centre FVIII stock entirely to heat-treated BPL product, as indicated by his letter to Dr Snape at BPL dated 19th February 1985. That letter was copied to Dr Parker-Williams and me, since we were the only other consultants in the department at that time. I cannot recall if this request was successful, or whether any US commercial concentrate was still stocked or used at the centre, or what specific products they were.

After Professor Flute left his post at St George's in July 1985, the title of Haemophilia Centre Director passed to me. However, in view of the multiple clinical responsibilities I had to take on as one of only two consultants in the Department of Haematology, I had little time to devote to haemophilia centre management (as opposed to the care of individuals with haemophilia). To the best of my recollection I made no alteration to the types or manufacturers of factor concentrates stocked and used at the centre. I stuck entirely to existing orders and policies. As far as I can remember, we used heat-treated BPL Factor 8Y (and 9A) almost exclusively. I cannot recall using any US-sourced plasma products at this time, although this could have happened due to temporary shortages of 8Y. Unfortunately, no records survive at St George's

of blood products stocked or issued by the department at this time.

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

As stated above, Professor Flute treated as many patients with UK plasma-derived cryoprecipitate and FVIII and FIX concentrate as supplies allowed him to. He used US plasma-derived commercial concentrate to fill the shortfalls caused by limited UK supplies. I do not know the specific reasons for his choice of one particular US concentrate (Factorate, Armour Pharmaceuticals). He only chose from the UKHCDO list of approved products.

Once Factorate had been used in patients, Professor Flute was strongly disposed not to switch to other companies' products. His opinion was that this would mean wider exposure to different multi-donor pools of plasma.

c. Where were the products sourced? From whom were they purchased?

Cryoprecipitate, BPL and Oxford products were sourced via the National Blood Transfusion Service. When BPL moved on to a commercial footing, concentrates were purchased directly from them.

US concentrates were purchased directly from the manufacturer's UK offices.

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

To my knowledge, no member of the Haemophilia Centre staff ever had any commercial interests (including holding shares or other investments) in Blood Product manufacturing, and accordingly they never entertained any commercial considerations in purchasing products.

Financial considerations were (and remain) a major and permanent driver of choice in clotting factor purchase, whether in the context of a limited, chronically overspent, departmental budget (St George's 1985-2000) or a planned budget provided by a Regional Specialised Commissioning Team (Pan-Thames Haemophilia Consortium [PTHC]: St George's 2000-2008) or similar commissioning operating under the terms of the National Tender for blood products (PTHC: St George's and GSTT 2005-2018). If a perceptibly equivalent product (in terms of safety and efficacy) is cheaper, it will be chosen as the dominant product.

e. What involvement did you have?

From **July 1985** until **1989**, I held sole responsibility for selecting the coagulation factors needed for the treatment of individuals with haemophilia and allied bleeding disorders registered or visiting the St George's Centre. My paediatric colleague Dr Sarah Ball participated in these decisions after she was appointed in **1989**. Senior laboratory staff ordered the products and handled invoices. From **April 2000**, until the onset of the National Tendering Process for Coagulation Factors in **2005**, we essentially retained this responsibility, but from **2001** there was also input from my new Haemophilia nurse colleague(s), and from **April 2000** choices needed to be discussed and approved by the Pan-Thames Haemophilia Consortium (PTHC), who progressively took on the cost of product infused into all patients registered with them, in the context of detailed specialist commissioning for Haemophilia and Allied disorders.

From the introduction of the National Tendering process in **2005**, our preferences in therapeutic product were communicated via the PTHC, but the type and volume of product allocated to the Centre was now determined by the contracts agreed as a result of the National Tendering Process. Centre Directors were therefore eliminated from the direct purchasing of product

except in an advisory capacity.

12. **What products were used for treating patients at the Centre, over what period of time and for which categories of patients? How were decisions taken at the Centre as to which products to use for individual patients? What involvement did you have in such decisions? Were patients given any choice, or involved in any discussions, as to which products to receive?**

- **1977-85** Frozen plasma (NBTS)
- Cryoprecipitate (NBTS)
- BPL Factor VIII concentrate (BPL Elstree / NBTS)
- Factorate (Armour)
- Oxford FIX concentrate (Bidwell)
- FEIBA

These products are the ones that I remember being used during this period. No documentation can be found at SGH, so this may not be a complete list. I had no involvement in these decisions, and therefore I do not know whether patient discussion or choice ware involved.

- **1985-9** Frozen plasma
- Cryoprecipitate
- BPL Factor 8Y (heat-treated)
- BPL Factor 9A (heat-treated)
- FEIBA (plasma-derived aPCC, heat-treated) for inhibitor patients
- Hyate-C (porcine FVIII) for inhibitor patients

It is doubtful that the amount of BPL product 8Y allocated to the Centre was sufficient for all treatment needs during this period, so it was very likely that heat-treated US factor concentrates were also used. Unfortunately, I cannot recall which, and no documentation of this usage has been retained at SGH. The letter from the Cutter representative indicates that it was not Koate HT. I have an incomplete memory of being invited to join an arrangement to supply Alpha Profilate HT managed by Dr Savidge at St Thomas' Hospital, but cannot remember whether I accepted or not. On the principal of sticking with a single US supplier held by Professor Flute, and almost certainly continued by me during my inexperienced initial period as Centre Director, it was likely to have been Factorate HT.

I was responsible for whatever products were purchased by the Centre at this time. Consent to treatment and the risks associated with it were discussed in detail with patients and/or their parents in the light of the ongoing HIV epidemic.

1989-97 As above, plus;

- Octoplas (S/D treated plasma, Octopharma)
- Monoclate P (affinity-purified FVIII, pasteurized), Armour
- Factor 8Y, BPL (FVIII)

- Factor 9A, BPL (FIX)

1997-2008

- Frozen plasma (NBTS)
- Octoplas (S/D treated plasma, Octopharma)
- Haemate P (FVIII/VWF)
- Advate (recombinant FVIII, Baxter)
- Helixate (recombinant FVIII, CSL Behring – manufactured by Bayer)
- Benefix (recombinant FIX, Baxter)
- Novoseven (recombinant FVIIa, NovoNordisk) for inhibitor patients
- FEIBA (plasma-derived aPCC, heat-treated) for inhibitor patients.

I retained primary responsibility for selecting the products used to treat individuals with bleeding disorders until 2000, when the process began to be increasingly tightly monitored by the Pan-Thames Haemophilia Consortium (PTHC). Then, from 2005, the range (and volumes) of individual concentrates from which a Director could choose became limited by the National Contract. Patient choice was also to a degree, limited, although individual preferences were taken into account as far as possible.

13. What was the relationship between the Centre and the pharmaceutical companies manufacturing/supplying blood products? What influence did that relationship have on the decisions and actions referred to above?

The relationship was typical of that between an NHS purchaser of a medicinal product and potential commercial suppliers of that product. Representatives of the pharmaceutical companies frequently sought appointments to discuss their products, and subsequent to an order being placed, kept in contact with the centre to discuss any ongoing issues. In the case of BPL, that relationship also involved the NBTS at first, although later BPL became simply another commercial company. Apart from pricing, purchasing and supply, there was no other influence on the decisions referred to above.

14. The enclosed 31 January and 28 May 1986 letters [BAYP0000008_077 and BAYP0000008_197] record attempts by a representative of Cutter Laboratories to sell you/the Centre Koate HT, a Factor VIII product.

a. Did you/the Centre purchase this or other products from Cutter? If so, were they purchased directly? If not, can you comment on why the letters included prices and the details of possible discounts?

I do not remember either receiving this letter or answering it, or any direct conversations with its sender. I doubt if it was the only such letter from pharmaceutical representatives I received at that time. As far as I can recall the Centre never purchased any products from Bayer (Cutter). The letter presumably contained prices and potential discounts because it was a sales pitch.

b. The 28 May 1986 letter noted that you were happy with the commercial Factor VIII you had been using and with the service you were receiving. Which Factor VIII product did this refer to and which company? What were the arrangements for you/the Centre to purchase it?

I do not recall making this assertion of 'happiness' at all, either verbally or in writing. As far as I can recall, BPL factor 8Y comprised most of the FVIII concentrate in use in the Centre at that time. As explained above, I had inherited Professor Flute's disinclination to switch patients from one therapeutic product to another unless there was a genuinely pressing reason, or the UKHCDO mandated it. Offers from drug representatives were not regarded as a significant reason to do so.

c. The 28 May 1986 letter offered to supply you/the Centre with some Koate HT free of charge. Did you/the Centre use this or other material that had been provided free of charge when treating patients?

As far as I can remember, no.

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

No external organization were involved in these responsibilities until Specialised Commissioning of Haemophilia was introduced in 2000, when purchasing became a jointly agreed procedure with the Pan-Thames Haemophilia Consortium; then, with the onset of the National Tendering process for coagulation factors (2005), both purchasing and selection became matters for the Business Unit of the Department of Health

16. What alternative treatments to factor concentrates were available in the 1970s and 1980s for people with bleeding disorders?

- Frozen Plasma (FFP: NBTS)
- Cryoprecipitate (NBTS)
- DDAVP (Desmopressin; from about 1983): synthetic vasopressin analogue able to increase endogenous VWF/FVIII in VWD and mild Haemophilia A. Not useful in Haemophilia B or severe haemophilia A.
- Tranexamic acid (or the earlier epsilonaminocaproic acid, EACA): topical, oral or parenteral administration: fibrinolytic inhibitor that acts as an adjuvant therapy to enhance action of FVIII / VWF.

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

FFP is a single-donor blood component with the same content of coagulation factors as normal blood. It remains the only therapeutic component with a level of FV, and is therefore needed to treat the rare individuals with severe inherited Factor V Deficiency. Because the FVIII in FFP is not concentrated, trying to administer enough FFP to stop a bleed in Haemophilia A is associated with life-threatening circulatory overload, as experienced in the history of haemophilia.

Cryoprecipitate (cryo) was introduced in the treatment of Haemophilia A in 1964: before its introduction, the median survival of an individual born with severe Haemophilia A was 16 years (Birch, 1963). It required intravenous infusion, usually as an i.v. drip. An effective total dose for a major bleed in an adult could be administered in a volume that rarely exceeded 500ml,

avoiding the danger of circulatory overload. In the UK, an individual dose was made up from frozen cryoprecipitate taken from ten to twenty individual blood donors. This was thawed out in the blood transfusion laboratory and pooled by transfer into a single blood bag for administration. The eventual product was therefore not a single-donor product but from a pool of donors: the sequential treatment, for several days, of a significant haemarthrosis or muscle bleed with cryo could expose the recipient to plasma from a hundred donors or more.

The drawbacks of cryoprecipitate were several: firstly, clumsy or inexperienced technique in thawing and pooling the cryo from multiple frozen bags into a single infusion bag could lose a substantial amount of the FVIII activity, or even risk bacterial contamination, and one was never sure of the FVIII dose infused. Secondly, cryo is full of cellular debris, including red cell membrane fragments sufficient to cause major blood transfusion reactions (so ABO Blood Group matched cryo must be given); and white cell and platelet fragments, as well as plasma proteins, capable of provoking severe febrile (non-haemolytic) transfusion reactions. After cumulative exposures the majority of haemophilia patients would experience these reactions to cryo (I recall the bed frame rattling with the intensity of the rigors that accompanied the infusions). These reactions eventually became unresponsive to routine injections of hydrocortisone and piriton administered in an attempt to forestall them. Some patients found these reactions so unpleasant that they developed phobic behavior, avoiding treatment for even major bleeds early enough for full efficacy.

Finally, because of its physico-chemical nature, UK cryo could not be treated with any of the effective antiviral methods of the time (pasteurization or solvent-detergent), which converted it to an insoluble mass. UK cryo of the time could not be directly compared with US cryo, which was often made from apheresis (single donor) plasma and could be in liquid or even freeze-dried formulations, making it easier to administer. Also, because more US families had domestic freezers, home therapy with cryo was possible in the US.

Desmopressin (DDAVP) can only be used successfully in individuals who synthesize enough FVIII to create a vascular store of the protein. This can be released into the circulation along with its carrier protein von Willebrand Factor (vWF) when the latter is stimulated to do so by the DDAVP, which is also effective in von Willebrand's Disease. In DDAVP responders, levels of circulating factor are achieved that can prevent abnormal bleeding after minor surgery and dentistry: they are rarely sufficient to cover major surgery. In the treatment of spontaneous bleeding, major bleeds are difficult to treat because they need elevated FVIII levels for several days; the effect of DDAVP only lasts for 24 hours and repeating the drug can lead to dangerous haemodilution and hyponatraemia. Useful responses to DDAVP only occur in individuals with baseline levels of >5iu/dL FVIII, i.e. in mild haemophilia A. DDAVP has no effect in Haemophilia B of any severity.

Tranexamic Acid is a useful adjuvant treatment when combined with FVIII or FIX in most circumstances, particularly when bleeding or surgery affects mucous membranes. However, it has extremely limited with no effect when used on its own.

18. **What was the policy and approach at the Centre as regards the use of cryoprecipitate for the treatment of patients with bleeding disorders?**

    a. **Did that policy and approach change over time and if so how?**

    b. **How, if at all, was the policy and approach informed by discussions with external parties?**

When I first arrived as a trainee, a sub-group of adults with severe haemophilia A comprising perhaps five or six individuals (I cannot recall the exact number), were still regularly treated with cryoprecipitate. Among them were the patients I described above who sustained severe febrile reactions despite pre-treatment with hydrocortisone and piriton. They hated the experience, which led to delayed treatment. Because the reasons for keeping them on cryo were due to limited concentrate (and financial) supplies, within a year or two, all had negotiated a change to concentrate. When it came to children with haemophilia, even if Professor Flute had wished to give their treatment in the form of cryo, the parents would not have allowed it; they would have sought care from other London Centres such as St Thomas's.

a. During the period when AIDS in haemophilia first emerged, in the medical literature and in the consciousness of patients and treaters (1982-3), I was engaged on different parts of the South Thames training rotation, away from the Centre for extended periods. At one visit to the Centre, the question of re-instituting cryoprecipitate treatment instead of US concentrate arose. I recall a discussion, possibly in the context of a weekly seminar for trainees, where Dr Richard Lee and I (both at that time Senior Registrars) jointly raised the issue with Professor Flute. I cannot date it with any accuracy, but it was probably in early 1983, possibly while we were attending a revision course in haemostasis prior to taking the MRCPath examination later that year. He dismissed the possibility on two main grounds: firstly, he considered it premature to attribute AIDS to an infectious agent, since similar T-cell abnormalities had been found in transfused individuals with blood diseases other than haemophilia (he referred to a recent publication in which T4/T8 lymphocyte ratios had been shown to be disturbed in multi-transfused patients with the bone marrow disease myelodysplasia), and his view was that it was a general immune response to chronic transfusion *per se*. Secondly, he explained that it was essential in times of uncertainty, particularly for smaller Centres, to stick closely to the current guidance from the UKHCDO, which at that time was not to discontinue US concentrate or revert to cryoprecipitate. He gave additional weight to the UKHCDO being supported by the Haemophilia Society in this opinion.

Even when everything became clear in 1984-5, and Prof Flute had attempted to obtain BPL heat-treated concentrate for all the Centre's patients, I do not recall a significant shift back to cryoprecipitate. Certainly, when I took up the responsibility for Haemophilia care in July 1985, I did not re-institute cryoprecipitate treatment. From then on our concern was centred on securing a supply of heat-treated and/or solvent-detergent treated concentrate, which we did.

b. As explained above, the discussions that informed Centre practice were with the UKHCDO and its officers.

19. What was the policy and approach at the Centre in relation to home treatment? So far as you are aware, when was home treatment introduced? Did the policy and approach change over time and if so how?

The introduction of home therapy at the centre was piecemeal. It necessitated the trained ability to self-inject (or inject a child on the part of a parent) and it could only be accomplished using concentrate. Some individuals were already successfully administering home therapy before 1980: nearly all had taken it up by 1990. We offered it to everyone as soon as safe concentrate became available.

20. What was the policy and approach at the Centre in relation to prophylactic treatment?

Did the policy and approach change over time and if so how?

Prophylactic treatment became the standard of care for severe Haemophilia (without inhibitors) in the UK – certainly in all patients less than 50 years of age, and many in older age groups as soon as the amount of safe concentrate purchased by the NHS became quantitatively sufficient. In general, the introduction of prophylaxis doubled the national requirement for FVIII. The majority of patients and their families who accepted prophylaxis did so by the early 1990's.

21. **What was the policy and approach at the Centre in relation to the use of factor concentrates for children? Did the policy and approach change over time and if so how?**

The discomfort and hospital attendance associated with the administration of cryoprecipitate to children, and its impossibility for home treatment, meant that factor concentrates were the treatment of choice for children as soon as they were produced. The approach of the Centre was to use BPL concentrate as far as possible in children, but unfortunately there was not enough available and often US concentrate was used.

From my involvement as Director in July 1985, all concentrate used in children with haemophilia A was heat-treated: as far as possible BPL 8Y. From 1989, our preference changed to high-purity immune-affinity purified heat-treated concentrate (Monoclate P), amongst other reasons for using it in children were its smaller injection volume, making it easier to administer. From 1997, children were the first cohort of patients at the Centre to transfer to recombinant FVIII and FIX. During the 1990's my paediatric haematology colleague Dr Sarah Ball played a major role in treatment policies in children at the Centre.

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

In general, in the modern era, the treatment needs of individuals defined as having "moderate" haemophilia (1-5iu/dL FVIII or FIX) have not been markedly less than those of severely affected individuals. In the past, fewer were put on prophylactic regimes, but this is no longer the case, since chronic musculoskeletal damage often occurs in moderate haemophilia: at a slower rate than in severe disease, but still capable of causing disabling arthropathy before the age of 40 yrs. . Individuals in the moderate category are heterogenous: having 1% FVIII is very different to having 4.9%. Furthermore, DDAVP will not elevate the FVIII level much above 10iu/dL in moderate haemophilia, inadequate to cover surgery or spontaneous bleeds. We administered factor concentrates to moderate individuals when they needed it. A note of caution here: one of the commonest errors in measuring FVIII during the era of manual assays was to find a trace of FVIII activity in the plasma of individuals who in fact have none (proven by later DNA analysis), then to 'round it up' to 1iu/dL and misclassify them as moderate. The SGH lab prior to 1980 may have sometimes done this. With improved techniques from 1980 onward, correct diagnosis of severe or true moderate haemophilia became the rule.

In mild haemophilia (5-50iu/dL) concentrate was only required for major surgery (where the FVIII or FIX level needed to be sustained at 100iu/dL for several days (e.g. neurosurgery), or trauma (thankfully rare). People with mild haemophilia will by definition be rarely transfused.

23. **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?**

None, to my knowledge. Parvovirus B19 affected some of our haematology patients with red cell transfusion-dependent anaemia, but no documented infections with this agent occurred in

haemophilia patients, despite the fact that heat-treatment is known not to eliminate the virus from concentrate.

Section 3: Knowledge of, and response to, risk

24. When you began work as the Centre, what did you know and understand about the risks of infection associated with blood and/or blood products? What were the sources of your knowledge? How did your knowledge and understanding develop over time?

When I began to attend the Centre as a junior trainee, I understood that blood transfusion could transmit syphilis, Hepatitis B, serum hepatitis, and a variety of tropical diseases; and that blood for transfusion, as a biological fluid, could become contaminated by bacterial growth during storage, which you had to identify by inspecting it for colour change or gas evolution, otherwise the recipient would be likely to suffer a terminal event. Like any British doctor trained during the 1970's, I was well aware of the Hepatitis B outbreak that killed patients, nurses and renal surgeons at the Glasgow Renal Unit, and I knew of the serendipitous discovery of 'Australia Antigen'. So I knew that blood and blood products could be infective, and therefore had to be screened for Syphilis and Hepatitis B. The knowledge came from textbooks, journals and mentors.

My knowledge broadened and became more detailed as I trained in Haematology and Blood Transfusion. In particular, before 1979, I learnt that most, if not all, individuals with severe haemophilia were getting infected with 'serum' hepatitis (at that time in process of being re-named Non A–Non B hepatitis, NANB) during their first few exposures to factor concentrate – mainly, but not exclusively, when it was of US origin.

Up until 1979, these infections were presented by their mentors to trainees as both inevitable and harmless. Most of the infections were asymptomatic – I recall someone (but not who) saying; that the patients didn't develop jaundice and were discovered only by a rise in the hepatocellular transaminase enzymes done routinely as part of liver function tests (LFTs). This led to the phenomenon being dismissed as 'transaminitis', rather than a 'real' hepatitis. In retrospect, this misreading of the infection may have been due to the comparatively dramatic impact of Hepatitis B (with florid outbreaks including clinical staff, acute jaundice, liver necrosis, and deaths, and if not, chronic hepatitis). It was at UKHCDO meetings commencing in 1979 that presentations by Dr Craske, Professor Preston, and Professor Christine Lee, alerted us to the serious nature of this long-term chronic disease.

The shocking penetration of AIDS into the UK haemophilia population, emerging from 1983 onward, the isolation of its viral origin in France and the USA, and the rapid development of serological tests for the (HAV / HTLVIII / HIV) antibody as a marker of infection, constituted a complete revolution in the understanding the impact of transfusion-transmitted infection and the priority given to safety.

It also brought into focus the large-pool plasma produced by commercial fractionation industry in the USA. It seems permissible to make a clear distinction between the pre-AIDS and post-AIDS World. Many aspects of transfusion practice, and medicine in general, were changed profoundly and forever.

25. What advisory and decision-making structures were in place, or were put in place, at the Centre and/or within the area covered by the Centre and/or nationally, to consider and

assess the risks of infection associated with the use of blood and/or blood products?

At St George's during the 1970's and after, the only forum that could be considered to be 'advisory and decision-making' was the Blood Transfusion Committee. This body was surgeon led; its remit was to ensure the prompt and plentiful supply of blood for surgical operations, while limiting the waste of this limited resource. Haematology input to the committee comprised (usually) Dr Parker-Williams from St George's and a representative of the medical team at the NBTS Regional Transfusion Centre at Tooting. To my knowledge, despite being technically part of its remit, the safety of blood was seen as being of secondary importance to the maintenance of supply: by far the most feared situation was running out of blood. The only blood product considered was Frozen Plasma for non-haemophilia patients with surgical bleeding.

After I became consultant in 1985, the minutes of this committee were circulated to me but I do not recall ever sitting on it. I do not recall any reference to transfusion-transmitted infection in them, and no contemporaneous minutes of this committee can be found.

On a South West Thames basis, I think it probable that NBTS Tooting held internal meetings on a regular basis during the 1970's and 1980's to consider transfusion safety, in particular the implementation of donor screening tests. I was never privy to these discussions, nor do I remember receiving any minutes of such discussions.

On a National basis, the advisory structures were to my knowledge and recognition connected to The UKHCDO, in the form of the Hepatitis and AIDS Working Parties, which reported to the Advisory Board. They in turn released advice and guidelines to Haemophilia Centres. Neither my predecessor Professor Flute nor I were members of either the Working Parties or the UKHCDO Advisory Board, since the St George's Centre was not a Reference Centre at that time. We, like most directors of smaller Centres, were not privy to the discussions that informed this advice.

26. **What was your understanding of the relative risks of infection from the use of commercially supplied blood products and the use of NHS blood products?**

    My understanding at the time (1977 – 95) was that the relative risk of infection from the use of US commercial blood products was substantially higher than that from the use of NHS blood products. However, the risk of infection from NHS blood products was not zero.

27. **When you began work at the Centre, what was your knowledge and understanding of the risks of the transmission of hepatitis (including hepatitisB and NANB hepatitis) from blood and blood products? What were thesources of your knowledge? How did that knowledge and understanding develop over time?**

    Please see my answer to question **24** above.

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

    When I took over as director of the Centre in July 1985, it was already routine for all treated patients with haemophilia and related bleeding disorders to have yearly liver function tests as part of their routine reviews, in order to monitor transaminase levels. I cannot recall whether any individuals showed significant changes in these levels. I do not have access to any documentation of the results of these tests.

In 1992, serological tests for the presence of anti-HCV antibodies in patient sera became available, and as far as I can recall they were carried out on-site at the SGH Virology Laboratory. As far as I can recall, these tests revealed that the majority of regularly treated patients at the Centre (about 70%) were carriers of the virus. The dates of acquiring the virus (sero-conversion) were not known because the Centre had no stored sera from patients.

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

    My predecessor had already applied to BPL / NBTS for supplies of heat-treated NHS concentrate to replace non-heat treated product. From July 1985, to the best of my recall and knowledge, no non-heated concentrate from any source was used at the Centre. Unfortunately, no contemporaneous records have been retained by SGH in order to confirm or refute this belief.

    As soon as effective vaccines became available, HBV and HAV vaccination was offered to all patients, whether treated or not, and individual antibody responses measured, with re-vaccination offered to all incomplete responders.

    As soon as recombinant coagulation factors became available, the Centre transited as soon as funding allowed to a recombinant-only treatment policy.

30. **What liver function tests and/or other forms of monitoring were undertaken at the Centre and how did that change over time? What was the purpose of such testing and monitoring?**

    Please see my answer to Question 28 above. The full LFT panel also included conjugated bilirubin and gamma GT levels. The purpose was to monitor patients for signs of hepatocellular inflammation (i.e. acute or chronic hepatitis).

31. **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?**

    Please see my answer to question **24** above.

32. **At the 20-21 November 1979 UKHCDO meeting [HCDO0000015_068], Dr Craske stated that there were two types of NANB hepatitis. What, at the time, did you understand these to be?**

    I was attending the 1979 UKHCDO meeting in a very junior capacity, on behalf of Professor Flute who was unable to attend. I cannot recall this statement, or how I interpreted it at the time. After 40 years, I do recall Dr Craske at the podium, and his talk persuading me that NANB was being taken seriously, but I cannot recall the detail.

33. **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? How did your knowledge and understanding develop over time?**

    Please see my answers to questions **18** and **24** above.

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

    In late 1982, I read the report of AIDS in haemophiliacs in the US CDC Mortality and Morbidity Weekly Reports, published as a supplement to The Journal of the American Medical

Association JAMA which was available at St George's Medical School Library. I knew that people with haemophilia were at risk of blood-borne infection because of their exposure to pooled plasma from many donors, so the association seemed quite likely to me.

35. **What steps did you take in light of that awareness? What steps were taken at the Centre?**

Please see my answer to question **18** above.

36. **What, if any, enquiries and/or investigations were carried out at the Centre in respect of the risks of transmission of HIV or AIDS? What was your involvement? What information was obtained as a result?**

When HTLVIII antibody testing became available at the Middlesex Hospital Laboratory under Professor Richard Tedder, Professor Flute arranged for the Centre's patients to be tested. This was alluded to in his letter to Dr Snape dated 19th February 1985, in which he refers to 'active investigation'. I had no involvement in the testing process. The information that was obtained as a result was that about 70% of our regularly treated patients, including several children, were seropositive for HTLVIII, indicating that they had been infected with the agent via their treatment for Haemophilia.

37. **What, if any, actions were taken at the Centre to reduce the risk to the patients of being infected with HIV?**

Up until mid-1983, as explained above, as far as I know no active measures were taken at the Centre in view of skepticism about the presence of an infectious agent in AIDS, together with the advice from UKHCDO. Continued attempts were made to avoid treating children and only rarely treat adults with US concentrate, and to give them UK concentrate as far as possible, mainly to avoid NANB exposure, but also a protection against any infectious agent present in US concentrate. I was not aware of what, if any, actions were taken at the Centre during 1984 in this regard since I was working mainly as the consultant haematologist at St James's Hospital Balham. I know that in February 1985, Professor Flute took the action of requesting the provision of BPL heat-treated FVIII concentrate from Dr Snape for all the Centre patients, clearly with the intention of protecting them from the AIDS virus. At that time, it seems he may have been unaware of the results of the serological tests in his patients referred to in my answer to question **36** above.

From the start of my tenure as Haemophilia Centre Director in July 1985, all concentrates used at the Centre were heat-treated, whether of UK or US origin. In addition, plasma donations from which concentrates were made underwent more stringent donor selection and screening using the HTLV III antibody test.

From 1989 onward, treatment of adults was, as far as possible, with affinity-purified US (and later UK) plasma-derived concentrates treated with heat, solvent-detergent or both: later, ultrafiltration was added as an additional safety step. Molecular screening for HIV was added to plasma donor selection.

From 1996, Recombinant products theoretically incapable of transmitting human infective agents were introduced as soon as they were available.

As a result of these sequential actions, I am confident that no patient with haemophilia was infected with HIV at St George's during my tenure as Haemophilia Centre Director.

38. Did you and your colleagues at the Centre continue to use factor concentrates to treat patients, after becoming aware of the possible risks of infection of HIV? If so, why?

Please see my answers to questions **18** and **37** above.

39. Did you take steps to ensure that patients were informed and educated about the risks of hepatitis and HIV? If so, what steps?

From 1985 onward, patients and their families were orally informed by myself, my colleague Dr Ball, and our HIV counsellor of these risks in a series of clinic meetings arranged in the Centre and Outpatient Clinics. Contact with The Haemophilia Society was advised, and leaflets from that organization were made available.

40. When did you begin to use heat treated factor products and for which categories of patients? From where did you obtain heat treated products? Did you experience difficulties in obtaining such products?

Please see my answer to question **37** above.

41. In the enclosed 19 February 1985 letter [CBLA0002049], which was copied to you, Professor Flute of St George's wrote to Dr Snape of BPL to request heat treated Factor VIII for a list of patients.

a. The letter described Professor Flute as "Director, Haemophilia Centre 111". Was Professor Flute director of the Centre prior to you? If so, when did you become director?

Yes, as indicated above, Professor Peter Flute was the director of the Haemophilia Centre at St George's until July 1985, when he retired from his roles there to become Postgraduate Regional Dean for the South West Thames Region. The role of Director passed to me at this time, along with consultant responsibility for the majority of all St George's inpatients and outpatients with blood diseases, including haemato-oncology, haemoglobinopathy, and thrombosis/anticoagulation services. The letter of 19 February was copied to me and to Dr Parker-Williams because we were the only two other consultants in the Department at that time. It is important to understand that the term 'Haemophilia Centre Director' had (and has) radically different implications outside the very big Reference (later Comprehensive Care) Centres such as The Royal Free and St Thomas's. Outside big centres it is always a part-time responsibility, although sometimes a dominant one.

b. So far as you can, please explain why Professor Flute's letter divided the patients into two categories. Why did category one include patients who had not received treatment in the past year and where few would do so in the year to come? Why were patients who had received treatment during 1984 in category two? What did the "active investigation "of these patients' HTLV III antibody status involve?

I was not privy to Professor Flute's thinking when he formulated these categories, so I cannot explain his categorization. I certainly did not divide patients up in this way when I took over their treatment.

As stated above the "active investigation" consisted of his sending samples for serological testing to The Middlesex Hospital. I believe that laboratory was deluged with samples at the time, as the only lab in London offering the service to Haemophilia Centres. The tests were therefore in a queue. Accordingly, it is unlikely that Professor Flute was aware of the results

when he wrote this letter. I have always had the impression that the results were one of the first things for me to receive as Director. I was certainly responsible for first giving the patients and their families their results.

42. At the 21 October 1985 UKHCDO meeting [LOTH0000018_008] Dr Craske stated that it "appeared from initial reports that dry-heating was not effective in destroying the hepatitis virus(es)". In response Dr Perry "reminded Dr Craske that there were 3 different types of dry-heating and suggested it was unwise to make generalised statements including all types of heating together."

a. Which hepatitis virus or viruses did you understand Dr Craske to be referring to?

Hepatitis B and NANB. He may also have included Hepatitis A, but I think that is unlikely.

b. What at the time did you understand the three types of dry-heating referred to by Dr Perry to be? So far as you understood, which, if any, of them was effective in destroying the hepatitis virus(es)?

My understanding at the time, as far as I can recall, was that dry-heating entailed heating the lyophilized product in its final vial. I also knew that BPL 8Y, our favoured product, was treated at a higher temperature than those of other manufacturers. I do not recall either Dr Craske's comment or Dr Perry's reply as this was 35 years ago. My priority in 1985 was that the AIDS agent was eliminated from the product. My understanding at the time, as far as I can recall, was that heat-treatment was broadly effective against NANB as well.

c. What, if anything, did you/the Centre do in response to Dr Craske's report at the meeting?

We continued our policy of treating everyone with heat-treated product.

43. At the 9 October 1989 UKHCDO meeting [HCDO0000015_035], Dr Craske reported that "the earlier heat treatment method had not been effective in reducing the incidence of hepatitis but the results so far with 8Y and 9A were encouraging." Which "earlier heat treatment method" did you understand Dr Craske to be referring to? What, if any, steps did you/the Centre take in response to his report?

Due to the passage of time of 30 years, I cannot remember these statements by Dr Craske, or what I understood by them at the time. There would not have been any reason to take 'steps' in late 1989, when the products we were using were BPL 8Y and 9A, supplemented with commercial US concentrate treated with the highly effective antiviral methods in current use by that time.

44. Do you consider that heat treated products should have been made available earlier? If not, why?

Yes, but I am subject to the same hindsight bias as everyone else when considering this question. In addition, during that 'earlier time' during which when heat-treated products 'should have been made available' (presumably the late 1970's and early 1980's) I had limited engagement with haemophilia, as explained above. Insofar as I understand the issues that delayed the introduction of heat-treated product, there were uncertainties about the safety, efficacy and yield of heated product.

Factor VIII activity was understood by haematologists of Professor Flute's generation to be highly labile and heat sensitive: FVIII solutions at ambient room temperature lose activity so

rapidly that bench assays have to include corrections for this loss during the assay itself. So they were very skeptical of deliberately heating it at much higher temperatures.

The concern was that the much higher heat needed to inactivate virus would either destroy FVIII function altogether or reduce the yield of active FVIII from starting plasma so much as to make therapy with concentrate economically unviable. The latter was obviously a major concern to the manufacturers.

In addition, it was feared that heat would alter the configuration of the FVIII molecule in a way that made in more immunogenic and provoke the development of Factor VIII inhibitors, a feared outcome with severe and immediate impacts on survival and quality of life in haemophilia.

Clearly manufacturers had to be as sure as possible that none of these negative outcomes occurred.

I know now that Alpha Therapeutics had produced a functional heat-treated FVIII concentrate (Profilate HT) suitable for clinical use by 1982. I do not know if production was sufficient to re-supply the UK in total. Certainly, I was unaware of this product until I learnt that St Thomas's were using it when I took over the Centre in 1985. At that time, I was not experienced or knowledgeable when it came to the commercial fractionation. It was conceivable that the UK could have had the foresight to switch wholesale to this product in 1982/3, but this would have contradicted the UKHCDO view that major changes in treatment policy due to AIDS would have been 'premature'. It is also probable that doing so would have been too late to prevent most of the HIV and HCV infections in UK haemophiliacs.

45. In the enclosed 31 January and 28 May 1986 letters [BAYP0000008_077 and BAYP0000008_197], the Cutter representative explained how Koate HT was heat treated.

a. The 31 January 1986 letter stated that Koate HT was treated at 60°C for 72 hours. The 28 May 1986 letter stated that it was treated at 68°C for 72 to 77 hours. What did you understand to be the reasons for the difference in temperature and duration?

I have no recall of receiving this letter or considering its content at all. I would not have given letters from the representatives of concentrate manufacturers much attention at the time, considering the massive information overload I was experiencing in all formats from patients, clinical colleagues and the clinical arena, not just in Haemophilia, but across all the major subspecialties I was responsible for in 1986.

b. The 31 January letter referred to inactivation and chimp studies. If you have copies of these studies, please provide them; if not please describe them as best you can. What did you understand the letter to be referring to by "the Hutchison strain of NANB" and "many other viruses known to be difficult to kill "?

Please see my answer to 45(a) above. I have no copies of the 'chimp' (sic) studies.

46. Did you 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?

Please see my answers to questions **17** and **18** above. Reverting to cryoprecipitate as treatment for any patient with Haemophilia A after I took on responsibility as Director in July 1985 would have been illogical, since heat-treated concentrate had then become available. Cryoprecipitate was still in use for some patients with von Willebrand's Disease and

afibrinogenaemia.

47. At the 29 September 1988 UKHCDO meeting [BART0002329], Dr Kernoff reported that Reference Centre Directors felt that heat treated materials were safer than cryoprecipitate in terms of viral transmission. Which heat treated materials did you understand Dr Kernoff to be referring to? Did you agree with the assessment that they were safer than cryoprecipitate? If so, on what basis and when did you conclude that they were safer?

I understood that Dr Kernoff was referring to all the heat-treated FVIII concentrates available from the UK and US at that time. I agreed with this assessment. As noted above, cryoprecipitate is a pooled product: a single adult dose would expose a recipient to plasma donations from 10 to 20 donors, and a course of infusions for a severe bleed could multiply that exposure three or fourfold. The HIV virus was now present in the UK population (and the HCV virus had been for many years). Cryoprecipitate at that time could not be treated with any of the effective anti-virus technologies. It was therefore unacceptable to use it where heat-treated alternatives were available. Such concentrates were also becoming available for individuals with vWD.

48. Do you consider that your decisions and actions, and the steps taken at 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.

I consider my decisions and actions, from the beginning of my responsibilities in July 1985, and the steps taken at the Centre from that point in response to known or suspected risks of infection, were adequate and appropriate. I do not see how they could have been any different given the available resources and knowledge.

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

I was only in a position to make such decisions or actions from July 1985 onward, by which time the use of infected products at the Centre had been effectively brought to an end by the introduction of heat-treated products. I have no evidence of individuals with haemophilia cared for at the Centre becoming infected with the HIV virus after this point in time. The same certainty is not possible in regard to HCV because serological testing for HCV did not become available until 1992, and the Centre had not kept stored sera for retrospective testing. However, I had no positive evidence of additional cases of NANB among Centre patients after this point.

50. 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?

To my current knowledge (from hearsay, largely informed by subsequent written sources such as Starr's revealing, book, 'Blood') during the 1970's and early 1980's plasma fractionation companies in the USA bid for large pools of frozen plasma assembled from up to 40,000 donors, traded on the North American plasma 'spot' market (Toronto, Canada) by 'plasma brokers'. The companies and brokers who participated in this market maintained a state of willful ignorance of the provenance of this plasma, which was widely known to have contained

donations from US prison populations, so-called 'skid row' blood donation facilities buying blood for cash from street people (including substance abusers) and even donations forced from central American villagers at gunpoint by paramilitaries. They performed screening for hepatitis B on the plasma pools but otherwise y fractionated them into Factor VIII concentrate.

I therefore consider *by far* the dominant contribution to the scale of infection of patients with bleeding disorders in the USA and UK to have been made by the commercial fractionators who made and sold infected FVIII concentrate, because they knowingly abandoned any control over the safety of their raw material. Another significant contribution to the scale of infection was made by the acts of plasma market makers and brokers involved in the sale of plasma.

The AIDS epidemic was a turning point that utterly transformed medical practice in ways analogous to the effect of a World War. The decisions and policies of the generation of haematologists that had dominated the UKHCDO and haemophilia treatment in the UK up to this point - pre-AIDS – were conditioned by the long period when haemophilia treatment was of limited availability and effectiveness.

Their attitude and reactions were dominated by determination never to withhold treatment and never to run short – let alone out - of treatment. This unwillingness to countenance the loss of effective treatment was shared by the Haemophilia Society.

The UKHCDO also took a position in many ways typical of British public health governance: Not to risk over-reaction, not to act prematurely, not to alarm the public, "the evidence is not yet conclusive", "we don't yet have proof "- responses still evident during the early phase of the current Covid-19 pandemic.

It is also true that the FVIII companies 'pulled the wool' over the eyes of medical opinion-leaders at the time. Armour, for example, would take visiting UK haemophilia doctors around their plasma-collection facilities where fresh–faced college students underwent plasmapheresis to provide a relatively safe source of product. However, Armour did not reveal to their visitors the massive supplementation by pools bought on the Canadian spot market. The eminent haemophilia doctor Peter Jones published a brave *Mea Culpa* admitting to having been deceived in this way.

However, taking all these things into account, the UKHCDO continued to hold the line, well into 1983, that the evidence of an infectious cause of AIDS was inconclusive, and that action would be premature, long after that position became obviously untenable. However, by then the scale of HIV infection in people with bleeding disorders in the UK was fully established.

In the case of HCV, by comparison with AIDS, there was ample warning. Every haemophilia treater in the US, the UK, and elsewhere knew that their patients were acquiring an infection from FVIII concentrate, and that this infection was marked by a significant rise in liver transaminase enzymes, i.e. it was a hepatitis, likely to be a viral hepatitis.

For circumstantial reasons, including a lack of symptoms during the acute phase, the absence of jaundice and cases of acute liver necrosis, the lack of a known pathogen and a blood test to demonstrate antibodies to it, the disease was widely considered to be non-serious. The progressive development of chronic hepatitis and cirrhosis remained silent because of the historic 'rule' that liver biopsy in haemophilia was hazardous and absolutely contraindicated. In the absence of evidence from liver biopsies, the assumption was made that this viral hepatitis was an inconvenience, but essentially harmless.

Such an assumption is the kind that doctors should not make. The overt, potentially fatal, acute severity of Hepatitis B was regarded as a distinguishing between the two viral illnesses, when attention should have been given to the likelihood that they were similar. I feel guilt on account of accepting this myth of harmlessness when it was first expounded to me, even though I was just a junior trainee with zero clout.

Accordingly, I think that those who formulated the advice promulgated by UKHCDO were late to recognize the reality of transfusion-transmitted HIV infection, and so may have made a minor contribution to the scale of HIV infection in patients with bleeding disorders.

The community of haemophilia specialists made a somewhat larger historical contribution (again much smaller than that of the companies) to the scale of the HCV infection – a much older disorder - by assuming that it was relatively harmless condition for much of the 1970's. However, it should be pointed out that throughout that time there were opponents of this view, and that it was members of the same community (including Dr Craske, Professor Eric Preston, Dr Mike Makris, and Professor Christine Lee) and the same organization (UKHCDO) who thoroughly corrected this assumption during the 1980's.

51. 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?

According to the wording of this question, it was and remains the case that inactivating viruses in whole blood and its primary cellular components (red cells, white cells and platelets) is still not technically possible. Transfusion-transmitted infection is prevented by the intensive screening of blood donors and donations with the most sensitive tests available.

Greater efforts should have been made to inactivate viruses in plasma and the clotting factor concentrates fractionated from it prior to 1980, because the fact that they were transmitting viral hepatitis had been realized from the time of their introduction into clinical medicine in the early 1970s.

Studies by Alter and colleagues in the US had shown the high prevalence of the condition in transfusion recipients by 1974, and he had good evidence from primate studies that the pathogen responsible was a small lipid-enveloped virus by 1979. It is unlikely that US commercial concentrate manufacturers were unaware of these findings, and that methods were available for study that could inactivate the virus by damaging its lipid envelope.

The eventual solution of heat-treatment was hardly innovative, since the effectiveness of pasteurizing complex biological liquids like milk, and even plasma fractions (albumin for infusion) was well known – and known, in the case of albumin, to eliminate post-transfusion hepatitis.

The manufacturers were presumably concerned about the effect of heat treatment on FVIII yield and product economic viability, but they were the only bodies in a position to measure this effect, which turned out to be tolerable.

Section 4: Treatment of patients

Provision of information to patients

52. What information did you provide or cause to be provided (or was, to your knowledge,

provided by others) to patients at the Centre about the risks of infection in consequence of treatment with blood products (in particular, factor concentrates) prior to such treatment commencing? Please detail whether, and if so, how this changed over time.

I have no knowledge of the information provided by my predecessor to patients or their parents / carers before initiating treatment.

During my tenure as Director of the Centre, I personally re-interviewed all treated patients and made sure they had correct information about the risks of infection via concentrates whether or not they had been infected. On the relatively rare occasions of consulting with a new severe patient (or their parents, since most new patients are children) I would explain everything I knew about these risks before initiating treatment. In all cases, valid verbal consent was obtained before starting. From 1985 onward an increasing number of well-produced and comprehensive information sheets and booklets became available from the Haemophilia Society, The US National Federation of Hemophilia, The World Federation of Haemophilia etc. The Centre obtained copies and patients were given these as follow-up sources to aid retention and as a basis for further discussions. From 1989 explanations given to parents of newly diagnosed children was taken on by my paediatric colleague Dr Sarah Ball. From 2000 onward the information resources became a library under the supervision of the haemophilia nursing team, and included a website and a guide to electronic sources. The exchange of information with people with haemophilia and their families has never stopped.

53. **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.**

Information about alternatives to treatment with factor concentrates was given at the same interviews. Clearly, this depended on whether such alternatives were a genuine treatment option. It would have been pointless explaining DDAVP or cryoprecipitate to someone with FIX deficiency (Haemophilia B), or DDAVP to a severe Haemophilia A patient or their family. I did explain the potential availability of cryoprecipitate to individuals with Haemophilia A, but no individual or their parent was ever interested in it after heat-treated concentrate became available.

54. **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?**

A patient, or the parent of a child, commencing home therapy needs to be physically taught how to safely store and make up the product (to dissolve the lyophilized factor in sterile water, and mix it properly), how to set up a sterile injection field and how to confidently insert a Butterfly needle into a peripheral vein. This is a sometimes fraught and always challenging one-on-one process and is one of the reasons that a haemophilia nurse is such a vital member of the haemophilia team. Before we were funded for such a nurse this was done with helpful haematology ward or paediatric ward nurses; sometimes the concentrate manufacturers would employ peripatetic qualified nurses who would visit to do the training, which was uniformly excellent. Written information was also provided, but home treatment was only possible with concentrate.

From the mid-1990s, home treatment in children became increasingly delivered with the help of Portacath devices. This was managed by paediatric colleagues and required further detailed management training for parents given by specialised nurses.

55. When did you first discuss AIDS or HIV (HTLV-III) with any of your patients? What did you tell them?

The first discussions I had with patients about AIDs were in the context of telling them about their HTLVIII antibody results in late summer and early autumn of 1985. I told adult patients whether the test was positive or negative. If it was positive, I communicated what I knew about the significance of that finding insofar as I understood it. None of my patients had at that time suffered any AIDS-defining illnesses, so I told them that having a positive test did not mean they would necessarily progress to symptomatic AIDS.

There were some HTLV-positive children. I initially told the parents (often in haemophilia at that time, the mother was the sole care-giver), and then discussed with them what the child should know. In general older children considered "Gillick-competent" were told, children less than ten years old, not.

56. Please describe how and when you learned that patients under your care/the care of the Centre had been infected with HIV. What tests were undertaken, where and over what period of time?

As explained above, the majority of these findings were the results of tests on blood samples taken by my predecessor in early 1985 and sent for analysis to Professor Richard Tedder's laboratory at the Middlesex Hospital. There was a wait before the results arrived, and to the best of my recall they arrived for my attention shortly after I took over as Director. They may have arrived on my desk in July.

Very soon, our own virology labs acquired the test, so any patient missed in the initial cohort was tested locally.

57. What if any arrangements were made for pre-test counselling?

For the initial batch of tests commissioned by Prof Flute, I don't know. It must be understood that the importance and essential nature of valid pre-test counselling became clear and accepted **due** to the AIDS epidemic. The concept, and the concerns it addressed, did not really exist in UK practice until then.

I am glad to say that things changed rapidly due to our appointment of a specialist counsellor for affected individuals with haemophilia, who rapidly brought our practice into line; and increasingly into contact, during shared care of our patients, with the Infectious Disease Medical and Nursing Teams based on McEntee Ward, St George's Hospital. Accordingly, all patients henceforth tested for HIV at the Centre had expert pre-test counseling.

58. 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?

To the best of my memory, I told affected adult individuals in person, in a confidential setting, usually an outpatient consultation room, sometimes with a supporter present at their request. Subsequent meetings, at which clarifications were made and questions answered as far as possible, included our Haemophilia HIV counselor with the patient's permission.

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

A positive HTLVIII / HIV antibody test is not a diagnosis. None of the antibody-positive patients

had had any AIDS-defining illness at this point: a minority have never developed any, so (with antiretroviral therapy) have never undergone transition to clinical AIDS despite the passage of nearly 40 years since their infection with the virus. One individual has never even developed a fall or imbalance in T lymphocyte numbers: it is presumed that he has some kind of genetically determined resistance to the virus.

In retrospect, it was therefore correct to explain that the significance to each individual was at that time uncertain. I explained that they had been put at risk of developing AIDS by acquiring the virus from the blood product they had been given as treatment, and that the disease at that time could lead to severe illness and death. I told them that they would be followed up closely and that I would refer them to the rapidly developing multidisciplinary team of AIDS clinicians in St George's Infectious Disease Unit - under Professor George Griffin - for shared monitoring.

I did not, as far as I can recall, advise (never 'told') affected individuals to keep their infection a secret. I probably did advise them to think carefully about whom they did tell outside their immediate family.

60. Were you aware of any discussions among clinicians about whether they should or should not tell their patients of their HIV status? If you were aware of such discussions, when and where did they happen, and what reasons were considered and discussed for informing or not informing people that they had HIV?

Nobody attempted to discuss the idea of not telling affected individuals the result of their HTLVIII antibody tests with me. It would have been in direct contradiction to my training at the Royal Marsden Hospital (RMH) (see above) and my concurrent 1985 haemato-oncology practice at SGH. The RMH ethos is to be utterly honest with patients with bad news, including the worst news. Only complete honesty can be the basis for valid patient consent to treatment (including palliative treatment). In addition to imbuing trainees with this principle, the RMH also gave us invaluable training in giving bad news. Part of that training was that bad news had to be given verbally, in person, in confidence, by the responsible consultant. So I am confident in retrospect that I gave our patients and their families this particular bad news in a way that was as non-traumatic as possible.

61. The minutes of the 21 October 1985 UKHCDO meeting [LOTH0000018_008] record that there was no agreed policy as to whom directors should disclose HTLVIII antibody results and that there was particular concern regarding children. What was your/the Centre's policy and practice on this issue? Did it change over time? If so, how and when?

These minutes are rather inexplicit; it may have mainly concerned communication with those other than the patient's family, for example the patients' General Practitioners. The concern about children would also have related to the complicated issue of informing their school.

There is no doubt that the communication of the HTLV results to the parents of affected children, and the question of what and how to tell the child, was a complex individual matter. Our practice was to defer telling senior school staff, including school nurses, until our counsellor was able to visit the school in question to carefully prepare the ground and arrange follow-up visits. As far as I can remember, and to the best of our knowledge at the time, school concerns and victimisation were avoided by these measures.

In terms of practice at the Centre, as far as I can recall, I informed the parents first, with the

child not present; the issue of what to tell the child was discussed with the parent(s) with a preference for giving a basic explanation to those children that in current terms would be considered 'Gillick competent'. As far as I can remember, the youngest child that I gave a simple account to, in the presence of his mother, was about nine years old (and to my knowledge is currently well on antiviral therapy).

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

Our policy was to test partners with their valid consent. Individual patients were advised to inform their partners of their HTLVIII seropositivity and to ask them to attend a joint consultation with the Centre team. We also offered individual consultations if the partner wished to be told individually. We did not contact partners without the patient's consent. At that consultation the partner was offered a blood test after pre-test counseling. If the partner agreed, blood was drawn for testing. As far as I recall, only one partner was found to be HIV positive during this process, and the couple shared other high-risk behavior.

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

I, with my counsellor colleague, gave detailed advice about safe sex practice, and she arranged the issue of condoms to affected individuals. Family members were seen if the patient requested it: we advised against testing, apart from the situation in home treatment where the parent was responsible for injecting the patient and dealing with sharps. No family members were discovered to be seropositive as far as I can recall. The information given to family members mainly emphasized the low risk of nearly all forms of non-sexual contact, sharing cutlery etc. We advised against sharing toothbrushes, although I know of no recorded case of this implement actually transmitting the virus.

64. What if any arrangements were made for post-test counselling?

All patients were enrolled in ongoing counselling, with the haemophilia counsellor, and for patients who developed AIDS-related illnesses, with the infectious disease unit nurse-counselors.

65. The minutes of the 21 October 1985 UKHCDO meeting [LOTH0000018_008] record differences of view as to the appropriateness and validity of a proposed survey of HTLVIII antibody prevalence in household/sexual contacts. What was your view on this issue? Did you/the Centre participate in the survey?

I have no recollection of this. My view was that it would have been a logical thing to do such a survey, given valid consent from all concerned. I can't remember us contributing to this survey.

66. How many patients at the Centre were infected with HIV? 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?

f. How many were children?

I am not able to give precise figures after such a long time and am unable to access any data collected at the time. To the best of my recollection, 15 -18 patients were found to be infected with HTLVIII.

a. 13-16 had severe haemophilia A;

b. One had moderate haemophilia A;

c. None had mild haemophilia A or B;

d. One had severe haemophilia B;

e. None had von Willebrand's Disease;

f. 3-4 were children

67. 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.

To the best of my recall, no such work was done at the Centre, which did not hold any historical serum samples from patients.

68. To the best of your knowledge, did any of the partners or other family members of patients of the Centre become infected with HIV, and if so how many?

Please see my answers to questions 63 and 64 above.

69. Enclosed are documents relating to a July 1989 application for a Medical Research Council grant for the continuation of a project entitled "Sequence variation in defined regions of the envelope gene of human immunodeficiency virus" [MRCO0000427_041 and MRCO0000427_042]. P.5 of the appendix records that "the haemophilia clinic at St George's sees more than 14 HIV-seropositive patients among whom are some with documented exposure to the same batch of infected factor viii concentrate (Dr David Bevan, Department of Haematology)". Please describe the work undertaken to establish which batches of infected Factor VIII the Centre's patients had been exposed to, including the reason(s) it was undertaken and the conclusions reached.

I had no input into this proposal for a study, or the grant application relating to it, whatsoever: otherwise, my name would have been on the grant application as a co-applicant and I would have been jointly accountable for its content. I would also have had sight of this grant application before now, which I do not recall having.

Despite searching my memory, I have no recall of any aspect of this proposed study. Nor do I recall at any time believing that HIV infections in my patients originated in, or could be traced to, a single batch of product. It is indeed likely that several patients would have been exposed to the same batches of infected product; but all of them would have been exposed to other such batches at other times.

At the time, the Centre had full documentation of all batches that individual patients had been exposed to, but this has all been lost, as far as I can determine, except possibly in the form of written entries in individual patient notes, which I do not have access to. I do not recall being

privy to any information about differing infectivity traced to different batches by the manufacturer or any other agency. Certainly, we did not attempt to discover this in-house

70. Were patients infected with HBV informed of their infection and if so, how? What information was provided to patients infected with HBV about the infection, its significance, prognosis, treatment options and management? What involvement did you have in this process?

No new infections with Hepatitis B were seen after my starting as Centre Director in July 1985. Concentrates and plasma donors that contributed to them had been effectively screened for this infection since the 1970's. I cannot recall a single haemophilia patient with chronic active hepatitis due to HBV.

We commenced routine Hepatitis B immunization as soon as the vaccines became available, as well as Hepatitis A immunization.

71. How many patients at the Centre were infected with HBV?

Some older patients may have been infected in the past and had thereby acquired immunity to the virus and recovered. I cannot recall how many.

72. Were patients infected with NANB hepatitis informed of their infection and if so, how and by whom? What information was provided to patients infected with NANB hepatitis about the infection, its significance, prognosis, treatment options and management? What involvement did you have in this process?

I have no knowledge of what, or whether, information was given to patients who had developed transaminase rises after exposure to concentrates prior to my taking up the Centre Director role in July 1985. Nor was I in a position to undertake retrospective investigation of Centre history in this respect.

As far as I can recall, no Centre patients developed symptomatic liver disease due to NANB during the period 1985-92, so engagement with NANB did not really occur until the Hepatitis C virus was discovered to be its cause in 1989, and HCV antibody testing became possible in the UK in 1992.

The rest of this question is anachronistic, since during the period when the hepatitis was known as NANB, there was little valid information one could give about 'its significance or prognosis', and none whatsoever on 'treatment options and management'.

73. When did you begin testing patients for HCV? How, when and by whom were patients informed of their diagnosis of HCV? Were they told in person, by letter or by phone? What involvement did you have in this process?

We began testing in 1992. I informed most of the patients of the results of these tests in individual consultations. I cannot remember the exact duration of the period, but most tested individuals had been given their results by the beginning of 1993.

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

All patients who had received blood products at the Centre were already registered at the Centre, and part of their Centre record was a log of all the blood products they had received. Therefore, it was a relatively simple to ensure that all who gave consent to such testing were

tested.

75. At the 18 September 1992 UKHCDO meeting [HCDO0000248_013], Professor Preston reported that, of the 100 Haemophilia Centres that had responded to a questionnaire, 77 carried out HCV testing, " 46% indicated that they discussed the results with their patients but 8% said the results were not discussed ".

a. Did you/the Centre carry out HCV testing at this time? If so, did you discuss the results with your patients? If the answer is no to either question, why not? So far as you are aware, why did a significant number of Haemophilia Centres either not carry out HCV testing or not discuss the results with their patients?

The answer to both these questions is yes (see my answer to question **73**).

b. It was also agreed at the meeting that patients should be tested annually for HCV. Did you/the Centre implement this measure and what was its purpose?

As far as I remember, we did introduce yearly HCV testing. The purpose was to know if any patient hitherto negative for HCV had seroconverted.

76. What information was provided to patients infected with HCV about their infection, its significance, prognosis, treatment options and management?

At the Centre, we explained their positive HCV antibody test, but that it did not usually signify immunity but ongoing infection. We explained that, on the basis of studies done in haemophilia patients in the UK, they were at risk of progression to chronic hepatitis and hepatic cirrhosis, but that it was not yet clear how many people this would happen to, or how long it would take in individual patients. We explained that the only way to recognize the development of cirrhosis was by liver biopsy*.

Initially, there were no treatment options to discuss, but a little later the option of Interferon treatment arose.

We advised patients to avoid alcohol, or at least to reduce their consumption.

*At St George's during this time, one of our colleagues was a Consultant Radiologist (Dr Anton Joseph) specialising in diagnostic ultrasound. He was an innovative and well-regarded expert who worked closely with SGH gastroenterologists and was certain that he could identify hepatic cirrhosis with conventional abdominal ultrasound (US). We referred our HCV-positive patients for ultrasound examinations by this clinician until, after a year or so, it became clear that there was a firm worldwide consensus that ultrasound could not detect cirrhosis.

77. How many patients at the Centre were infected with HCV?

I cannot recall the exact number and have no access to any numerical records from the time in question. My estimate is that about 15 individuals were HCV positive in 1992.

78. 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.

Patients were notified of their test results promptly.

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

By 'public health implications', I take this to mean the possibility of infecting others. Initially, we extended the safe sex guidance given to HIV positive individuals to those who were HCV positive, and this continued to be given despite the growing evidence that sexual transmission of HCV was rare. If we had had any current patients who were chronic HBV carriers, we would have counselled them in safe sex. We asked our patients to inform any dental or general surgeons they consulted of their risk status.

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

Patients with HIV who had developed severe T-lymphocyte deficiency or clinical AIDS were warned that they were at risk of opportunistic infections, and to contact the Infectious Disease (ID) team as soon as possible if they developed any new symptom. This information was given to them by members of the ID team.

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

Please see my answers to questions **63** and **79** above.

82. 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?

Blood samples were taken frequently from patients attending the centre. Purposes included performing clotting factor assays to determine factor levels at diagnosis, in response to being treated, or during surgical episodes; for infrequent pharmacokinetic studies; screening for coagulation factor inhibitors; monitoring haemoglobin levels to determine the severity of blood loss during haemorrhagic episodes; general health screening for diabetes, renal function, bone and endocrine function, and liver function. Samples were also taken, less frequently, to determine HIV, HCV and HBV infection status and HBV and HAV antibody levels after immunization. We always explained the purpose of the test. We did not ask consent to the storage and 'use' of the samples since the Centre did not store or use the samples for anything other than the immediate analytic process itself. Consent was recorded in the patient notes in the case of viral testing.

83. Were patients under your care 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?

While under my care, from July 1985, to the best of my recollection, no patient was treated with factor concentrates or other blood products without their expressed and valid consent.

In general, this consent was obtained in a categorical sense, that is, to a period of ongoing treatment with a single product. Consent was not renewed for every subsequent infusion of the approved product, or issue of the product for home treatment, unless the patient asked for a review.

This consent was obtained anew, in the context of patient choice, if a patient was offered a change in treatment because of technical advances in theoretical safety, such as changing from intermediate purity to high-purity factor concentrate in the early 1990's, or from plasma-derived to recombinant product in the late 1990's).

Consent was also re-obtained in the context of patient choice if a product change was entailed by the National Contract.

Renewed consent in the context of patient choice was also obtained in the light of emergent safety issues like vCJD.

In all these cases, the eventual choice of product and the patient's consent was recorded in the patient's clinical notes.

84. Were patients under your care 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?

No patients under my care were tested for HIV or hepatitis without their express and informed consent, to the best of my knowledge. I do not understand the addition 'for any other purpose'.

Tests for HIV or Hepatitis were regarded as consented to only if the patient had received full pre-test counseling from a member of the Centre team.

Consent was recorded in the patient's clinical notes.

As indicated above, many patients under my care had been tested for HIV prior to my taking over as Director of the Centre, and I cannot vouch for the consent they may have given at that time.

85. Please detail all decisions and actions taken by you or with your involvement with regard to a category of people referred to as 'previously untreated patients' (PUPS).

All Haemophilia Centres will encounter PUPs from time to time in the form of infants with newly diagnosed severe haemophilia A or B. This will be a rare event outside big reference centres (later Comprehensive Care Centres, CCC). To the best of my recollection the Centre only encountered two or three PUPs of this kind during my tenure.

Decisions about their care were taken in concert with my paediatric haematology colleague Dr Sarah Ball, with advice from the Great Ormond Street CCC, particularly concerning the first doses of therapy and the initiation of prophylaxis after placement of an indwelling device such as a PortaCath. I cannot recall the detail of these complex and highly individual decisions in these rare cases so long ago. I do recall that the outcomes were good, however, due to the care and skill of paediatric colleagues.

The other type of 'PUP' seen at the Centre were patients of any age with moderate or mild haemophilia, who had never needed treatment with factor concentrates. My decisions in this category of patient was to avoid exposing them to concentrate, using DDAVP and tranexamic acid whenever feasible to treat mucosal bleeding or cover dental surgery. Treatment with concentrate was reserved for situations such as major surgery. In that case, the product used was the safest available at the time. During 1985 – 1989 this would have been considered to be BPL 8Y or 9A, while from 1990, my preference was affinity-purified FVIII, and later rFVIII.

86. The minutes of the 29 September 1988 UKHCDO meeting [BART0002329] record that directors were encouraged to enter PUPS into a study of 8Y/9A, and that Dr Hill thought that parents should be encouraged to enter their children. Were any of your/the Centre's patients involved in this study, either before or after the meeting? If so, were any of them PUPS and/or children?

As far as I can recall, we did not enter any patients into this study.

87. How was the care and treatment of patients with HIV/AIDS managed at the Centre? In particular:

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

We developed very close links with the St George's Infectious Disease (ID) service, which was in the process of becoming one of the major AIDS treatment centres in London. Therefore, there was no need for haematologists at the Centre to become *ad hoc* HIV specialists. We referred all our seropositive patients to clinicians of the ID team (particularly to Dr Mark Wansborough-Jones) from the outset. They took over all AIDS-related aspects of the patient's treatment and monitoring.

b. What treatment options were offered over the years to those infected with HIV?

Initially, patients were offered prophylaxis against AIDS-related opportunistic infections (Co-trimoxazole, pentamidine inhalations, topical and oral antifungal agents). If they developed overt clinical disease to opportunistic agents, they were admitted to the ID ward for high-dose treatment with these and other antimicrobials for pneumocystis carinii pneumonitis, toxoplasma encephalitis, or invasive fungal disease.

In the pre-AZT era this care became a desperate holding operation as patients progressively succumbed to the onslaught of multiple opportunistic infections. We lost four patients quite quickly, including one who was 13 years old. I had seen similar organisms cause disease in immunosuppressed leukaemia patients, but never in concert like this, rapidly invading multiple organs despite high-dose antimicrobial therapy. The sense of helplessness in the face of a new disease that was outpacing the chasing clinicians was terrifying.

In 1987, AZT was the first therapeutic agent to salvage some patients and give breathing space: it was offered to patients as soon as it was available. But as soon as the initial storm seemed over, patients began to succumb to another wave of diseases. Aggressive Hodgkins Disease, Burkitt Lymphoma, and rapidly progressive brain tumours caused death in patients, despite care and treatment by St. George's oncologists.

Real progress in treating AIDS really began with the introduction of Ritonavir and other protease inhibitors in 1995, together with AZT and other agents in the combinations termed Highly Active Anti Retroviral Therapy (HAART). I remember a patient seemingly faced by certain death with severe bone marrow failure due to invasion with atypical TB. After starting ritonavir he walked out of ITU within a fortnight.

Our ID colleagues were early and expert users of HAART and our patients got the benefit of these advances as early as possible. The expert use of active agents of several classes, and their flexible and individualized use in suitable patients enabled by accurate laboratory measurement of CD4 counts and HIV viral load, were offered and managed in our patients by leading HIV clinicians (Dr Wansborough-Jones and Dr Derek Macallan, and the ID specialist nursing team). By then the number of available agents, the complexity of drug maintenance regimes, including drug holidays, sidestepping drug resistance, and the use of combined formulations to simplify therapy, had left me far behind.

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

Full and complete information, in all its evolving aspects, was provided to patients by the expert ID

team. The Centre took responsibility for counselling and monitoring patients in respect of the subtle increase in bleeding episodes that followed the institution of Ritonavir in some patients; this usually responded to a modest increase in either the dose or frequency of FVIII prophylaxis.

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

Close follow-up and detailed monitoring (of symptoms, side effects, new events, CD4 counts, HIV viral load measurements) was carried out by ID specialists at HIV clinics, where all HIV medication was prescribed. The Centre continued to see these patients for regular Haemophilia review.

88. How was the care and treatment of patients with HBV managed? In particular:

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

b. What treatment options were offered over the years?

c. What information was provided to patients about the risks and benefits

of specific treatments and about side effects?

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

As explained above, to the best of my recollection there were no patients with active HBV cared for at the Centre during my tenure there, so I cannot answer these questions.

89. How was the care and treatment of patients with NANB hepatitis managed at the Centre? In particular:

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

We now know that nearly all cases of NANBH were due to HCV. During the period that this hepatitis was known as NANBH (approximately during the years 1974 – 1989) the clinical response in UK haemophilia centres – including the St George's Centre - tended to be one of passive acceptance, compared to the increasing awareness that followed the discovery of the HCV virus in 1989, and a test for the presence of anti-HCV becoming widely available (1992). This was compounded by the massive impact of the HIV epidemic in haemophilia – leaving a reduced level of attention for what was a largely subclinical condition.

During the NANBH period, most if not all individuals who had sustained transaminase rises (hepatitis) after early exposure to commercial concentrate had no clinical symptoms of liver disease. This was true of the SGH patients. Accordingly, no need was perceived for specialist referral to liver specialists (who at that time at SGH would have been gastroenterologists). This inaction was also conditioned by the assumption that liver biopsy was simply not an option in severe haemophilia because of its danger and cost.

Accordingly, to the best of my memory, I cannot recall any referrals to specialist care during the time of NANBH.

b. What treatment options were offered over the years?

No treatment options were offered for asymptomatic NANBH during these years. There were no treatment options for NANBH at this time.

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

As above (b), none.

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

As above (b), none.

90. How was the care and treatment of patients with HCV managed at the Centre? In particular:

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

As far as I can remember, specialist hepatology at St George's in the early 1990's was provided by gastroenterologists. They saw little value in adding asymptomatic HCV seropositive individuals to their busy clinics, particularly when transaminase increases were modest and liver ultrasound normal in most patients (see my answer to **q76** above). Their position was that they be contacted if a patient developed liver problems. That approach was understandable given that no effective treatment was available for HCV until 1994 at least.

Patients with HIV / HCV co-infection were monitored for both diseases by the ID team.

b. What treatment options were offered over the years? When did you begin to treat patients with interferon?

Interferon alpha of lymphoblastoid or recombinant origin, given subcutaneously as monotherapy over 3-6 months was shown to cause sustained virological responses in about 38% of treated individuals, in major trials published in 1996 or after. Slightly better results were obtained with pegylated recombinant IFN in studies published after 2000. The low rates of response were due to high numbers of individuals dropping out of the trials because of intolerable side-effects.

ID physicians or gastroenterologists seeing centre patients offered them therapy with these interferons. Take up by patients was extremely limited (see **90c** below); as far as I remember, the few who did start therapy were unable to complete the course because of severe fatigue and increasing depression. The addition of ribavirin to IFN later did not make much difference to this state of affairs.

I personally did not prescribe interferon or interferon/ribavirin.

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

A full account of the general malaise and potentially severe psychological distress that could complicate treatment was given to all patients, along with a HCV response rate below 50%. Unsurprisingly, hardly any patients agreed to IFN therapy as a result.

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

Centre patients continued under follow-up and monitoring at these clinics: eventually, a combination of gradually progressive liver compromise, reliable non-invasive detection of hepatic cirrhosis, the entry of a new generation of hepatologists working with new national guidelines, and of highly active new drugs - eventually leading to effective non-interferon regimes - persuaded most HCV patients to undergo effective antiviral therapy. I had left by this stage, but some St George's patients came to take up this later model of HCV care at St Thomas's.

91. At the 18 September 1992 UKHCDO meeting [HCDO0000248_013], after Dr Savidge and

Professor Bloom had said they would use interferon for patients with significant hepatitis, the consensus of opinion " seemed to be that the use of an unlicensed product was not justified". What was your/the Centre's policy and practice on using interferon at this time?

I find these statements surprising, since in 1992 interferon was yet to be tested in HCV in any major prospective trial; so it was unproven as well as unlicensed. Our policy and practice is described in my answer to **90b** above.

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

Children affected by HIV were managed jointly by my paediatric colleague Dr Sarah Ball and Dr Graham Davies, consultant paediatrician specializing in immunodeficiency. To the best of my memory, I do not recall any children at that time with HCV attending the centre.

93. **What if any involvement did you and/or colleagues at the Centre have with any clinical trials in relation to treatments for HIV and HCV?**

We had no direct involvement in any such trials.

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

Please see my answers to **q63** and **q64** above

95. **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?**

As far as I recall our counsellor was funded by Wandsworth District Health Authority.

96. **What if any difficulties did you encounter in obtaining sufficient funding for the treatment of people who had been infected with HIV and/or HCV?**

Funding for the treatment of people with HIV was channeled through the ID unit. They may have had difficulties, but I was not aware of any.

97. **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.**

See q93.

98. **Please list all research studies that you were involved with during your time at the Centre. In relation to those research studies that could be relevant to the Inquiry's Terms of Reference, please:**

I was at the Centre from 1985 - 2008. Here is the requested list of all the research studies I was involved in during that time. As can be seen, only a single project (5) out of the 57 listed involved patients of the Centre in any way. The list reflects the scope of my multi-subspeciality practice during those years. In order to save space, I have left out the names of all the co-authors (often the most important authors) of the studies. The relevant journal references are given so that they can be consulted if this information is required.

- Malignant histiocytosis of the intestine: a T-cell lymphoma. Lancet. 1985 Sep 28;2(8457):688-

91.

- Monosomy 7 and multipotential stem cell transformation. Br J Haematol. 1985 Nov;61(3):531-9
- Effects of arginine vasopressin (AVP) infusions on circulating concentrations of platelet AVP, factor VIII: C and von Willebrand factor. Thromb Haemost. 1986 Feb 28;55(1):34-6.
- Human platelet arginine vasopressin. Clin Endocrinol (Oxf). 1986 Apr;24(4):427-33.
- Serial studies of T-lymphocyte subpopulations in HIV seropositive haemophiliacs. Clin Lab Haematol. 1987;9(2):109-14.
- Direct effect of interleukin 2 on chronic lymphocytic leukaemia B cell functions and morphology. Clin Exp Immunol.1987 Jun;68(3):677-84.
- The correlation of breakpoint cluster region rearrangement and p210 phl/abl expression with morphological analysis of Ph-negative chronic myeloid leukemia and other myeloproliferative diseases. Blood. 1988 Feb;71(2):349-55.
- Desmopressin therapy in patients with acquired factor VIII inhibitors. Lancet. 1988 Feb 13;1(8581):366.
- Alteration of the mechanical properties of sickle cells by repetitive deoxygenation: role of calcium and the effects of calcium blockers. Br J Haematol. 1989 Jun;72(2):260-4.
- Hemodynamic changes during sickle cell crisis. Am J Cardiol. 1989 Nov 15;64(18):1211-3.
- Protein C London 1: recurrent mutation at Arg 169 (CGG----TGG) in the protein C gene causing thrombosis. Nucleic Acids Res. 1989 Dec 25;17(24):10513.
- The Kasabach-Merritt syndrome: treatment with intermittent pneumatic compression. Arch Dis Child. 1990 Jul;65(7):790-1.
- The clinical effects of prolonged treatment of patients with advanced cancer with low-dose subcutaneous interleukin-2 Br J Cancer. 1991 Feb;63(2):275-8.
- Decreased expression of complement receptor type 2 (CR2) on neoplastic B cells of chronic lymphocytic leukaemia. Clin Exp Immunol. 1991 Mar;83(3):423-9.
- Use of immunoglobulin gene rearrangements to show clonal lymphoproliferation in hyper-reactive malarial splenomegaly. Lancet. 1991 Mar 2;337(8740):505-7.
- Abnormal neutrophil adhesion in sickle cell anaemia and crisis: relationship to blood rheology. Br J Haematol. 1991 Jul;78(3):437-41.
- Coagulation-factor deficiencies and abnormal bleeding in Noonan's syndrome. Lancet. 1992 Jan 4;339(8784):19-21.
- Surface and molecular expression of complement-receptor type 2 of neoplastic CD5+ B cells in chronic lymphocytic leukemia. Ann N Y Acad Sci. 1992 May 4;651:494-7.
- Unique expression of von Willebrand factor by type IIA von Willebrand's disease endothelial cells. Br J Haematol. 1992 Jul;81(3):401-6.
- Splenic lymphoma with villous lymphocytes in tropical West Africa. Lancet. 1992 Sep 5;340(8819):575-7.
- Secondary leukaemia after MMM combined modality therapy for breast carcinoma. Lancet. 1993 May 15;341(8855):1289.

- Splenic sepsis in sickle cell disease. Br J Haematol. 1994 Jan;86(1):187-9.
- The radiological features of adult T-cell leukaemia/lymphoma. Clin Radiol. 1994 Feb;49(2):83-8.
- Aprotinin inhibits fibrinolysis, improves platelet adhesion and reduces blood loss. Results of a double-blind randomized clinical trial. Eur J Cardiothorac Surg. 1994;8(6):315-22;
- Pre-operative aspirin decreases platelet aggregation and increases post-operative blood loss--a prospective, randomised, placebo controlled, double-blind clinical trial in 100 patients with chronic stable angina. Eur J Cardiothorac Surg. 1994;8(8):404-9.
- Three novel mutations in the protein C (PROC) gene causing venous thrombosis.Blood Coagul Fibrinolysis. 1995 Apr;6(2):138-
- Detection and characterization of seven novel protein S (PROS) gene lesions: evaluation of reverse transcript-polymerase chain reaction as a mutation screening strategy. Blood. 1995 Oct 1;86(7):2632-41.
- Erythrocyte aplasia and systemic lupus erythematosus. Lupus. 1995 Oct;4(5):407-11.
- Immunoglobulin gene polymerase chain reaction to distinguish hyperreactive malarial splenomegaly from 'African' chronic lymphocytic leukaemia and splenic lymphoma. Trans R Soc Trop Med Hyg. 1996 Jan-Feb;90(1):37-9.
- Trousseau's syndrome in association with ovarian carcinoma. Cancer. 1996 Jun 15;77(12):2544-9.
- A prospective randomised controlled trial of postoperative autotransfusion with and without a heparin-bonded circuit. Eur J Cardiothorac Surg. 1996;10(1):38-47.
- Comparison of immunofiltration assay of plasma D-dimer with diagnostic imaging in deep vein thrombosis. Br J Haematol. 1997 Mar;96(4):846-9.
- Circulating villous lymphocytes--a link between hyperreactive malarial splenomegaly and splenic lymphoma. Trans R Soc Trop Med Hyg. 1997 Mar-Apr;91(2):171-4.
- Hypercoagulable abnormalities and postoperative failure of arterial reconstruction. Eur J Vasc Endovasc Surg. 1997 Apr;13(4):363-70.
- Automated red cell exchange in sickle cell disease. Br J Haematol. 1997 May;97(2):256-8.
- Hypercoagulable states in patients with leg ischaemia. Br J Surg. 1998 Jun;81(6):811-4.
- Cardiopulmonary bypass with danaparoid sodium and ancrod in heparin-induced thrombocytopenia. Ann Thorac Surg. 1998 Aug;66(2):567-9.
- Three novel PROC gene lesions causing protein C deficiency. Clin Genet. 1998 Sep;54(3):231-3.
- Experiences of hospital care and treatment seeking for pain from sickle cell disease: qualitative study. BMJ. 1999 Jun 12;318(7198):1585-90.
- Risk factors and thrombosis after airline flight. Thromb Haemost. 1999 Jun;81(6):995-6.
- Automated erythrocytapheresis in the treatment of severe falciparum malaria. J Infect. 1999 Nov;39(3):233-6.
- Management of patients with sickle cell pain in the community. J R Coll Physicians Lond. 1999 Nov-Dec;33(6):587-8.

- Red cell exchange, erythrocytapheresis, in the treatment of malaria with high parasitaemia in returning travellers. Trans R Soc Trop Med Hyg. 2000 Jul-Aug;94(4):353-6.
- Management of intracranial bleeding associated with anticoagulation: balancing the risk of further bleeding against thromboembolism from prosthetic heart valves. J Neurol Neurosurg Psychiatry. 2000 Sep;69(3):396-8.
- The effect of treatment with Campath-1H in patients with autoimmune cytopenias. Br J Haematol. 2001 Sep;114(4):891-8.
- Thromboelastography: a reliable test? Blood Coagul Fibrinolysis. 2001 Oct;12(7):555-61.
- Platelet pheresis is not a useful adjunct to blood-sparing strategies in cardiac surgery. J Cardiothorac Vasc Anesth. 2002 Jun;16(3):321-9.
- Sickle cell disease: Pain, coping and quality of life in a study of adults in the UK. Br J Health Psychol. 2002 Sep;7(Part3):331-344.
- Pain management and symptoms of substance dependence among patients with sickle cell disease. Soc Sci Med. 2003 Nov;57(9):1683-96.
- Understanding the causes of problematic pain management in sickle cell disease: evidence that pseudoaddiction plays a more important role than genuine analgesic dependence. J Pain Symptom Manage. 2004 Feb;27(2):156-69.
- Prevalence and risk of thrombophilia defects in vascular patients. Eur J Vasc Endovasc Surg. 2004 Aug;28(2):124-31.
- A population study to define the incidence and survival of multiple myeloma in a National Health Service Region in UK. Br J Haematol. 2004 Nov;127(3):299-304.A protective contribution of the Q allele of the R353Q polymorphism of the Factor VII gene in individuals with chronic stable angina? Int J Cardiol. 2005 Apr 28;100(3):395-9.
- Analgesic addiction and pseudoaddiction in painful chronic illness. Clin J Pain. 2006 Mar-Apr;22(3):316-24.
- The prevalence of thrombophilia in patients with symptomatic peripheral vascular disease. Br J Surg. 2006 May;93(5):577-81.
- Thrombotic thrombocytopenic purpura precipitated by acute pancreatitis: a report of seven cases from a regional UK TTP registry. Br J Haematol. 2009 Feb;144(3):430-3.
- Usefulness and limitations of a Bayesian network model as a mortality risk assessment tool in sickle cell anemia. Am J Hematol. 2009 May;84(5):312-3.

Research studies that could be relevant to the Inquiry's Terms of Reference :

Mahir WS, Millard RE, Flute PT, Bevan DH. Serial studies of T-lymphocyte

subpopulations in HIV seropositive haemophiliacs.

Clin Lab Haematol. 1987;9(2):109-14. doi: 10.1111/j.1365-2257.1987.tb01391.x. PMID: 2957143.

a. Describe the purpose of the research.

To detect and follow T-lymphocyte numbers and subpopulations (T-helper/inducer and T-suppressor/cytotoxic cells) using monoclonal antibodies in 12 patients with haemophilia who were HIV antibody positive.

b. Explain the steps that were taken to obtain approval for the research.

This project would have required approval by the St George's Pathology Research Committee in terms of scientific validity.

It would also have required approval by the Wandsworth District Health Authority Research Ethics Committee before it could proceed. This committee would have examined and approved the consent procedures to the study and would also have required sight of a written information sheet for patients asked for their consent.

To the best of my recollection, I did not attend either of these committees in respect of this study. The attendees were likely to be Dr Mahir, the primary investigator and Dr Millard, her supervisor, an academic haematologist working in the department at that time.

c. Explain what your involvement was.

The Director of the Haemophilia Centre would be required to approve any research involving Centre Patients, and as a rule would therefore be cited as a co-author. This project started under Professor Flute, but since it was planned to continue the observations into my tenure, I was on there as well. I had no involvement (apart from that of an occasional interested on-looker) in the immunofluorescence benchwork, and although I would have read the manuscript before submission, I do not recall writing any of it.

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

research.

The HIV antibody results informing the study were those provided by The Virology Department at The Middlesex Hospital as part of the patients' standard NHS care. The serological tests were not repeated as part of the study. Accordingly, that Department was not 'involved' in the research.

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

Dr Mahir was funded by a scholarship from the Government of Iraq.

Consumables, etc. would have been funded from Departmental discretional funds held by Professor Flute; this was so-called 'own account' research.

f. State the number of patients involved.

12 patients were involved.

g. Provide details of steps taken to inform patients of their involvement

and to seek their informed consent.

Formal written signed consent would have been required from patients entering the study, after verbal information and a written patient leaflet approved by the ethics committee had been read.

No record of these consents has been retained 35 years later, nor is any account of ethical approval or patient consent given in the published manuscript, which would be impossible now. However, I am sure that correct and ethical consent procedures were followed according to the practice at the time: Dr Millard was a very conscientious and ethical clinical scientist.

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

Please provide the same details in relation to any epidemiological or similar studies in which you were involved, insofar as relevant to the Inquiry's Terms of Reference.

Relating to this research:

Mahir WS, Millard RE, Flute PT, Bevan DH. Serial studies of T-lymphocyte

subpopulations in HIV seropositive haemophiliacs.

Clin Lab Haematol. 1987;9(2):109-14.

Epidemiological studies: see q.99 below.

99. The Inquiry understands that the various research studies undertaken at the Centre, or that you otherwise contributed to or were involved in or provided data for, included or may have included the following:

a. A project entitled "Sequence variation in defined regions of the envelope gene of human immunodeficiency virus" in the late 1980s, funded by the Medical Research Council.

Please see my answer to **q67** above. I was not involved in this proposal at all. There is no evidence that the proposal was actually funded by the MRC or that the study it proposed ever took place. I can certainly find no reference to it in the medical literature.

b. A BPL study of 8Y in the early 1990s.

I think this refers to the BPL PUP study reported by Hill et al in the BJH in 1993 that confirmed that BPL 8Y was virologically safe. To my regret, the Centre did not enter any patients into this study (to the best of my recollection). I had no involvement with it.

c. "Mortality before and after HIV infection in the complete UK population of haemophiliacs", Nature, Vol 377, 7 September 1995.

d. "The importance of age at infection with HIV-1 for survival and development of AIDS in UK haemophilia population", The Lancet 1996, 347: 1573-1579.

e. "Mortality from liver cancer and liver disease in haemophilic men and boys in UK given blood products contaminated with hepatitis C", The Lancet, 1997, 350: 1425-31.

f. "Immune status in HIV-1 infected men and boys with haemophilia in the United Kingdom", AIDS, 1998, Vol 12 No 8.

g. "Treatment of haemophilia in the United Kingdom 1981-1996", Haemophilia, 2001, 7, 349-359.

h. "HIV and mortality in the UK haemophilia population: demonstration of a causal relationship".Please set out what you recall of these research studies and explain what involvement you had in them.

These epidemiological papers, including a Nature publication of international importance in understanding the HIV epidemic, were written by Dr Sarah Darby and others on the basis of anonymised data from the UK haemophilia population held by the National Haemophilia Database (NHD).

My involvement consisted of signing off the yearly haemophilia returns from Centre 111, containing details of treatment, seropositivity, and death notifications in our patients. These returns formed the basis of the data analysed in the studies. I had no direct involvement with the NHD, the data analysis of the studies, or any other aspect. I would be proud to have been more closely involved, since these studies constitute an essential, scientifically important and honest accounting of the impact of HIV on the UK haemophilia community.

100. Please provide details of any articles or studies that you have published insofar as relevant to the Inquiry's Terms of Reference and please provide a copy (if you have one) of "A field guide to the bleeding disorders for the general practitioner". The Practitioner 1982; 226: 25-32.

Please see my answer to **q98**. I do not regard the Practitioner article as relevant to the Inquiry's Terms of Reference. It was purely about the recognition of bleeding disorders in Primary Care, and made little or no reference to treatment.

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

I understand the ethical principles that should guide research to be those enshrined in the Helsinki Declaration (1964) and its revisions.

The Declaration governs international research ethics and defines rules for 'research combined with clinical care' and 'non-therapeutic research.' The Declaration of Helsinki was revised in 1975, 1983, 1989, and 1996, and is the basis for Good Clinical Practices used today.

Issues addressed in the declaration of Helsinki include:

- Research protocols should be reviewed by an independent committee prior to initiation
- Informed consent from research participants is necessary
- Research should be conducted by medically / scientifically qualified individuals
- Risks should not exceed benefits

To the best of my memory, I did apply the principles of the Helsinki Declaration to the research studies referred to above.

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

No patients at the Centre were involved in Centre research studies without their express and informed consent.

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

Anonymised patient data, collated by the National Haemophilia Database, was used as the basis for epidemiological research of the type described in **Q99c-h.**

Express and informed individual consent to this usage was not obtained, since the Haemophilia Registry and Database operated throughout this period on the basis of 'patient implied consent with an opt-out'.

Such an arrangement was regarded as appropriate for databases used for direct care - for example, if commissioner funding of ongoing treatment for an individual depended on their being registered, as often the case in haemophilia.

As far as I can recall, we were also informed over the years that databases required for public health purposes – for example to know the number of individuals with haemophilia in the UK in

order to plan for the required volume of FVIII concentrate – could also apply 'patient implied consent with an opt-out'.

Over the years, clinicians were assured that this arrangement had been assessed as compliant with the Data Protection Act and had been reviewed and approved by the Information Commissioners Office and local Caldicott Guardians, and the Department of Health, as well as the responsible forerunners of these bodies. I believe that these provisions are now considered to be inadequate for research purposes and are being reviewed again.

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

To the best of my knowledge, I never shared any patient data with third parties (unless the use of that term includes UKHCDO and the NHD) without their consent. I do not know if such data was shared by NHD / UKHCDO.

105. The enclosed April 1991 memorandum from JK Smith [BPLL0005964] refers to a practice whereby the Protein Fractionation Laboratory ("PFL") provided certain products, mostly free of charge, on the understanding that clinical data would be provided in return. You were included on the list of AT III and Factor XI users. Did you provide clinical data to PFL in return for AT III and Factor XI free or at a reduced charge? Did you do the same for Factor VIII?

This memorandum refers to so-called 'minor products', in particular plasma-derived Factor XI and Antithrombin concentrates; they would probably be classified as 'orphan' products now. These were occasionally used during my tenure. They were unlicensed and produced by BPL under Crown Immunity.

These products were neither produced nor used in sufficient volume to allow valid clinical trials of safety and efficacy: hence BPL asked users to collect simple post-treatment information on paper forms that came with the product, such as the reason for use, severity of the treated FXI or AT deficiency, and whether the treatment was effective or caused unwanted effects. We probably did return the information, but I cannot remember for sure whether we received free product. Such an arrangement certainly never applied to FVIII.

106. What was the policy at the Centre as regards recording information on death certificates when a patient had been infected with HIV or hepatitis?

As far as I can remember, the Centre had no fixed policy on this matter. Death Certificates were completed by the patients' attending doctors, who were usually members of the Infectious Disease or Haematology team; some deaths were reported to the Coroner, and at least one Coroner's Inquest was held.

107. What were the retention policies of the Centre in relation to medical records during the time you were practicing there?

The Centre did not have independent medical record retention policies. These policies were a matter for the St George's Hospital Medical Records Department, and latterly for St George's Healthcare Trust Medical Records Department.

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

The Centre did not maintain separate files for any patients.

109. Did you 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 hospital where you worked? If so, why, what information and where is that information held now?

I have never kept hospital notes, patient records or information of any kind at my home, or anywhere other than within the clinical and office spaces of the hospital.

I had intermittent contact with the Centre as a junior trainee from late 1977, but only became Director in July 1985.

Section 5: Treatment of Patients

110. In December 1974 the Department of Health announced additional funding with the primary aim of making the NHS self-sufficient in Factor V111 blood products within two to three years. The Inquiry understands that you began working at the Centre in 1974. Whether or not that is correct, please answer the questions in this section as far as you can.

a. Were you aware of the Department of Health's aim of achieving self-sufficiency when you began working at the Centre?

I was aware of the concept of self-sufficiency. I was probably aware that the Department of Health had expressed an aspiration towards it.

b. What did you understand the term "self-sufficiency" to mean? In particular, did you understand it to mean self-sufficiency in providing Factor VIII blood products prophylactically, or solely in response to bleeding incidents?

I took it to mean self-sufficiency in all blood products: i.e. able to manufacture adequate supplies for all haemophilia treatment needs, including prophylaxis, from plasma donated by unpaid volunteer UK blood donors. However, it must be said that for the first 2 or 3 years of my tenure, prophylaxis in adults was not yet general praxis in the UK.

c. Did your understanding of what "self-sufficiency" meant change at any time? If so, when and why?

My understanding of the term self-sufficiency did not change.

d. What was your understanding of how others defined "self-sufficiency"?

I assumed that they defined it in the same way.

e. What if any role did you play, at any time, in any arrangements or initiatives designed to help achieve self-sufficiency.

None whatsoever. My time was completely taken up with my multiple clinical roles at St George's.

111. How were estimates made of how much Factor VIII blood product would be required for use in England and Wales? In particular:

a. What was the role of the director of the Centre in making such

estimates, and how did this change over time?

During the years 1985-2000, the director of a relatively small Centre like SGH had little input to, or influence over, these national estimates or targets.

From 2000, the Pan Thames Haemophilia Consortium compiled estimates for future usage in the London Region and used them to inform the National Tender process. So our role expanded a little.

b. What was your role (if any) in making such estimates and how did that change over time?

See answer a. above.

c. What was the role of UKHCDO and how did this change over time?

UKHCDO used the reported treatment volumes in the annual returns from UK Centres to compute the estimated requirement for the next year. They were the only source for this data, so the role was absolutely central to the process.

d. What assumptions would underpin the estimates (including assumptions as to how the blood products would be used)?

There was a general assumption of a year-on-year increase due to the gradual adoption of prophylaxis in all age groups, and an increase in musculoskeletal surgery as more patients survived to require joint replacement procedures.

e. How would the estimate be made (e.g. by whom were they made, when and through what process)?

By members of UKHCDO in concert with the NHD, after discussions at the Advisory Board and AGM of the UKHCDO.

f. How were the estimates shared with other interested parties?

I was not privy to this process, so cannot say.

g. How did any of these processes change over time?

See my answer to **q111f** above.

112. How were annual figures derived for how much Factor VIII blood product had been used over the course of a year?

From the usage figures in the UKHCDO Annual Returns.

a. What was the role of the director of the Centre in providing such figures, and how did this change over time?

I did not compile them, laboratory staff did. I checked them and lab secretarial staff sent them to UKHCDO.

b. What was your role (if any) in providing such figures, and how did this change over time?

See my answer to q112a above.

c. What was the role of UKHCDO and how did this change over time?

See my answers to **q111f** and **q112** above

d. How would the calculations be made (e.g. by whom were they made, when, through what process and using what data)?

See my answer to **q111** above.

e. How were those figures broken down geographically (e.g. by country, region or any other unit)?

I do not know.

f. How were the figures shared with other interested parties?

I do not know.

g. How did any of these processes change over time?

They remained fairly stable, as far as I know.

113. Were there significant differences between the estimates that were made and actual use? If so, why?

I do not know.

114. To what extent, if at all, did England and Wales (in your view) achieve self-sufficiency of Factor VIII blood products? Why, if this is your view, was self-sufficiency not achieved? Do you consider that more could have been done to achieve self-sufficiency and if so what?

Self-sufficiency in any blood product is either achieved or it is not: there is no such thing as 'an extent 'of self-sufficiency. In England and Wales (E&W), it was never achieved in respect of FVIII. Prior to 1985 – say from 1976-81, when self-sufficiency might have made a difference to the scale of the Haemophilia HIV epidemic in the UK – production fell a very long way short. There was insufficient plasma fractionation capacity, linked to the fact that the National Blood Transfusion Service was not configured to provide large volumes of plasma to fractionate, but rather to produce an ample supply of whole blood for transfusion.

In 1985, after an initial burst of financial investment in plasma fractionation capacity, self-sufficiency was achieved in Scotland, and BPL managed to make enough safe FVIII (8Y) from E&W donor blood to satisfy close to 40% of the FVIII need. That showed that self-sufficiency was feasible if production at BPL had been scaled up, and the supply of plasma from the NBTS had been optimized (probably by expanding their apheresis donor programme). However, self-sufficiency from 1985 onward would have made little difference to the incidence of HIV and HCV in the UK population, since safe imported heat-treated and SD-treated concentrates were available by then. Furthermore, any such investment in self-sufficiency would have been negated by BSE/vCJD a few years later.

To protect the UK haemophilia population from the eventual scale of the HIV and HCV epidemics through self-sufficiency, at the very least the following interlinked advances would need to have been in place well before 1980:

Massive new financial investment in fractionation capacity at BPL / SNBTS.

Reconfiguration of the NBTS and its staffing to roughly double the amount of plasma obtained from donor blood and apheresis donors.

A sea-change in the perception of the threat of NANB on the part of clinicians and

manufacturers, including recognition of the import of the work of Harvey Alter in the 70's that pointed to a 'small, lipid-coated virus', and the will on the part of concentrate manufacturers to demonstrate the efficacy of heat-treatment.

The possibility that these radical changes could have occurred in synchrony was zero. The massive investments required would never have been released by the UK Treasury, soon wedded to the doctrine that privatized provision was always to be preferred to investment in public works. For these reasons, I have come to regard the argument around self-sufficiency as a counterfactual distraction.

115. Do you consider that there was a failure by haemophilia clinicians to provide timely and accurate estimates of future demand for Factor VIII blood products and/or a failure by haemophilia clinicians to identify the foreseeable increase in use of such products once they became available?

No, absolutely not. To the best of my knowledge, the yearly estimates of FVIII demand provided by UKHCDO are considered to be the most accurate predictions of future service requirements provided to healthcare commissioners across the whole spectrum of specialized services. This has sometimes been the source of some irritation, since it removes one reason for withholding funding.

116. If self-sufficiency had been achieved in Factor VIII products, what, in your view, would have been the effect on the numbers of patients infected with (i) hepatitis B, (ii) hepatitis C, and (iii) HIV. Please comment on when self-sufficiency would have needed to be achieved (in your view) in order for any material difference to have been made in respect of each of these viruses.

Please see my response to **q114** above. I am unable to speculate about the effects of something that didn't happen.

FVIII self-sufficiency would have had little or no effect on the numbers of UK patients infected by hepatitis B, which was already being excluded from imported product by donor screening.

Self-sufficiency alone, without heat-treatment and before HCV screening, would probably have reduced the numbers of Hepatitis C infections in UK PWH if in place by the early 1970s. HCV would not be eliminated because it was already present in the UK donor population and UK product would still be a large-pool product. Introduced any later than the early seventies, it would have prevented fewer infections.

Self-sufficiency introduced before 1979, without heat-treatment and before knowledge of, and screening for, HIV, would probably have significantly reduced the numbers of HIV infections in UK PWH, mainly by delaying product infection until effective screening and heat-treatment was introduced. However, some infections would also have occurred from UK product before 1985 as the HIV virus entered the UK donor population in the eighties. There was such an outbreak due to self-sufficient SNBTS FVIII concentrate.

117. To the best of your knowledge, did England and Wales achieve self-sufficiency in respect of Factor IX blood products?

To the best of my knowledge, I don't know.

118. If self-sufficiency in respect of Factor IX blood products was achieved, did you nonetheless use commercially produced products in preference to domestically

produced products? If so, why?

As far as I can recall, I used mainly BPL FIX. I cannot recall using commercial products before Benefix (recombinant FIX) became available. Then I would have switched for theoretical safety reasons.

119. The minutes of the 21 September 1990 UKHCDO meeting [BART0002382] record Professor Bloom as stating that " in 1979-85, when he was Chairman, all the Haemophilia Centre Directors and the Haemophilia Society were pushing the Department of Health to purchase imported products; everyone knew the result of that ." During that time, was the Centre pushing for the purchase of imported blood products and if so why? Were you aware of other Haemophilia Centres pushing for the purchase of imported products as described by Professor Bloom? What did you understand Professor Bloom to mean by "everyone knew the result of that"?

I was not involved in the management of the Centre until mid-1985. My predecessor, in view of his letter to Dr Snape (qv) was evidently 'pushing for' (requesting) BPL product rather than imported product from the beginning of 1985. Before then, if the Centre and the Haemophilia Society were indeed 'pushing for' imported FVIII, it was because there was nowhere near enough FVIII treatment for our patients' needs without it. 'Appealing for' might have been a more appropriate term. The same would have been the case for other Haemophilia Centres.

"Everyone knew the result of that". In 1990, yes, his audience knew that imported FVIII was contaminated with HIV before heat-treatment in 1985, and increasingly, they knew of the irresponsible safety risks that had been taken by its manufacturers. However, that contamination was the fault of those who sold it, not those who requested its purchase in good faith.

120. In the same minutes, Professor Bloom stated that "Directors were under some pressure to use products like Monoclate, Hemofil M etc." Were you under pressure to use those or any other products? If so, from whom and why? Professor Bloom also stated that he was "concerned about hidden dangers with the American concentrates. One needed to consider the risks of paid volunteer donors." Did you share Professor Bloom's concerns and if so why? What did you understand Professor Bloom to mean by "the risks of paid volunteer donors"?

I was never under any pressure to use any particular product. I was being asked by hospital general and financial management (active by 1990) not to use more expensive products without good reason, and new affinity-purified FVIII concentrates like Monoclate P were definitely more expensive, so any 'pressure' was in the opposite direction to that perceived by Professor Bloom.

I did share Professor Bloom's concerns. After the horror of HIV, 'concern' about 'hidden dangers' in concentrates from any source was universal. It was this fear that led many of us to consider it fully justifiable to move to highly-purified FVIII, on the basis that (crudely put) the more you select for the FVIII in plasma (e.g. by binding it to antibodies as in Monoclate) the more you select against other chemical entities - including infectious agents of unknown type.

In the USA all donors are volunteers: some are unpaid, some paid (or 'compensated' at a level supposedly inadequate to constitute an 'incentive to donate'). By 1990 the rigorous regulatory environment that emerged in response to the contamination scandal insisted that plasma used

for FVIII manufacture was sourced from long-term apheresis donors, repeatedly tested for viruses with sensitive molecular assays over many visits: none of their plasma used until several consecutive negative results accumulated over time. The companies were still profit-driven corporate entities, but their ability to trade became dependent on never transmitting an infection ever again. The 'old' paid donor giving blood for drug money or early prison parole no longer existed by 1990. Commercial plasma-derived FVIII concentrate, after state-of-the-art heat or SD treatment and ultrafiltration, had become safe, and remains proven to have been so.

121. In a letter to The Independent newspaper, published on 12 April 1991 [UHMB0000006_064], you responded to an article published on 9 April 1991 [HSOC0002632] and commented on NHS reforms.

a. Please explain what you meant by a "cost-cutting war among haemophilia treaters and Factor 8 manufacturers", and why you believed it would reduce the safety of the blood supply.

This rather naïve (and crudely edited, although I have no unedited copy) letter must be put in context. St George's, like the entire hospital sector, was struggling to cope with the Thatcher/Enthoven Internal Market in 1991. Low-volume high-cost services for chronic diseases, like Haemophilia Centres, were particularly targeted for 'efficiency savings' and even closure, since they risked unbalancing hospital budgets. The centre was under pressure to use the cheapest available product, irrespective of whether it was best for patients.

The sentence in question was edited, removing an important comma after 'treaters'. I was not invoking an absurd idea of 'treaters' engaging in a cost-cutting war against 'manufacturers', but of a potential 'race to the bottom' by both. Given that the safety measures I described in my answer to **Q120**, including increased purity, were all expensive, there was a clear risk to safety in such a race.

b. Please explain what you meant by "legalistic defences which saw [the Government] through".

I was referring to the 'Bolam Test' of medical negligence applied at the time, which made it very difficult for the victims of HIV to sue doctors, hospitals or the Department of Health for negligence in the face of the UKHCDO's ongoing advice to continue treating with imported product. I think I was also referring to legal 'waivers' concerning the Macfarlane Trust being presented to people with haemophilia as part of the Government response to their class action, although this was probably only hearsay in April 1991.

When you stated that the Government could "never again claim to be surprised by the contamination of crude preparations of bulk plasma by unknown viruses or other infectious agents", which blood products and viruses or other infectious agents were you referring to? Were you expressing doubt as to whether the Government (and any others) were in fact "surprised by the contamination" and if so why?

This related to the argument in paragraph 2 of my response to **Q120.** I strongly agreed with those UK clinicians who considered that the adoption of high-purity FVIII was an important step in 'future-proofing' FVIII safety, since HIV showed that novel organisms with hitherto unpredicted effects could suddenly invade the blood supply; it was no good to simply protect against known pathogens: in future they might not be enveloped viruses susceptible to heat, or viruses at all.

The official contention was that the HIV epidemic was an unforeseeable event due to a completely novel virus, that couldn't be 'seen coming'. My doubt about that excuse was that it simply would not do, next time around.

c. Please explain what you were referring to when you stated that "a scandalous linkage has been arranged between the proportion of BPL products bought and the price that the hospital concerned will be charged for totally different blood products such as red cells and platelets".

Because BPL was linked closely to the NBTS, they proposed that hospitals not buying BPL FVIII would be charged more for cellular blood products like red cells and platelets. Conversely, the more BPL product we bought, the less we would pay for platelets.

It will be recalled that at that time I was also the consultant responsible for treating leukaemia patients at St George's, so the threat of paying more for the platelets on which their lives depended, because of my preference in terms of FVIII, struck me as scandalous. It was this proposal from BPL that provoked the letter. To the best of my recollection it was dropped soon after; I expect mine was not the only negative response.

d. Please explain why and how you considered that the "ethos of the gift relationship in blood and plasma donation" was "previously exemplified to the highest degree by the Blood Transfusion Service and its Blood Products Laboratory at Elstree".

Because Richard Titmuss's definition of the Gift Relationship, as expressed in his book of that title, was based upon, and had been perfectly exemplified by the NBTS, until the misconceived attempt to apply 'market forces'.

122. In the enclosed 24 April 1991 letter to, amongst others, all Haemophilia Centre directors [UHMB0000006_063], the managing director of Armour commented on the letter you had written to The Independent . Did you agree with his letter? If not why not?

I did not agree with his quoting it in what was, essentially, promotional literature. As I replied, my letter did not mention any particular commercial product, and was not promoting any.

123. In a follow-up 15 May 1991 letter [UHMB0000006_066], Armour stated that copies of your (and another) letter to The Independent had been included in its 24 April 1991 letter in error, that the reference to your and others' names did not imply agreement with all of the points it made, and that you should not be taken to endorse the product of any specific manufacturer. Had you contacted Armour to request that it issue a letter of this nature? If so please say why.

Yes, I had contacted them. I considered it would have compromised me if Haemophilia Directors and others had concluded, from the Armour letter of 24th April, that my letter to the Independent was in any way a puff for their product.

Section 6: Blood services and BPL and PFL

124. Please outline the interactions and dealings you had with the blood services, whether on a regional or national level, and/or with BPL and PFL during the time that you worked at the Centre.

I had the usual interactions and dealings with the Tooting Regional NBTS Centre that any consultant haematologist working within their orbit would have, such as contributing to routine orders for red cells and platelets; arranging special blood for transfusion and red cell exchange

for multi-transfused sickle cell patients (NBTS responses uniformly helpful and excellent); ringing begging for platelets in the middle of the night when my registrar's request had been declined; attending regular users' meetings at which senior NBTS medical staff would tell us in very reasonable terms to use less blood and platelets…

On a National Level, and with BPL, there were occasional exchanges of 'customer's letters', but no direct involvement.

125. Do you know what if any consideration was given to increasing production of cryoprecipitate, or producing a product with lower risk, in response to the risks associated with factor products, and what if any involvement did you have with any blood service (regionally or nationally) and/or BPL/PFL in relation to this?

I had no knowledge or involvement with this issue during my tenure as Centre Director.

126. What if any discussions or meetings or interactions did you have with any blood service (regionally or nationally) and/or BPL/PFL in relation to:

a. the risk of infection with hepatitis from blood products;

b. the risk of infection with HIV/AIDS from blood products;

c. the steps to be taken to reduce the risk of infection?

I can recall no personal discussions or meetings with the NBTS, BPL or PFL on these matters.

127. What if any involvement did you have with any decisions or actions taken by any blood service (regional or national) and/or BPL/PFL in response to the risks arising from blood and blood products?

I had no involvement with any such decisions.

128. What was the system at the Centre for keeping records of the blood or blood products that were used?

Up until the late 1980's, it was predominantly a paper system, with patient, dose, product name and batch number written by hand in laboratory ledgers and copied into patients' medical notes. Later, this data became computerized on laboratory spreadsheets, but continued to be recorded in patients' medical notes.

129. The enclosed 14 June 1990 letter from Dr Snape to you [BPLL0003080] referred to a recall which led to "unnecessary concern" among users who had not received the product. Please describe the incident which led to Dr Snape's letter and, if available, provide your 11 June 1990 letter (to which he was responding).

I have no clear memory of this event, and no copy of my letter. From Dr Snape's reply, I infer that there had been a recall of a specific batch of BPL F8Y, this had appeared in the press, and one or more of my patients (or their families) who had been treated with F8Y but not been exposed to the batch in question had been upset when they read about it. Dr Snape courteously explained that this had been a leak rather than a deliberate press release.

Section 7: UKHCDO

130. Please describe your involvement with UKHCDO (including any of its working parties, committees or groups).

During my time as Director at St George's (1985-2008) my involvement with UKHCDO was as

an ordinary member, attending the combined yearly AGM and Scientific Meeting and signing off the Annual Returns. I was not a member of any of its working parties, committees or groups; I was too busy with clinical work at St George's to devote any time to them, and St George's was not a large enough Centre for UKHCDO to request my participation.

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

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

To promote and enable the best care for haemophilia and other inherited bleeding disorders, by:

Maintaining a national register of all patients known to have these disorders, and collecting data on treatment usage, to allow computation of the treatment needs of this group.

Helping to maintain and audit a network of recognized National Haemophilia Treatment Centres where patients and their families affected by these rare diseases could consult clinicians with expertise, and a laboratory could reliably diagnose the conditions and latterly, auditing the facilities of these Centres.

Supporting the multidisciplinary haemophilia teams at these Centres by holding regular meetings to promulgate guidelines and other assistance towards best practice.

Contributing to all aspects of improvement in the care of these disorders by supporting research.

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

The number, structures, composition and roles of the myriad committees and working groups of the organization that have existed since I joined UKHCDO in 1985, the names and remits of which have constantly changed to meet changing priorities, is too vast a subject for me to effectively recall or describe, since I was never an office-holder in the organization, far less an historian of it.

c. The relationships between UKHCDO and pharmaceutical companies.

I have not been involved in, and therefore have no certain knowledge of, any such relationships. Insofar as I understand, pharmaceutical companies do make a contribution to UKHCDO funding.

d. How UKHCDO was funded.

I do not have certain knowledge of UKHCDO was or is funded. I have never held office as UKHCDO Treasurer or had any direct involvement with the sources of funding of the UKHCDO. Insofar as I understand it, there were/are contributions from grant income from The Department of Health, Membership fees, Triennial Audit fees, and pharmaceutical companies.

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

Information and advice was disseminated by UKHCDO at its Annual General Meetings (AGM), and in the minutes of the AGM, to all members of UKHCDO and to its affiliated organizations, including the Haemophilia Society. UKHCDO would also circulate guidelines and advisory memos when the occasion arose. Latterly, its website has disseminated this information electronically.

f. Any policies, guidance, actions or decisions of UKHCDO in which you

were involved and which relate to:

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

ii. the manufacture of blood products;

iii. self-sufficiency;

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

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

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

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

viii. heat treatment;

ix. other measures to reduce risk;

x. vCJD exposure; and

xi. treatments for HIV and hepatitis C.

During my tenure as Haemophilia Centre Director at St George's Hospital (1985-2008) I was not involved in any UKHCDO policies, guidance, actions or decisions in any of these areas.

Section 8: Pharmaceutical companies/medical research/clinical trials

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

As I understand the terms 'consultancy' and 'blood products', I have never offered ongoing consultancy services to any company. I gave a single piece of advice to **Octapharma AG,** a Swiss company, at a meeting in Dusseldorf (about 1992) to the effect that their novel Solvent-Detergent treated frozen plasma (Octoplas) would have a likely role as replacement for untreated standard FFP in treating patients with the rare, potentially fatal, disease Thrombotic Thrombocytopenic Purpura (TTP). Individuals with TTP need multiple plasma exchange procedures (PEX) in order to survive and recover, and cases of HCV had occurred after consequent multiple exposures to single donor (unpaid donor, self-sufficiently British) untreated FFP. Within five years Octoplas had become the standard replacement fluid for PEX in TTP in the UK. Of course, they may well have had the same advice from others.

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

Octapharma AG paid for business class flights to Dusseldorf and a single night at a hotel there. I probably received a fee for this single meeting but cannot remember the amount. It was certainly less than 500 Euros.

134. Have you ever sat on any advisory panel, board, committee or similar body, of any

pharmaceutical company involved in the manufacture, importation or sale of blood products? If so, please provide details of your involvement and of any financial or other remuneration you received.

Not in the context of blood products, as far as I can recall.

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

I have never received any such financial incentives.

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

I have never received any such non-financial incentives.

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

I have never received any such funding.

138. What regulations or requirements or guidelines were in place (at any time relevant to your answers above) concerning declaratory procedures for involvement with a pharmaceutical company? If you were so involved, did you follow these regulations, requirements and guidelines and what steps did you take?

I cannot remember what procedures were in place at St George's between 1985 and 2008. They probably entailed getting permission from a line-manager to ensure any time required was taken as entitled leave. Whatever they were, I would have followed them.

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

No. I have never undertaken medical research into pharmaceutical products manufactured from human blood.

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

Please see my answer to **Q139** above.

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

Please see my answer to **Q139** above.

142. The Inquiry understands that you had a role in the International Health Consortium in the 1990s. Insofar as relevant to the Inquiry's Terms of Reference, please describe the work of the Consortium and your role within it.

I cannot recall any such role, or organization. I can find no record of any organization of that name in the UK. I was briefly involved with The Tropical Health Education Trust, based at the London School of Tropical Medicine, in the context of the work I did in Ghana during the 1990's. It has no relevance to this Inquiry.

Section 9: vCJD

143. When and in what circumstances did you first become aware of the risks of transmission of vCJD associated with the use of blood and blood products? How did your knowledge develop over time?

I cannot remember when and where, but by 1996 I was certainly aware that UK citizens had begun to develop vCJD. That there was a consequent theoretical route of onward transmission by blood and blood product transfusion would have immediately occurred to any haemophilia doctors.

UK cases of fatal vCJD in three blood transfusion recipients, linked to donations from individuals who themselves had gone on to develop vCJD, confirmed that transfusion of non-leukodepleted blood is capable of transmitting the disease.

I knew that UK plasma was not being used for coagulation factor fractionation after 1999. BPL began to fractionate US donor plasma. I know now that no person with haemophilia has developed vCJD in the UK, so the risk of transmission by non-cellular fractionated blood products remains theoretical.

144. Please describe your involvement in decisions as to what information to provide to patients about vCJD at (a) the Centre and (b) St Thomas's.

I was involved in these decisions at the St George's centre (until 2008) but not at St Thomas's, where, by the time I arrived, the information had already been provided to patients.

Please also answer the following questions:

a. What procedures were put in place for informing patients about possible exposure to vCJD?

We prepared to inform patients by letter (see below), to be followed up by individual consultations if the patient requested it.

b. What steps were taken, and when, to tell patients of possible exposure to vCJD?

See **Q144a** above.

c. What information was provided, and when, to patients about vCJD?

See Q144a above.

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

See Q144a above and our generic letter [WITN1194004]. The counseling offered was to be delivered by myself, by my then paediatric colleague Dr Miguel Ortin (Dr Sarah Ball having retired), or by our Haemophilia Nurse Specialists Helen Greensmith and Allison Greig.

e. What precautions were recommended, and why, in relation to patients notified to be at risk?

The precautions recommended were all for 'public health purposes'; not to donate blood or tissues (not possible anyway for people with haemophilia or any kind of bleeding disorder), and to inform dentists, surgeons, gastroenterologists and any other clinician considering invasive or endoscopic procedures of their 'additional risk' status.

145. The enclosed 24 August 2004 letter from BPL [HCDO0000134_079] listed batches of

blood product received by the Centre. If available, please provide a copy of the notification letter to which it referred. If not, please describe the contents of that letter as far as you are able to. The Inquiry understands that both of the letters relate to vCJD risk. Is that correct? What steps did you/the Centre take in response to receiving them?

This letter, HCDO0000134_079, is not addressed to me or the Centre at St George's, but to my namesake Dr Phillip Bevan at St Richard's Hospital Chichester, so I cannot answer this question.

146. Enclosed is a generic letter from you and colleagues, dated 16 September 2004, regarding vCJD risk [WITN1194004]. The letter asked the patient if they wanted to know whether they had received any batch of clotting factor known to contain plasma from individuals who later developed vCJD.

Please explain why you offered patients this choice and, if available, provide the information pack referred to in the letter. How did your/the Centre's patients respond to being offered this choice?

As far as I can remember, offering this choice was recommended by the UKHCDO. However, this distant in time I cannot refer to, or retrieve any, documentation to that effect. It seemed a reasonable thing to offer, because no test was (or is yet) available to detect whether an individual had been infected with the prions responsible for BSE/vCJD, the true natural history of the disease was unknown, and no treatment was available.

A PWH might therefore justifiably ask "what is the value to me of knowing this now, since doing so would only put me in a position of uncertainty?" and conclude that there was no value, or negative value, in the context of their own life, given the numerous unknowns.

My colleagues and I concluded that individuals should be given the right to know or not to know; the right not to be passive recipients of the information. Most patients appreciated being given this choice. When it came to the decisions actually made, I remember individuals who were strongly for, and others strongly against, being informed.

I cannot provide a copy of the information pack referred to in the letter.

147. The enclosed 6 October 2004 letter from a colleague at Mayday University Hospital [HCDO0000254_826] records that you had queried UKHCDO's standard patient letter with respect to vCDJ risk, and that you had " developed a less alarming patient letter for those patients who have only ever received recombinant products or non-UK plasma sourced products. " Why and in what ways did you query the UKHCDO standard letter? Please provide a copy of the alternative letter that you developed.

I do not hold, and cannot access, any copy of the alternative letter. I believe that it informed individuals, or the family members of individuals, that they had never been exposed to any of the BPL products considered to be of increased risk – for example those who we were sure had received recombinant product only. We felt that the UKHCDO standard letter (which required detailed close reading to understand) would have been pointlessly alarming to, for example, the parents of a young child who had only ever received recombinant FVIII.

148. The enclosed February 2009 email correspondence with a colleague in Torbay Hospital [TORB0000099] related to whether a patient was at risk of vCJD for public health purposes. You stated that the patient was not transfused at St Thomas's with UK-plasma-derived pooled clotting factor concentrate because it was St Thomas's policy not

to use UK factors during the period 1980-2001. What was the source for your knowledge of St Thomas's policy during that period? So far as you can, please explain the policy further, including why it was adopted, when it was implemented and when it came to an end.

My source for that knowledge was communication from CCC staff members who had worked during the period of Professor Savidge's tenure as Director (1980 -2007). As far as I know, Professor Savidge's reasons for not using BPL products were complex and included the theoretical safety and comparative purity of the product, together with financial and/or contractual issues I was never privy to. As a policy, it ended when I became Director in 2008, although in practice recombinant product had largely taken over by then.

149. In the enclosed witness statement [WITN3866001], Dr Alexandra Rice refers to inconsistencies in advice she received in early 2012 as to whether, in light of vCJD risk, she could perform a diagnostic frozen section on a patient's tissue sample. Is Dr Rice's description of the advice you provided accurate? If so, what was the "official guidance" you relied on when advising that a frozen section should not be performed in these cases regardless of the tissue type? So far as you are able to say, why did your advice differ from that provided by the National CJD Research and Surveillance Unit?

My input into this issue seems to have taken place entirely in the form of a telephone conversation with Dr Louise Tillier, the haematologist covering the Royal Brompton Hospital (RBH) at the time, and sadly I cannot remember anything about it.

From Dr Rice's statement, she took the advice from Dr Tillier (advised by me), and Dr Phadke, a consultant neuropathologist at Queens Square, not to do a frozen section biopsy in a patient. Contrary advice was later given by Dr Mead, a consultant neurologist at the National Prion Clinic, and Professor Ironside at the National CJD Research and Surveillance Unit, which allowed the frozen section to take place after a week's delay.

The 'official guidance' I relied on was probably that of the NHS vCJD Clinical Governance Advisory Group published in 2003. I don't think frozen section is specifically mentioned in that guidance, and at the time of the telephone call I doubt if I had it to hand. I probably concluded that a lung biopsy might include lymphoid tissue, conferring a medium degree of risk. In addition, there may have been a degree of ambiguity about the patient's risk status. I would have given the advice in good faith, and followed the precautionary principle in giving it, as I'm sure Dr Phadke and Dr Tillier did.

Dr Mead – and certainly Professor Ironside – contributed to writing the NHS vCJD guidelines. The writers of guidelines will always have a more complete knowledge of their minutiae than end users. If a view on a specific issue like frozen section is formed during the preparation of guidelines, but not included in the final publication, the guideline writers are going to be the only ones to know.

I am very sorry that the patient experienced a delay in getting an important biopsy done, with all the uncertainty and worry that entailed. This episode shows exactly the kind of difficulty that can occur when clinicians try to apply the precautionary principle in medical decision-making.

Section 10: The financial support schemes

150. What if any involvement did you have with the different trusts or funds (the Macfarlane Trust, the Eileen Trust, the Caxton Foundation, the Skipton Fund) which were set up to

provide financial support to people who had been infected? Please provide as much detail as you can.

I had no involvement with any of these Trusts or Funds.

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

As far as I can recall, I, or our HIV counsellor, would have given all available information to our patients and where appropriate their families.

152. At the 29 September 1988 UKHCDO meeting [BART0002329], directors were asked to encourage registration with the Macfarlane Trust. What if any steps did you/the Centre take in response in response?

Please see my answer to Q151 above. The patients and families would have been strongly advised to register with the Macfarlane Trust.

153. Did the Centre have any policy or any guidance for staff members in relation to referring patients to the trusts and funds for support? If so please provide details.

The Centre did not have any written policy or guidance on this issue. Such decisions were taken in individual consultations with patients and families either by me, or my HIV Haemophilia Counsellor colleague.

154. 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?

To the best of my memory this information was provided on application forms presented to us by patients rather than directly to the Trusts or Funds. The information addressed issues of severity and whether particular problems could be attributed to the transfusion-transmitted infection.

155. What kind of support or assistance was provided by you and/or the Centre to patients making applications for financial assistance?

Whatever support and assistance was required and we could do. I cannot remember individual instances.

156. Did the Centre, or any of their staff, act as a gateway for determining whether a particular patient met the eligibility criteria for the receipt of assistance from any of the trusts and funds? If so, please explain who set the criteria, what they were and how they were applied.

I have no recall of setting or determining any such criteria during my time at St George's.

157. Was the Centre or any of its staff involved in determining applications made by patients for assistance from the trusts or funds? If so, please describe that involvement.

No.

158. 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?

I consider these bodies to have been conscientiously run with a clear intention of delivering as much help as they could to patients. However, I consider the charitable '*Ex Gratia*' and 'discretionary' nature of the funds, together with the limited money at their disposal, a grave disservice to the patients infected with HIV and HCV. My view is that these funds were designed by HM Government as devices to evade proper restitution to individuals infected by HIV and HCV by their NHS treatment.

159. The Inquiry understands that you wrote letters of support for patients applying to the Macfarlane Trust. Please describe the kinds of supporting letters you provided.

I cannot remember any individual letters, or what was in them. I hope they were helpful.

Section 11: HCV lookback

160. In **the enclosed 16 January 1996 letter [NHBT0090819_004], Dr Doughty ofthe South Thames Blood Transfusion Service noted that you had expressed an interest in counselling a patient with regards to the hepatitis C look-back programme that was then being carried out. Please describe your involvement in the look-back programme, both with respect to counselling and any other role.**

My colleague Dr John Parker-Williams took on the first look back because he was responsible for blood transfusion at St George's. I counseled the patient mentioned in Dr Doughty's letter because she was a patient of mine who had developed HCV after a life-saving course of plasma exchange using NBTS fresh frozen plasma. She was the patient that generated my interest in S/D treated plasma, as expressed to Octapharma AG.

161. Please provide details of any involvement you had in the HCV look-back programmes organised by the Department of Health in 2010 and 2013.

The main part of this work at St Thomas's CCC was taken on by my colleague Dr Graeme Thomson.

162. At the 3 October 2011 UKHCDO meeting [HCDO0000510] it was "generally agreed" that the burden the look-back was placing on Haemophilia Centres was too great. Was this your/St Thomas's experience? If so please explain how.

This was not our experience. We were better staffed than many other Centres, and we had Dr Thomson.

Section 12: Current Haemophilia care and treatment

163. The Inquiry understands that you worked at St Thomas's until at least 2014 (and assumes that you subsequently ceased clinical practice). In answering the questions in this section, which are aimed at enabling the Inquiry to understand how haemophilia care is currently provided and how the provision of care and treatment and the approach to patients may have changed over the years, please draw upon your practice at St Thomas's around the time that you stopped working as a clinician, and where appropriate your earlier work and experiences at the Centre.

Please see my answer to Q1 above. I was Consultant Haematologist, Haemophilia Comprehensive Care Centre Director, and Clinical Lead for Haemostasis and Thrombosis from May 2008 until January 2017. I then retired from full-time NHS practice, including as Director and Lead, but returned to work part-time as a clinician in the Thrombosis service at GSTTuntil January 2018. A further year was spent working part-time in haemophilia and thrombosis at

GSTT until my complete retirement in March 2019.

164. Please describe:

a. how the provision of care and treatment for bleeding disorders was organised at St Thomas's when you ceased clinical practice; and

Provision of care and treatment at GSTT continued to be based in the large purpose-built Comprehensive Care Centre (CCC) on the first floor of North Wing, refurbished with charitable funds during my tenure.

The CCC contains a treatment room, clinic rooms, waiting rooms, the haemophilia nursing team station, a physiotherapy suite and a temperature-controlled storage room for therapeutic products. It has its own business suite housing staff running the home therapy / delivery systems, the CCC registry, and other management functions.

A paediatric Haematologist, Dr Jay Alamelu, was appointed during my tenure, and a separate paediatric haemophilia unit, in Evelina Children's Hospital on the St Thomas' site, was established. A transition clinic for adolescent patients is held in the adult Centre.

The CCC runs separate adult clinics for Haemophilia, for Severe and Mild bleeding disorders, for Women with bleeding disorders (including Obstetrics & Gynaecology), telephone clinics, and joint clinics for HIV / haemophilia, Orthopaedics / haemophilia, HCV/ haemophilia (including a nurse-led fibroscan clinic).

b. your roles and responsibilities at St Thomas's at that time.

I was Consultant Haematologist, Haemophilia Comprehensive Care Centre Director, and Clinical Lead for Haemostasis and Thrombosis at the Trust.

165. Please outline the treatments provided to patients with bleeding disorders at St Thomas's at the time that you stopped working there.

The majority of patients with severe Haemophilia A and B were established on self- or family member- infused prophylaxis with recombinant FVIII or IX, and therefore received their product direct from the manufacturer via third-party home delivery companies. Most reported their factor usage and any breakthrough bleeds on the NHD Haemtrak system operated on their home computers.

A small number of patients with Haemophilia A were treated with heat / SD treated high purity plasma-derived FVIII due to personal preference, or past immune tolerance treatment for inhibitors.

Individuals with inhibitors who failed or declined immune tolerance treatment were provided with bypassing therapy rVII (novoseven or FEIBA) via the centre.

Individuals with severe VWD were treated with heat / SD plasma-derived VWF-rich concentrates (Wilate). Individuals with severe fibrinogen disorders were treated with pasteurised plasma-derived Fibrinogen Concentrate (Riastap). Concentrates are also available for rare disorders.

DDAVP / Tranexamic Acid are widely used in mild bleeding disorders.

166. Please describe how, in recent years, you typically obtained your patients' consent to treatment. In particular:

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

Patients were carefully briefed by CCC team clinicians about any risks or side effects that may occur due to treatment. The main such risk is that an inhibitor develops; this can happen early in treatment or after many years of successful treatment, Patients are instructed to report any change in the response to treatment that might signify inhibitor development.

The theoretical risks of infection from plasma-derived factor concentrates are fully explained to their recipients, along with an account of the safety steps taken to avoid HIV, HCV, HBV and prion diseases.

Patients who receive recombinant products are given a short account of the history of blood-borne infection, chiefly to reassure, but also to make sure they never accept routine treatment with a plasma-derived form elsewhere.

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

Side-effects of recombinant concentrates are vanishingly rare. When starting a new treatment, individuals are informed that rare allergic responses can occur, and to report them if they do. Some rarely used concentrates (e.g. FXI) carry a risk of thrombosis – if so, the patient is informed that we usually modify the dose to avoid this (FXI is not used outside hospital).

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

The risks of not treating bleeds promptly in severe haemophilia is emphasized from the outset of therapy and reinforced by all members of the multidisciplinary team. Close personal attention to all aspects of care is the particular skill and value of haemophilia nurses, with the Centre physiotherapist also having a central role integrating the message with regular musculoskeletal assessments.

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

See the answer to **165c** above. We were also able to demonstrate to our patients, through our data resulting from regular and complete musculoskeletal assessments, that due to prophylactic treatment, all of our young patients (under 25) had maintained completely normal joint and musculoskeletal function.

167. Did you, in recent years, routinely take blood samples from patients attending St Thomas's? If so, what information did you provide to patients about the purposes for which the samples are being taken? Did you obtain patients' consent to the storage and use of the samples and if so how and was that recorded?

All our patients with severe haemophilia were aware that they would have regular blood tests (at least once a year) to detect the development of inhibitors. Individuals with moderate haemophilia were screened for inhibitors if they had been exposed to factor, for example around surgery. At the same time routine testing for anaemia and assessment of renal function was done. Hepatic function and markers were tested regularly at the joint HCV clinic. Viral serological testing was not done routinely except for yearly review of individuals: molecular testing for viral load during regular assessments at the joint HIV and HCV clinics were done to

reveal any development of drug resistance. At all times the patients were kept informed of the testing and its rationale and gave valid verbal consent recorded in their clinical notes. None of these samples were stored or used for any other purpose than the analysis in question.

DNA mutation analysis to discover the cause of genetic haemophilia and other conditions is usually only performed at the outset of care, after careful counselling. Because of the reproductive implications of such testing, and because it is a legal obligation to store the DNA obtained, detailed written consent is obtained for molecular testing, and the laboratory will not accept samples without the consent form, which is filed in the laboratory.

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

See **Q 167** above. Consent to fibroscan examinations and hepatic ultrasound in HCV clinic patients were also obtained by the operator and recorded in the patients notes.

169. How many current patients at St Thomas's (at the time you stopped working there)

(a) were infected with HIV through blood products;

To the best of my recollection – 50;

(b) were infected with HCV through blood products;

To the best of my recollection – 175

(c) were infected with HBV through blood products;

To the best of my recollection – 0

(d) were co-infected with HIV and HCV through blood products?

To the best of my recollection – 50

170. What if any involvement did you/St Thomas's have in the treatment of St Thomas's patients for HIV and/or HCV and/or HBV in recent years? Were there multidisciplinary clinics (e.g. haematology and hepatology), and if not would such arrangements have been feasible and beneficial?

As indicated above, there were such multidisciplinary clinics at GSTT, which were not just beneficial but essential. A consultant member of the haemophilia team (sometimes me, more often my colleague Dr Thomson) and the senior member of the nursing team responsible for fibro-scanning would attend the HCV clinic with Dr Terry Wong: and a consultant (as above) attended the HIV clinic with Dr Ranjababu Kulasegaram.

171. What if any psychological services were available at St Thomas's in recent years? Did you have a psychologist as part of the staff team? Was there psychological support specifically for those infected with HIV and/or hepatitis in consequence of infected blood products?

The Haemophilia CCC has had longstanding and extremely valuable input from the Department of Clinical Psychology at GSTT. Several members of the team were attached to the CCC on a rotational basis. Most of their work involved patients affected by HIV and HCV, but the psychological impact of a severe lifelong inherited bleeding disorder doesn't stop there.

72. What if any other support services were available at St Thomas's in recent years?

A complementary therapist provides a regular clinic for the many patients that find her work helpful.

For some older patients who depend on orthotic footwear we have an expert on site Surgical Appliances department who works in consultation with the CCC Physiotherapist.

Social Work support is no longer provided on site at acute hospitals, but the CCC both liaises with, and recommends patients consult, local authority based social work support.

173. What was the impact of the infection of patients with HIV and/or hepatitis through blood products:

a. upon patients at (a) the Centre and (b) St Thomas's (without identifying any individual patient);

As described above, the early impact of HIV at St George's on patients was lethal for some and terrifying for nearly everyone (including doctors). It must have been similar at St Thomas's, but I wasn't there. Later, as therapy evolved, it became 'life-changing' for all affected patients: the lives they thought they would have turned out to be different. With HCV, in a way the impact has been reversed: it is now, 35 to 50 years later at St Thomas's, that the legacy of cirrhosis and hepatoma is being expressed, after many years of malaise and lives put out of joint.

b. the ways in which decisions about treatment and care were taken, andtreatment and care were provided, at (a) the Centre and (b) St Thomas's?

I can really only speak for the St George's Centre because the ways decisions about treatment and care were made, not just in haemophilia but across the entire field of medicine, were changed utterly, and over a very short time, by AIDS. Concepts such as counselling, particularly pre-test counselling and patient autonomy in treatment choice and consent, did not exist in practice pre-AIDS. The experience of AIDS demolished the old paternalistic model of medical decision-making forever. Blood contamination resulted in concepts such as Patient Safety and Clinical Governance to enter the arena.

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

a. change or influence your professional practice and approach and if so how?

As noted above, I have always been as honest as I could be with patients. Obtaining truly valid consent to non-surgical treatment and testing, particularly when the results of such a treatment or test could have existential import to the patient, I have come to see as an equally important aspect of honest practice. It was the AIDS epidemic and the skills of counsellors that taught me that.

The experience of travelling alongside haemophilia patients battling these terrible iatrogenic diseases led to my deciding on a late move to a CCC that would allow me to research novel therapies that could eliminate exposure to blood products in haemophilia altogether. I hope to have helped that along a bit, in concert with many others.

b. change or influence the practice and approach of your colleagues at (a) the Centre and (b) St Thomas's and if so how?

It evidently influenced their practice and approach of valid consent in the same way.

c. change or influence, in recent years, the way in which haemophilia

care was provided at (a) the Centre and (b) St Thomas's and if so how?

The two departments now form (with Lewisham) an integrated network of haemophilia provision in South London, so that St George's haemophilia patients have access to elements of CCC care, resulting in true shared care of children with haemophilia.

Section 13: Other Issues

175. 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.

To the best of my recollection there have never been any such complaints to any of the named bodies, or others, originating from my work either at St George's or Guy's & St Thomas's.

176. 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.

I do not believe that there are any other matters of relevance not already answered above.

Statement of Truth

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

Signed: ... GRO-C

Date: 9th NOV 2020