Witness Name: Dr Angela Thomas
Statement No.1: WITN4741001
Exhibits: WITN4741002-14
Dated: 12 March 2021

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF PROFESSOR ANGELA THOMAS

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 16 November 2020.

I, Professor Angela Thomas, will say as follows: -

Section 1: Introduction

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

1.1. Name: Angela Eleine Thomas
1.2. Address: GRO-C Edinburgh, GRO-C
1.3. Date of birth: GRO-C 1957
1.4. Professional qualifications: MB BS (Honours in Pathology) (London) 1980; MRCP (UK) 1983; MRCPath 1988; FRCP Edin 1994; PhD (London) 1995; FRCPCH 1996 - 2017; FRCPath 1997

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

2.1 August 1980-February 1981: Surgical House Officer Professorial Surgical Unit, St Bartholomew's Hospital, London. Responsible for clerking admissions to the ward, looking after in patients, assisting with surgery and undertaking emergency, surgical on call. Rota 3 in 5 (132 hours per week)

2.2 February 1981-August 1981: Medical House Office to Dr Ferguson, Northampton General Hospital, Northampton. Responsible for clerking planned and emergency admissions to the ward and caring for in patients. Participated in a 2 in 5 emergency on call rota (91 hours per week)

2.3 September 1981-October 1981: Locum appointment as Senior House officer for cardiac unit at the Brook General Hospital, Greenwich Health Authority. General inpatient duties and assisting with invasive cardiac procedures such as pacing. On call for cardiac service 1 in 3.

2.4 November 1981 - June 1982: Senior House Officer Thoracic Medicine, South Western Hospital, Stockwell and St Thomas's Hospital London. In patient care at the South Western Hospital and emergency department duties at St Thomas's Hospital. Rota 1 in 2 (104 hours per week)

2.5 June 1982-June 1983: Senior House Officer Medical rotation at St Bartholomew's Hospital, London. Four months general medicine at St Leonard's Hospital, Hackney under Prof Dame Parveen Kumar; 4 months oncology at St Bartholomew's Hospital under Professor Andrew Lister and 4 months gastroenterology at St Bartholomew's Hospital under Professor Sir Tony Dawson. In all posts I cared for in patients with general medical or specific medical problems according to rotation, outpatient duties and medical on call of between 1 in 5 to 2 in 5.

2.6 July 1983-July 1984: Medical Registrar in general medicine and gastroenterology at Greenwich District Hospital, Greenwich Health Authority. I cared for patients with general medical or specific medical problems according to placement, outpatient duties and medical on call of 1 in 4.

2.7 July 1984-December 1984: Haematology Senior House Officer, Royal Free Hospital, London.

2.8 January 1985-May 1986: Haematology Registrar, Royal Free Hospital, London. During my time at the Royal Free Hospital I rotated through different disciplines in haematology including malignant haematology and bone marrow transplantation, including children, with Professor Victor Hoffbrand and Professor Grant Prentice; Bleeding and thrombotic disorders with Dr Peter Kernoff and Professor Ted Tuddenham; benign haematology, morphology, laboratory and blood transfusion with Dr Sue Knowles. All posts included inpatient and outpatient care and haematology on call.

2.9 June 1986-July1989: Senior Registrar in Haematology St Bartholomew's Hospital, London working with Dr John Amos, Professor Alan Waters, Professor Mike Murphy, Dr Adrian Stephens and Professor Andrew Lister. Rotated through all disciplines of haematology apart from congenital bleeding disorders.

2.10 August 1989 - July 1992 Rayne Institute initially Charing Cross Hospital then lab moved to University College Hospital. PhD Thesis: Genetic Variation at the α and β fibrinogen loci and its association with plasma fibrinogen levels: ethnic differences and environmental interactions. During this time I had 2 sessions for clinical work, continuing one haematology clinic per week initially at Charing Cross Hospital and then subsequently at UCH. The clinics involved care of patients with general, malignant and coagulation haematological problems.

2.11 August 1992-December 1992: lecturer in Haematology Charing Cross Hospital covering all aspects of haematological care.

2.12 January 1993-June 2017: Consultant Paediatric Haematologist, Royal Hospital for Sick Children, Edinburgh. This post included both in-patient and out-patient management of children with a wide range of haematological disorders both benign and malignant. Inpatient care was mainly devoted to those with acute leukaemia or immune dysfunction. The department is recognised as a Children's Cancer and Leukaemia Group Centre. I provided a clinical neonatal haematology advisory service at the Royal Infirmary and saw paediatric patients with bleeding and thrombotic disorders at a weekly clinic at the Edinburgh Haemophilia Comprehensive Care Centre. Professor Ludlam was the Director of the Haemophilia Centre at that time, but as I had responsibility for paediatric patients, I was designated a co-director with responsibility for the clinical paediatric service. I became Director of Haemophilia Centre from the time of Professor Ludlam's retirement at the end of December 2011 until June 14th 2017 with responsibility for administrative aspects of the service and in addition, the clinical paediatric service. I had 1 session per week for this responsibility. I was lead clinician for the integrated haematology/biochemistry laboratory at RHSC (April 2000) and was head of the haematology laboratory before that (Jan 1993-March 2000). The haematology laboratory has Clinical Pathology Accreditation for a combined paediatric haematology and biochemistry service and is recognised for training by the Health Professions' Council.

2.13 August 2015: I was made Honorary Professor University of Edinburgh, College of Medicine and Veterinary Medicine.

2.14 Medicines Regulation

In addition to my clinical post, I have 19 years' experience in the licensing and regulation of medicines, with particular expertise in the field of vaccines, biological medicines and advanced therapies.

2.15 Membership of committees involved in regulation:

*denotes Ministerial appointment

**Commission on Human Medicines November 2005 – December 2018*
Vice-Chair January 2015 - December 2018

Chair CHM Vaccines and Biologicals Expert Advisory Group Nov 2005 – May 2013
Advises on the quality, safety and efficacy of biological products including vaccines and advanced therapies.

Chair CHM Clinical Trials, Vaccines and Biologicals Expert Advisory Group May 2013-Dec 2018

At my request, the Clinical Trials group and the BVEAG merged as most products in the high risk trials were biologicals and the quality and after aspects of the products required critical assessment before the trials could proceed.

CHM Oncology and Haematology Expert Advisory Group
Vice-chair 2010 – 2013, July 2014-December 2014; acting chair 2013-July 2014 and from Jan 2019 - September 2020; currently member

National Emergency Stockpile Quality Panel (DoH and Ministry of Defence) April 2010-December 2018
Advises the Emergency Preparedness Group of the Department of Health regarding UK Medicines Strategic Stockpile Expiry

Chair Transmissible Spongiform Encephalopathies ad hoc group, July 2010
To review the Commission on Human Medicines position regarding blood products and vCJD and advise on safety of plasma supply and of manufacturing processes and facilities.

**Chair Regulatory Oversight Committee April 2009-2013*
Oversees conflicts or potential conflicts of interest between the Health Protection Agency and National Institute for Biological Controls and Standards

**Committee on Safety of Medicine Jan 2002 – October 2005*
Biologicals subcommittee, vice-chair September 2003 – October 2005
HRT working party to October 2005
GTAC/CSM working party, chair 2003-2004
Medicines Consolidation Legislation working group 2011

European Medicines Agency:
Advisor to Haematology Oncology Special Advisory Group from 2003
Chair of ad hoc Haematology Special Advisory Groups from December 2009-January 2020.

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

3.1 Member of the British Society for Haematology ?1994-present

- Paediatric Subcommittee of British Society for Haematology ?2000-2011
- Scientific Secretary from April 2002
- Chairman from April 2004-2010
- President Elect April 2011-2012
- President April 2012- April 2013

No official position now; simply a member

3.2 Member UKHCDO 1993 until June 2017

- Paediatric Subcommittee 2000 – 2004; 2009-2012
- Treasurer March 2004 - November 2009
  As treasurer I was responsible for the finances of the association, collecting of subs, payment of expenses and ensuring that the accounts were correct and filed on time with the Charity Commission.

4. Please confirm whether you have provided evidence to, or have been involved in, any other inquiries, investigations, criminal or civil litigation i n relation to human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Creutzfeldt-Jakob disease ("vCJD") in blood and/or blood products. Please provide details of your involvement and copies of any statements or reports which you provided.

4.1 I have had no involvement in any previous inquiries, investigations, criminal or civil litigations as described.

5. In relation to each section that follows, please consider whether you have any information about the decisions/policies/care provided at the Royal Infirmary of Edinburgh prior to you taking up your position i n 1993. If you do, please set that information out under the relevant section below.

5.1 I have no information about the decisions/policies/care provided at the Royal Infirmary of Edinburgh prior to my taking up my position on 1st January 1993.

Section 2: Decisions and actions of the Haemophilia and Thrombosis Centre at the Royal Infirmary of Edinburgh (RIOE)

6. Please describe the roles, functions and responsibilities of the RIOE during the time that you worked there. Please provide an account of the RIOE history, its establishment and its activities during this time.

6.1 The Haemophilia Centre was part of the RIOE at the Lauriston Place site when I started my post in Edinburgh in 1993. The RIOE, both the old RIOE and the new RIOE at Little France, is a hospital for all aspects of adult care. The Haemophilia Centre is run as an outpatient and day care centre for adults; for children it runs predominantly as an outpatient facility although some children were brought for initial assessment and advice out with clinic times. Inpatient care for adult patients with haemophilia was provided at the RIOE while for children it was provided at the Royal Hospital for Sick Children (RHSC). Emergency assessment was also carried out through the A&E department at the RHSC. In January 2002, the new RIOE at Little France opened and the Haemophilia Centre transferred there at some point after that and the move of all the hospital facilities was completed in 2003. As stated above, provision of care was as for the Lauriston site.

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

7.1 Professor Christopher Ludlam, Haemophilia Centre Director until December 2011, was responsible for the administration of the centre and the clinical care of adults with coagulation disorders. He also ran the clinical trials.

7.2 Dr Rosie Dennis was an associate specialist at the Centre until April 2017. She was responsible for the clinical care of the adults but also assessed children who presented to the haemophilia centre out with formal outpatient clinic times.

7.3 Dr Janet Andrews was not a haematologist but was undertaking a specific research project involving clinical joint assessment. I do not know what type of contract she held; she was not a senior colleague.

7.4 Sister Billie Reynolds Lead nurse for the haemophilia Centre. Her post involved assessing patients and giving treatment prescribed by one of the haemophilia medical staff; teaching patients and parents/carers about haemophilia and how to give home treatment including intravenous treatment; monitoring stock and stock control.

7.5 Staff Nurse Susan Hook (Trainor at that time) as for Billie Reynolds. She later became a Charge Nurse - then as Hook - and then went on to become a nurse practitioner. In between her post as Staff Nurse and Charge Nurse she worked in the cell separator unit at the Royal Infirmary. Her duties were similar to those of Billie Reynolds but at a more junior level until she became a charge nurse and then nurse practitioner. As a charge nurse and nurse practitioner, she was line manager at the Haemophilia Centre for the nursing staff and some of the other staff, including operational managers, working with data capture of the patients' treatment and factor usage. This was in addition to her clinical duties. Operational managers were appointed at haemophilia centres to coordinate product purchase and usage in 2003.

7.6 Staff Nurse Irma Shea: Her post involved assessing patients and giving treatment prescribed by one of the haemophilia medical staff; teaching patients and parents/carers about haemophilia and how to give home treatment including intravenous treatment.

7.7 Dr Lishel Horne was a Consultant Haematologist and responsible for the clinical care of adult patients with coagulation disorders.

7.8 Dr Julia Anderson was a Consultant Haematologist and responsible for the clinical care adult patients with coagulation disorders.

7.9 Dr Pamala Kanagasabapathy was a Consultant Haematologist who replaced Dr Horne for a couple of years before moving to another post at St George's Hospital London. She was responsible for the clinical care of adult patients with coagulation disorders.

7.10 Dr Ryan Rodgers, Consultant Haematologist, was responsible for the clinical care of adults patients with coagulation disorders. I think he was appointed in 2015. Dr Rodgers took on the post of Haemophilia Centre Director after my retirement in June 2017.

8. Please describe:

a. your role and responsibilities at the RIOE and how, if applicable, this changed over time;

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

8.1 My association with the RIOE was as a Consultant Paediatric Haematologist responsible for the clinical care of paediatric patients (from birth to 18 years of age) with coagulation disorders. These were predominantly congenital bleeding disorders but I did have some patients with congenital thrombotic disorders. Clinical care included the participation in clinical trials where appropriate. As I was not allowed to have any interests of any kind with Pharma due to my position on the CHM, I was never the lead investigator for any of the trials from 2003 onwards. I instigated a programme of prophylaxis for those patients with severe haemophilia and/or a severe bleeding type. I also promoted home treatment and through the nursing staff's expertise, ensured that families were taught and supported to enable them to do this safely. All inpatient work with was undertaken at the Royal Hospital for Sick Children in Edinburgh. From January 2012, I became the Haemophilia Centre Director for the administrative side and thus oversaw the stock management and general running of the centre. I was not a line manager for any of the staff. I did not look after any of the adult patients and was not involved in their treatment strategy. I had no patients under my care with HIV or Hepatitis C. I ensured that the children were offered vaccination against hepatitis A and B at the appropriate ages.

9. Professor Ludlam's evidence to the Penrose Inquiry indicated that you were appointed primarily for the care of children at the RIOE from 1993 onwards [PRSE0006014 page 23 line 19]. Is this correct? If not, when were you appointed primarily to provide the care of children at the RIOE.

9.1 Yes, this is correct.

10. To the best of your ability, can you provide details of how your role operated alongside that of Professor Ludlam's at the RIOE in the care of children. In answering this question please consider what roles you were responsible for, and what required collaboration, if any, with Professor Ludlam. Please provide examples and details where possible.

10.1 I had prime responsibility for the clinical care of the children with congenital coagulation disorders. I would occasionally cover the haemophilia centre on call and Professor Ludlam would occasionally cover for my patients on call. I would discuss clinical management problems with Professor Ludlam, such as surgical management of patients and patients with inhibitors. I would inform him if I needed a specific product such as rVIIa for a patient with inhibitors or if I planned to change standard practice such as develop home treatment, introduce prophylactic therapy or consider participating in a trial. Professor Ludlam too would inform me if there was a trial involving children that he thought I might like to consider. Specific examples are set out below.

10.2 patient who had developed factor VIII inhibitors required an indwelling intravenous catheter and thus an operation. I wanted to use rVIIa cover and discussed this with Professor Ludlam who sanctioned the provision of the rVIIa.

10.3 Professor Ludlam told me of a trial of recombinant factor IX (rFIX) in surgical patients with haemophilia B and I recruited a patient to this trial. The patient would otherwise have been given a plasma derived product.

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

11.1 I do not know how many patients in total there were but to be a Comprehensive Care Centre at that time, 40 patients with severe bleeding disorders had to be registered. I have no knowledge of the numbers of adult patients who were registered. In terms of paediatric patients, I had about 10-15 with severe bleeding disorders. I also looked after patients with milder bleeding conditions which included mild haemophilia A and B, other coagulation factor defects such as haemophilia C (factor IX deficiency) and patients with von Willebrand Disease.

12. To the best of your knowledge, what decisions and actions were taken, and what policies were formulated, by the RIOE, 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?

12a.1 On starting my post, the majority of paediatric patients were either using the high purity SNBTS FVIII product or moved from their previous product as part of a trial as they needed treatment. By 1993, Scottish and Northern Ireland Haemophilia Centre Directors had completed their previously untreated patient (PUP) study of SNBTS factor VIII concentrate, which showed that no patient had developed abnormal liver function tests or antibodies to HCV. This product was produced locally, with plasma from Scottish donors, and results showed no transmission of known adventitious agents and was thus the treatment of

choice for the paediatric patients with haemophilia A. The few patients I looked after with Haemophilia B used a heat treated factor IX SNBTS product and then moved to recombinant factor IX when it was available. I cannot remember if any patient had to use Replenine in the interim.

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

12b.1 Safety was the main reason for choice of product and this was particularly in terms of transmission of adventitious agents. Consideration of inhibitor formation was also important but there was little evidence for preference of one product over another at this time. The SNBTS factors had been shown to be efficacious and safe.

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

12c.1 I am not aware of any commercial or financial considerations in choice of products for the paediatric patients.

d. What if any involvement did you have?

12d.1 There was no clinical reason to change the products that were being used or introduced as above at the time I started. There was concern about viral transmission and so I was keen to move to recombinant products when they were available. I was not involved specifically in agreeing contracts on purchase of product although I would have been involved in discussions at the Coagulation Factor Working Party (see below).

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

13.1 For the paediatric patients I remember using SNBTS high purity factor VIII and SNBTS heat-treated factor IX concentrate. For patients with inhibitors, I used an activated prothrombin complex concentrate and then as it became available and for those who responded well to it, rVIIa. For those with mild haemophilia A I used DDAVP which causes a rise of endogenous factor VIII which can be sustained over a couple of days. I think that the change to recombinant products was introduced from around 1996. The first product used was Recombinate (Baxter) and then Kogenate (Bayer) also marketed as Helixate (Aventis) and then later a 2nd generation product (see 17) B-domainless factor VIII, ReFacto (Wyeth) followed by the 2nd generation products Kogenate FS and Helixate NexGen. A 3rd generation product (see 17), Advate, was later used. A variety of different manufacturers was used in case of supply problems. This did occur in the early 2000s with the Bayer (and thus Aventis too) product resulting in a shortage of supply of that particular product. Recombinant factor IX was licensed in 1997 and I moved the few patients under my care to that product as soon as I was able. I cannot remember the date. I do not know what the adult patients were prescribed.

14. On 6 December 1996 you co-signed a letter to the Scottish Government regarding their unilateral decision, without consultation with Haemophilia Centre Directors, about the choice of concentrate product [LOTH0000053_045]. In your experience, was there a lack of collaboration and consultation between Haemophilia Centre Directors and the Scottish Government on product choice? If so, how did this impact the policies and approach adopted by the RIOE regarding product usage? As a result of this letter or otherwise, did the Scottish Government subsequently collaborate with Haemophilia Centre Directors on product choice?

14.1 Yes, I did sign this letter. In my experience and from memory there were regular discussions at meetings of the Coagulation Factor Working Party which included the Haemophilia Centre Directors, SNBTS and representatives of the Scottish Office Department of Health. At these meetings, use of products as well as volume and trends of use were discussed, along with choice of products. I do not remember other incidents of this sort where a unilateral decision on product choice was made by the Scottish Office of the UK Government or the Scottish Government after Devolution in 1999.

15. What was the relationship between the RIOE and the pharmaceutical companies manufacturing/supplying blood products? What influence did that relationship have on the RIOE decisions and actions?

15.1 I was not involved in individual discussions with the pharmaceutical companies over purchase of product.

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

16.1 As far as I am aware, the Haemophilia Directors of Scotland and Northern Ireland met regularly, several times a year, to discuss management and treatment of patients with haemophilia. I cannot remember if these meetings were separate from the Coagulation Factor Working Party meetings but it may be that they preceded them in some or all instances. In 2003, as Co-chairs of the Haemophilia Directors of Scotland and Northern Ireland, Professor Lowe and Professor Ludlam met with the Chief Medical Officer for Scotland to request that the NHS in Scotland develop a procedure to replace SNBTS factor concentrates progressively with recombinant concentrates. This was agreed and a consortium established for this purpose. The main concern was safety and thus transfer to recombinant products, with the individual patient's agreement, was offered as such products became available for use. It was recognised that some patients did not want to change products and these wishes were accommodated as far as possible. Thus the great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK.

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

17.1 For paediatric patients, the change was predominantly from high purity SNBTS factor VIII to one of 3 different manufactured recombinant factor VIII products. The older children were prescribed Recombinate and the younger children Kogenate or Helixate (the same product but marketed under a different name by the two companies concerned) as the latter was made up in a smaller volume and thus more suitable for smaller children. When ReFacto, a 2nd-generation product, was available as this was albumin free, some children were also prescribed this product. I cannot remember whether this was new patients or whether some children were transferred from an earlier generation product. I tried to ensure that where more than one child was affected in a family, the brothers were on the same product. Other 2nd generation products were used which did not contain any human albumin - Helixate NexGen and Kogenate FS - and the paediatric patients on the equivalent 1st generation product were transferred to these. Advate, a third-generation rFVIII product, that is a product manufactured without additional human or animal plasma proteins, became available and some paediatric patients were transferred to this or commenced on this at their first treatment. For children with Haemophilia B, transfer to recombinant Factor IX (BeneFIX) was made once the product was available and all newly diagnosed patients were given this product. I do not have information about the adult patients.

18. What were, in your view, the advantages and disadvantages of alternative treatments? What use did the RIOE make of them? 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?

18.1 DDAVP was the treatment of choice for paediatric patients with mild Haemophilia A who required treatment for only a few days. Tranexamic acid was often prescribed in addition to DDAVP or factor replacement therapy for patients with all severities of haemophilia to help stabilise the clot, particularly helpful for mucosal bleeding such as nose bleeds, and reduce the use of factor concentrate.

19. The attached draft minutes from a meeting of representatives of Haemophilia Directors, Health Care Purchasers, Health Care Providers and the Scottish Office held on 17 February 1997 indicates that '...commercial factor concentrate therapy has previously been necessary in Scotland because of occasional shortfalls of SNBTS factor VIII and IX' [BART0002136]. What was the policy and approach adopted by you and/or the RIOE as a result of any shortfall in SNBTS factor VIII and IX? What product was used by you and/or the RIOE in the event of SNBTS factor VIII and IX shortage?

19.1 As far as I am aware, the children were prioritised not to change product. I do not remember any change in product for them apart from to recombinant factor concentrate. I do not know what the policy was for the adults.

20. What was the RIOE policy and approach 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?

20a.1 I do not know what the policy was for the adult patients. For the paediatric patients, cryoprecipitate was not used for the treatment of Haemophilia A. I cannot remember if I ever prescribed it for patients with severe von Willebrand Disease (vWD); it is a source of von Willebrand Factor. Many patients with VWD are managed with DDAVP and tranexamic acid and that was my treatment of choice. Patients with Type 2b vWD should not be given DDAVP; I had one patient with this particular variant but I cannot remember if I ever prescribed cryoprecipitate for him; I don't think I did.

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

20b.1 Not applicable

21. What was the RIOE policy and approach in relation to prophylactic treatment? Did the policy and approach change over time and if so how?

21.1 Soon after I started in January 1993, there were reports in the literature of successful prophylactic treatment for preventing bleeds in children with severe Haemophilia A. I started to introduce this into my practice probably during 1994. Patients were identified initially using the criteria of frequency of bleeds and ability to give factor intravenously at home. A training programme was put in place and delivered by the experienced nursing staff who would 'sign off' a family when they were satisfied that the factor could be given safely at home. As more data became available, prophylaxis was introduced on a systematic basis either after the 2nd significant bleed or before the age to 2 years, whichever came sooner.

22. A letter from Dr Cachia to Dr Ludlam in 1996 states that the Health Board for Tayside had funded replacement recombinant therapy rather than prophylactic therapy. It notes that some parents had asked for prophylaxis for their children [LOTH0000088]. Did you have parents of patients request prophylaxis? What was the RIOE policy and approach in relation to requests made by parents for particular treatments?

22.1 I do not remember a problem with supply of factor concentrate limiting this programme. Once prophylaxis became an established treatment, I would discuss it with parents and carers soon after the diagnosis of severe

haemophilia and make a joint decision with the families when it should start and when training could begin.

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

23.1 Please see answers to questions 12,13,17,18.

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

24.1 Patients with moderate Haemophilia A or B can bleed significantly after an injury or with surgery. Treatment with factor concentrate is appropriate under these circumstances. Patients with moderate Haemophilia A do not respond to DDAVP. Patients with mild haemophilia A were mostly given DDAVP as first line therapy. If the bleeding post injury or with surgery continued more than a few days, then factor concentrate would be needed as endogenous stores of fact VIII are exhausted after a few days and/or the side effects of DDAVP such as sodium and water retention become significant.

25. The attached minutes identify that 'severe [haemophilia] patients in the east tended to use more concentrate than severe [haemophilia] patients in the west' [GRAM0000120]. To the best of your knowledge, was this the case? Suggested reasons for the variance are detailed in the minutes. Do you agree with these? If not, please provide details as to the reasons you believe there was a variance.

25.1 From the records of use this was the case. I also note in document GRAM0000120, section 4, point 2 bullet point 4 that reasons are put forward to explain the differing use of factor in the East compared with the West of Scotland. These are plausible, highlight the need for more detail than the audit collected at the time and would explain the variance in use.

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

26.1 In the paediatric population, no patients were infected with HIV, HCV or HBV. Anti-bodies to human parvovirus B19 are higher in those who have received blood and blood products. In the paediatric population parvovirus is a common, self-limiting disease which may be asymptomatic and infection gives life-long immunity. Immunity against it was not routinely tested.

Section 3: Knowledge of, and response to, risk

General

27. When you began work as a consultant at the RIOE, 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?

27.1 I understood that certain viruses could be transmitted from blood and blood products and that these viruses included Hepatitis A, B and C, and HIV. I was also aware that blood donors were screened for specific viruses and other infections such as malaria and syphilis as these could also be transmitted through blood transfusion. I knew that in the UK donors whose blood was used for blood and blood products would have been screened at least twice before their blood could be used for transfusion and manufacture of blood products. Later in the 1990s, the Nucleic Acid Amplification Technology (NAT) was used for pooled plasma testing which was more sensitive. I also understood the quantal nature of virus transmission and that dilution by pooling of multiple donations does not prevent transmission. This explains why pooled plasma is a greater risk for transmission of any contaminating virus. Information was gleaned from the literature, scientific meetings, discussion with colleagues and also from my work as chair of the Biologicals and Vaccines Expert Advisory Group of the Commission on Human Medicines.

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

28.1 For the paediatric patients, initial use of product was a high purity factor VIII (Liberate, SNBTS) which was solvent-detergent treated which effectively eliminated HIV and HCV, and a heat treated SNBTS factor IX product (DEFIX). The children continued with these products and were gradually changed over to recombinant products as they became available. It was of prime importance to ensure that children received products that had been virally inactivated and thus least likely to transmit adventitious agents as they had never been exposed to the earlier blood products where transmission had occurred.

29. By the time you began work at the RIOE what was your understanding of the relative risks of infection from (i) the use of commercially supplied blood products, and (ii) the use of NHS blood products?

29.1 When I started at the RIOE I understood that the older commercially supplied blood products probably had a higher risk of transmitting infection than NHS blood products due to the pool of donors used. The NHS donors were unpaid and therefore giving blood for altruistic reasons and thus thought to be less likely to be able to transmit infections such as HCV and HIV. However, as pre donor testing became broader and more sensitive and viral inactivation of blood products was introduced, I understood that the risk differential was likely to be minimal. The paediatric patients however, were all prescribed NHS products and then recombinant products.

Hepatitis

30. When you began work as a consultant at the RIOE, what was your knowledge and understanding of the risks of the transmission of hepatitis (including hepatitis B and NANB hepatitis/hepatitis C) from blood and blood products? What were the sources of your knowledge? How did that knowledge and understanding develop over time?

30.1 As for 27.

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

31.1 As for 28. I also arranged for the children to be vaccinated against hepatitis A and B prior to treatment if possible. Note that the licence for hepatitis B vaccination allowed vaccination from birth but for Hepatitis A vaccination, the licence was from 1 year of age. Twinrix, covering both Hepatitis A and B, was licensed from 1 year of age and unless hepatitis B vaccination was needed before this, I would introduce Twinrix at 1 year of age for those who agreed after discussion. I did not treat any of the adult patients.

HIV and AIDS

32. What was your knowledge and understanding of HIV (HTLV-III) and AIDS and in particular of the risks of transmission from blood and blood products during your time working at the RIOE? What were the sources of your knowledge? How did your knowledge and understanding develop over time?

32.1 As for 27.

Response to risk

33. Did you or your colleagues at the RIOE take steps to ensure that patients were informed and educated about the risks of hepatitis and HIV? If so, what steps.

33.1 I discussed the risk of hepatitis transmission from use of Liberate (theoretical in this case as there had been no transmission in the trials - see 12a) and DEFIX, advised vaccination against Hepatitis A and B (there is not Hepatitis C vaccine) and also advised that the products had not transmitted HIV.

34. At any stage, did you or your colleagues at the RIOE revert to treatment with cryoprecipitate for some or all of the patients? If so why was this and how was it determined which patients would be offered a return to cryoprecipitate and which would not? If not, why not?

34.1 I do not know.

35. Do you consider that your decisions and actions, and those of the RIOE in response to any known or suspected risks of infection were adequate and

appropriate? If so, why? If not, please explain what you accept could or should have been done differently.

35.1 I think that actions for the paediatric population were appropriate. I cannot comment on the actions for the adult population.

36. 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?

36.1 The haemophilia community was very concerned about viral transmission from use of blood products and were seeking ways of improving safety through viral inactivation during manufacture and use of recombinant products. The UKHCDO recommended the use of recombinant products where possible.* Unfortunately, the latter were significantly more expensive and thus transfer to such products required increased funding which in Scotland was negotiated through discussions with the Scottish CMO as described in 16. It was recognised that some patients did not want to change products and these wishes were accommodated as far as possible. The great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK.

* Guidelines on the selection and use of therapeutic products to treat haemophilia and other hereditary bleeding disorders. UKHCDO. First published: 28 January 2003 [WITN4741002]

Section 4: Treatment of patients at the RIOE

Provision of information to patients

37. What information did you provide or cause to be provided (or was, to your knowledge, provided by others) to patients at the RIOE with a bleeding disorder 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.

37.1 There was a folder/booklet with generic information regarding haemophilia and its treatment given to the parents/carers of newly diagnosed paediatric patients with haemophilia and the age appropriate information for the children themselves which did include information about factor concentrate and risks of infection. The information was updated as new products became available. I informed most if not all parents, carers and patients where appropriate that they could read more about the specific product that they were being given from the Patient Information Leaflet (PIL) - the packet insert that comes with any medicine. Specific information sheets were given to patients with bleeding disorders at the RIOE regarding the risk of nvCJD. I think that paediatric patients were included but only where they had been given plasma derived

products or recombinant products that contained human albumin. I cannot be sure of the details. For those in the Liberate trial, which had already started at the time I commenced my appointment at the RHSC, an information sheet about Liberate was given to the patients but I can't remember precisely what it said.

38. 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.

38.1 In most cases there was no alternative. DDAVP and TXA were used when appropriate. I introduced a physiotherapy programme and assessment to ensure children were strong and fit to limit bleeds due to lack of conditioning. The physiotherapist from the RHSC spent some of her time with me and became expert in the physiotherapy treatment of children with bleeding disorders.

39. 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?

39.1 The senior nursing staff, Charge Nurse Hook and Staff Nurse Shea provided written information updated at least yearly and a comprehensive training programme, initially at the haemophilia centre and then in the patient's home. Once the parent(s)/carer was competent they were 'signed off' and home treatment commenced. Home visits were arranged to assess how treatment was going and as a check from time to time. Home delivery was commenced in May 2007 whereby parents/carers along with the medical and nursing staff agreed what volume of factor was required and how frequently it would be delivered and the parents kept records of use. The agreed amount of factor was delivered to the home on a regular basis to ease the burden of caring for a child with haemophilia as some patients lived a significant distance from the centre.

HIV

40. By the time you began work at the RIOE had patients been informed of their HIV status? Were policies in place regarding consultation with patients to discuss AIDS or HIV (HTLV-III). Did you discuss AIDS or HIV (HTLV-III) with any of your patients?

40.1 I don't know; none of the paediatric patients was HIV positive.

41. Please provide any information you can regarding the practice at RIOE before you started work as a Consultant in relation to the following issues:

- **What if any arrangements were made at RIOE for pre-test counselling?**

- **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?**

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

- **What was the RIOE 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?**

- **What, if any, information or advice was provided to partners or family members of people who were at risk of infection with HIV or were infected with HIV?**

- **What if any arrangements were made at the RIOE for post-test counselling?**

41.1 I do not know the details for the adult patients. No paediatric patients were infected with HIV.

42. How many patients at the RIOE 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?

42.1 I was not involved in this work.

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

43.1 None of the paediatric patients had HIV. I do not know details of the management of the adult patients.

Hepatitis B

44. Were patients infected with hepatitis B informed of their infection and if so, how? What information was provided to patients infected with hepatitis B about the

infection, its significance, prognosis, treatment options and management? What if any involvement did you have in this process?

44.1 I do not now

45. How many patients at the RIOE were infected with hepatitis B?

45.1 I do not know

NANB Hepatitis/Hepatitis C

46. When did the RIOE begin testing patients for hepatitis C? How, when and by whom were patients informed of their diagnosis of hepatitis C? Were they told in person, by letter or by phone? What if any involvement did you have in this process?

46.1 Testing for Hepatitis C was available for patients at the RIOE when I started in 1993. I do not know when testing for Hepatitis C started at the Haemophilia Centre. I had no involvement of communicating results of tests to adult patients. No paediatric patient developed Hepatitis C. My normal practice would be to either tell the parent/carer the result in person at the next appointment - the results were invariably negative - or ring the result through if requested.

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

47.1 I think that the paediatric patients who were taking part in the Liberate trial had testing as part of the trial. It was routine to test for hepatitis C on a yearly basis I think. Once patients were on recombinant product, the routine testing may have been stopped but I can't remember for certain. Patients who had been on recombinant products did not have routine hepatitis C testing.

48. What steps, if any, were taken by the Centre and/or by you to ensure that all patients who had received blood products were and invited to be tested?

48.1 I do not know how many adult patients were infected

49. How many patients at the RIOE were infected with hepatitis C?

49.1 I do not have this information for adults. No paediatric patients under my care had hepatitis C

Delay/public health/other information

50. 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.

50.1 Not applicable to the paediatric patients.

51. To what extent, if at all, were public health implications of HIV, AIDS, hepatitis B, NANB hepatitis and hepatitis C taken into account, when taking decisions as to what information or advice to provide to patients or what treatment to offer patients?

51.1 I did not need to take them into account as the paediatric population were treated with concentrates free from transmission of HCV, HBV and HIV.

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

52.1 The possibility of parvovirus was discussed with some parents/carers if they asked about other infections but was not routine for the reasons given in 26. The theoretical risk of nvCJD (theoretical because there were no reports of patients with haemophilia developing nvCJD) was discussed for those who had received plasma derived or 1st generation recombinant products. For patients who had only received recombinant products discussions centred around them being at no greater risk than the general population.

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

53.1 Not applicable.

Consent

54. How often were blood samples taken from patients attending the RIOE 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?

54.1 Routine tests were taken on a yearly basis - not sure how much was stored - I think that I probably did gain consent if there was storage as I was aware from other areas of practice that consent was required for long term storage. For storage of genetic material, written information was given to parent/carer and child if appropriate and consent gained for both testing and storage of DNA for possible future use either as part of quality control or if new tests were available for the disease in question.

55. Were patients under your care or under the care of your colleagues at the RIOE 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?

55.1 No, the children were always treated with either the consent of their parents/carers or their consent once old enough. I do not remember specifically

gaining written consent - certainly not at first but later I quite probably did. The consent forms were probably kept in the notes but may also have been kept in the abbreviated notes that were maintained within the haemophilia centre.

56. 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?

56.1 No, I would tell the parents/carers what I was taking tests for. For the majority of the time I worked as a consultant, I did not record explicit consent in the notes unless it was part of a clinical trial. However in the last year or two that I was working, there was general advice for all branches of medicine to record consent in the notes and this I did.

PUPS

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

57.1 Previously untreated patients with a confirmed diagnosis of haemophilia A or B would have a treatment plan made ahead of first treatment with choice of product, dosage and testing strategy. This would be discussed with the parents/carers at the time of the plan and then at the time of the first treatment. The purest products were used as outlined in answers to questions 12,13 and 17.

Research

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

a. Describe the purpose of the research.

58a.1 Trial of Liberate SNBTS: unblinded uncontrolled study looking at the efficacy and safety of Liberate, a pdFVIII concentrate.

58a.2 Prevalence of Parvovirus antibodies in patients with haemophilia versus those without haemophilia.

58a.3 Prevalence of TT virus in different paediatric age groups and adults in different countries.

58a.4 Use of Benefix in surgical patients with haemophilia B: an uncontrolled study of use of rFIX in surgical patients.

58a.5 European Paediatric Haemophilia Study (Pednet Registry) - a European wide collection of observational data in paediatric patients with haemophilia A and B from birth.

58a.6 Immune Tolerance Therapy (ITT) trial in patients with haemophilia A and inhibitors: randomised trial of high dose versus low dose FVIII treatment.

58a.7 Home recording of factor use using a specifically programmed iPad.

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

58b.1 The trial was on going when I started my consultant post in 1993.

58b.2 The trial would have been presented to the Lothian Research and Ethics Committee and approval obtained.

58b.3 The trial would have been presented to the Lothian Research and Ethics Committee and approval obtained.

58b.4 Professor Ludlam arranged for the approval of the trial; I may have undertaken some of the paperwork.

58b.5 I gained approval for the UK as a whole at the time the study commenced in the UK. I also gained local approval through the Research and Ethics Committee Lothian.

58b.6 ITT - multi centre study - local approval through the Research and Ethics Committee Lothian.

58b.7 Home recording of factor use - multi centre study - local approval through Research and Ethics Committee Lothian.

c. Explain what your involvement was.

58c.1 Recruiting patients and gaining consent and prescribing the FVIII.

58c.2 I arranged collection of leftover plasma from blood samples from children who had had blood taken at A&E RHSC and children who had received treatment for haemophilia.

58c.3 I arranged for collection of leftover plasma from blood samples from children of all ages at RHSC who did not have haemophilia.

58c.4 Recruitment, consent, liaising with surgeon, giving treatment.

58c.5 Recruiting patients and gaining consent, collecting and entering data into computer programme. Later in the trial the data entry was undertaken by dedicated trial staff.

58c.6 Recruitment and gaining consent, supervising treatment, collecting samples and recording clinical and treatment data.

58c.7 Recruiting patients and taking consent.

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

58d.1 SNBTS

58d.2 SNBTS

58d.3 SNBTS, Dept of Medical Microbiology University of Edinburgh and the Haemophilia Centre RIOE

58d.4 Baxter

58d.5 PedNet network - https://pednet.eu

58d.6 UKHCDO and other worldwide haemophilia organisations. Trial coordinated by Professor Charlie Hay and Dr Donna diMichele (New York)

58d.7 Baxter - I think

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

58e.1 Not aware of specific funding; no funding for my participation
58e.2 Not aware of specific funding; no funding for my participation
58e.3 Not aware of specific funding; no funding for my participation
58e.4 Financial arrangements, if any, were between Baxter and Professor Ludlam. I undertook the care of the patient as part of normal clinical care.
58e.5 €275 per patient registered and for whom data were entered was paid into a dedicated paediatric haemophilia research fund with overall control through a Lothian Hospitals Trust Fund body or similar. A smaller annual sum was paid per patient in the same way until the data were collected by trial staff.
58e.6 I participated in this trial within my normal NHS clinical duties. I am not aware that there was any financial arrangement
58e.7 Baxter provided the programmed iPads for the patients. I am not aware of other funding.

f. State the number of patients involved.

58f.1 Not sure 10-15 perhaps
58f.2 Not sure
58f.3 No patients; 148 samples
58f.4 1
58f.5 15-20
58f.6 2
58f.7 <5

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

58g.1 My standard practice was to introduce the concept of the trial and explain what was involved. I would give written information and allow the parent/care or patient to have time to read the information. This may have been over a few days or even weeks. After that I would ensure any questions were answered and then ask the parent/carer or patient to sign the consent form.

58g.2 For the study on prevalence of parvovirus antibodies (2) I can't remember specifically but my standard practice was to inform parents when blood was being taken if any plasma was to be used for other tests. Information was made available in the Accident and Emergency Department at the RHSC for the time that the plasma samples were being collected. There were notices, and there may have been leaflets, explaining that any left over plasma from blood tests may be used for parvovirus antibody tests with an option to opt out. The staff in the A&E department would have been responsible for asking the parent/carer or patient.

58g.3 For the study on prevalence of TT virus I think that the same type of approach was taken but I can't remember specific details.

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.

58h.1 *Prowse C, Dow B, Pelly SJ, McIntosh E, Reading S, Lowe GD, Gibson B, Cachia P, Thomas A, Dennis R, Ludlam CA. (1998) Human parvovirus B19 infection in persons with haemophilia. Thromb Haemostas 80:351.* [WITN4741003]

58h.2 *Simmonds P, Prescott LE, Logue C, Davidson F, Thomas AE, Ludlam CA. (1999) TT virus - part of the normal flora? J Infect Dis 180: 1748-1750. [WITN4741004]*

58h.3 *Ludlam CA, Lee RJ, Prescott RJ, Andrews J, Kirk E, Thomas AE, Chalmers E, Lowe GDO. (On behalf of haemophilia directors of Scotland) Haemophilia care in Scotland 1980-1994. (2000) Demographic characteristics, hospital admissions and causes of death. Haemophilia 6: 494-503 [WITN4741005]*

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

59.1 No, express consent was always obtained and consent forms signed.

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

60.1 No data were used without express consent.

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

61.1 No data were used without express consent.

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

Papers

62.1 *The impact of nursing practice on the outcome of central venous access devices in children with haemophilia. Khair K, Ranta S, Thomas A, Lindvall K (2017) Haemophilia 23: e276-e281.* [WITN4741006]

62.2 *Bleeding before prophylaxis in severe haemophilia; paradigm shift over 2 decades. Nijdam A, Altisent C, Carcao MD, Cid AR, Claeyssens-Donadel S,*

Kurnik K, Ljung R, Nolan B, Petrini P, Platokouki H, Rafowicz, Thomas AE, Fischer K. (2015) Haematologica 100: e84-e8 [WITN4741007]

62.3 *FVIII Product Brands and Inhibitors in Children with Severe Hemophilia A. Gouw SC, van Bom JG, Ljung R, Escuriola C, Cid AR, Claeyssens-Donadel S, van Geet C, Kenet G, Mäkipernaa A, Molinari AG, Muntean W, Kobelt R, Rivard G, Santagostino E, Thomas A, van den Berg M for the PedNet and Rodin Study Group (2013). N Engl J Med 368: 231-239* [WITN4741008]

62.4 *European principles of haemophilia care. Colvin BT, Astermark J, Fischer K, Gringeri A, Lassila R, Schramm W, Thomas A, Ingerslev J. (2008) Haemophlia 14(2) 361-378* [HSOC0021039]

62.5 *Early factor VIII exposure and subsequent inhibitor development in children with severe haemophilia A. Chalmers EA, Brown SA, Keeling D, Leisner R, Richards M, Stirling D, Thomas A, Vidler V, Williams MD, Young D. (2007) Haemophilia 13(2) 149-155* [WITN4741009]

62.6 *Chalmers EA, Williams MD, Richards M, Brown SA, Liesner R, Thomas A, Vidler V, Pasi KJ, Hill FG; The Paediatric Working Party of UKHCDO (2005) Management of neonates with inherited bleeding disorders--a survey of current UK practice. Haemophilia 11(2): 186-187* [WITN4741010]

62.7 *Ludlam CA, Lee RJ, Prescott RJ, Andrews J, Kirk E, Thomas AE, Chalmers E, Lowe GDO. (On behalf of haemophilia directors of Scotland) Haemophilia care in Scotland 1980-1994. (2000) Demographic characteristics, hospital admissions and causes of death. Haemophilia 6: 494-503* [WITN4741005]

62.8 *Simmonds P, Prescott LE, Logue C, Davidson F, Thomas AE, Ludlam CA. (1999) TT virus - part of the normal flora? J Infect Dis 180: 1748-1750* [WITN4741004]

62.9 *Prowse C, Dow B, Pelly SJ, McIntosh E, Reading S, Lowe GD, Gibson B, Cachia P, Thomas A, Dennis R, Ludlam CA. (1998) Human parvovirus B19 infection in persons with haemophilia. Thromb Haemostas 80:351* [WITN4741003]

Chapters

62.10 *'The neonate with haemophilia' in Textbook of Haemophilia, editors Lee, Berntorp, Hoots, publishers Blackwells;* 1st edition 2004 [WITN4741011], 2nd edition 2010 [WITN4741012] and 3rd edition 2014 [WITN4741013]

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

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

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

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

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

63.1 No paediatric patients developed HIV/AIDS.

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

64.1 Not applicable.

65. How was the care and treatment of patients with hepatitis B managed at the RIOE? 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?

65.1 No paediatric patients developed hepatitis B.

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

66.1 Not applicable.

67. Prior to your appointment, do you have any knowledge as to how the care and treatment of patients with NANB hepatitis was managed at the RIOE? 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?

67.1 No, I have no knowledge of that.

68. How was the care and treatment of patients with hepatitis C managed at the RIOE? 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?

68.1 No paediatric patients developed Hepatitis C.

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

69.1 Not applicable.

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

70.1 No paediatric patients were infected with HIV or hepatitis.

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

71.1 Not applicable.

72. Did the RIOE 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?

72.1 I don't know.

73. What (if any) difficulties did you/the RIOE encounter in obtaining sufficient funding for the treatment of people who had been infected with HIV and/or hepatitis C?

73.1 Not applicable.

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

74.1 None.

Recombinant

75. A letter from Dr Cachia to Dr Ludlam in 1996 discusses the funding of recombinant by Tayside Health Board. The letter records your advice regarding the treatment of a particular patient [LOTH0000088].

a. Did you provide guidance and opinions to other Centres about the treatment of children if requested? If so, how was this communicated?

75a.1 Yes, I did provide advice. This may have initially been verbal but normal practice would be to follow up with written advice.

b. To the best of your knowledge, what was the policy and approach adopted by the Lothian Health Board for the funding of recombinant treatment at the RIOE?

75b.1 I never had a problem obtaining recombinant factor concentrates for treatment of the children.

Records

76. What was the RIOE policy with regard to recording information on death certificates when a patient had been infected with HIV or hepatitis?

76.1 I do not know as I was not involved in the care of adult patients.

77. What were the retention policies of the RIOE in regards to medical records during the time you were practising there?

77.1 I think that records were retained indefinitely.

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

78.1 Each patient had their own set of paper notes. The haemophilia centre maintained a separate file for each patient in addition with details of treatment, factor consumption and other information. I didn't use these files very often and if so, I can't really remember why.

79. Are you aware of whether any of your senior colleagues maintained separate files for some or all patients? If so, why did they do so? Where were those files located; and where are those files now?

79.1 As for 78. I think the files were kept as a short file of essential information so that if a patient's notes couldn't be found, the information was easily available.

80. 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 RIOE? If so, why, what information and where is that information held now?

80.1 The paediatric patients had a set of paediatric notes at the Royal Hospital for Sick Children Edinburgh. I ensured that a copy of all correspondence was present in both sets of notes but in patient or out patient notes were not duplicated. Just as I was leaving, an electronic notes system was being introduced. I never held any records in my home.

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

81.1 No, I do not hold any records.

Section 5: UKHCDO

82. Please describe your involvement with UKHCDO (including any of its working parties, committees or groups), including how you came to become Treasurer of the UKHCDO.

82.1 I became a member of the UKHCDO sometime around 1994. Although Professor Ludlam was the Director of the Haemophilia Centre at that time, as I had responsibility for paediatric patients, I was designated a co-director so that I could attend the UKHCDO meetings to allow the contribution of my expertise in the treating of such a patient population. I was a member of the paediatric working group during some of that time and also the inhibitor working group but I cannot remember the dates. I became treasurer around 2004 for 3 years or so when Professor Gerry Dolan came to the end of his term. I was appointed after my name was put forward by the executive and agreed by the members.

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

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

83a.1 The United Kingdom Haemophilia Centre Doctors' Organisation is an association of medical practitioners who work within the Haemophilia Centres of England, Scotland, Northern Ireland and Wales and have an interest in the care of people with Haemophilia or other inherited bleeding disorders. The aims of the organisation are:

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

83a.2 The UKHCDO is required by the Department of Health to collect data on diagnosis, management and complications of bleeding disorders. This information was kept in the National Haemophilia Database, which was located in Oxford but moved to Manchester in 2002. I think that money was paid into the UKHCDO account from the Government for the running of the database/collection of data after I had been treasurer for about a year.

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

83b.1 There is an executive committee consisting of the chair, vice-chair, secretary and treasurer and an advisory committee consisting of the directors of the haemophilia centres around the UK. More recently the chairs of the working parties and other additional members have been included. Various working parties were set up to look into different aspects of haemophilia care as needed. They were reviewed every so often, probably triennially, to see if they should continue. They reported to the UKHCDO members at each meeting and members could write papers/guidelines to be reviewed and ratified as needed.

c. The relationships between UKHCDO and pharmaceutical companies.

83c.1 Procurement of factor concentrates: initially I think that the UKHCDO negotiated contracts with the different companies on behalf of the Haemophilia Centres in England. Haemophilia directors in Scotland agreed funding of factor with the Scottish Government and then negotiated contracts with the companies. From February 2003, tendering was undertaken through the OJEU process for the UKHCDO but Scotland I believe still negotiated separately.

- Some sponsorship for UKHCDO educational meetings.

d. How decisions were taken by UKHCDO.

83d.1 Members took decisions jointly informed by either the working party output and/or experts (possibly). Some decisions were taken by the executive alone but I can't remember precisely what these were.

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

84.1 Individual directors took information back to disseminate locally; also guidelines and advice were available on the website and through societies such as the Haemophilia Society.

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

- **the importation, purchase and selection of blood products;**
- **the manufacture of blood products;**
- **self-sufficiency;**
- **alternative treatments to factor products for patients with bleeding disorders;**
- **the risks of infection associated with the use of blood products;**
- **the sharing of information about such risks with patients and/or their families;**

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

- **heat treatment;**

- **other measures to reduce risk;**

- **vCJD exposure; and**

- **treatments for HIV and hepatitis C.**

85.1 In 1996, the UKHCDO recommended that recombinant Factor VIII was the product of choice for those with haemophilia A. I supported this and in particular for children to have recombinant products as priority. Primary considerations were the avoidance of adventitious agents and no increase in inhibitor production.

85.2 I was an author of 'The use of enhanced half-life coagulation factor concentrates in routine clinical practice: guidance from UKHCDO' published Haemophilia 2016 Jul;22(4):487-98. [WITN4741014]

85.3 No advice given re manufacture

85.4 No advice given re self sufficiency

85.5 I would have recommended or supported guidance on alternative treatments such as DDAVP and use of rVIIa in children where appropriate.

85.6 I would have recommended or supported any guidance on discussions with families regarding risks of infections associated with the use of blood products. This was part of the routine care that I delivered.

85.7 I would have recommended or supported any guidance on the sharing of information about such risks with patients and/or their families. This was part of the routine care that I delivered.

85.8 I would have recommended or supported any guidance on ensuring consent was taken for all the testing and storage of blood for treatment and for research. This was part of the routine care that I delivered.

85.9 I did not give specific advice regarding heat treatment. The recommendation at the time I started at the Haemophilia Centre was of dual inactivation of blood products; one of the inactivating steps was heat treatment.

85.10 I would have recommended or supported and guidance on use of recombinant products where possible over blood products; careful recording of products used and use of other non-blood products where possible.

85.11 In 1996 a new variant of Creutzfeldt-Jakob disease (vCJD) emerged. This supported the recommendation by the UKHCDO of use of recombinant products.

85.12 I did not advise on treatments for HCV or HIV.

Section 6: Pharmaceutical companies/medical research/clinical trials

86. On the attached declaration of personal and non-personal interests of the Committee on Safety of Medicines as at 31 December 2002, your interest with Chugai Pharma is noted at page 58 and 96 [MHRA0009363]. Please provide details of the nature of your relationship with Chugai Pharma.

86.1 Chugai Pharma paid for me to attend the British Society for Haematology Annual Scientific Meeting held in Brighton in 2002.

86.2 2001-2003: Study to examine the effects of G-CSF on neutrophil function and number in premature neonates. Funded by Chugai Pharma £9,000 over 2 years to cover consumables.

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

87.1 No.

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

88.1 2001 Study of single agent antibiotic therapy in febrile neutropenic children. Consumables funded by Wyeth Laboratories £20,000. The funding was thus non-personal. Wyeth did produce a recombinant Factor VIII product 'Recombinate' but the arm of the company that funded this study was the anti-microbial arm.

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

89.1 No.

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

90.1 No.

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

91.1 No.

92. 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.

92.1 No.

93. What regulations or requirements or guidelines were in place at the time 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?

93.1 From January 2002 until October 2005 as a member of the Committee on Safety of Medicines, all interests of any sort had to be declared: personal specific, personal non-specific, non-personal specific and non-personal non-specific. I had few interests at this time and both, as detailed above, were for attending scientific meetings but I no longer have the details. All interests were declared in the CSM Annual Reports. From October 2005, when I became a Commissioner on the Commission for Human Medicines, MHRA, a condition of appointment was that we had no personal interests in any pharmaceutical company. Any interests that did arise, which would have been non-personal, were declared as necessary during any meetings of the CHM and published in the CHM Annual Report. I have not provided any advice or held a consultancy with any pharmaceutical company involved in the manufacture and/or sale of blood products

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

94.1 SNBTS: participation in the trial of safety and efficacy of Liberate for licensing as detailed above (trial1); participation in use of an SNBTS IgG product. SNBTS is not a pharmaceutical company so this may not count. No remuneration was received.

94.2 I also recruited one patient into a trial investigating the efficacy and safety of a recombinant factor IX product in patients with haemophilia B undergoing surgery. The trial was run by Baxter in order to gain a licence for their product. I did not receive any remuneration for my participation.

94.3 I recruited patients for a trial where parents/carers or paediatric patients collected data on use of factor at home on a specially programmed iPad which

was provided by Baxter (I think). I did not receive any remuneration for this study.

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

95.1 The results from the study of patients receiving Liberate were used by SNBTS for the licensing purposes of its pdFVIII product, Liberate.

95.2 The results from the study of surgical patients with haemophilia B to which I contributed one patients were used by Baxter for licensing purposes of its recombinant FIX product Benefix.

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

96.1 Yes; there was a register kept at the Royal Hospital for Sick Children and I ensured that I made an entry whenever I had received any sponsorship.

Section 7: vCJD

97. When and in what circumstances did you become aware of the risks of transmission of vCJD associated with the use of blood and blood products?

97.1 Probably around 2003/2004 when there were reports of nvCJD being transmitted by blood transfusion. Information would have been from medical - specifically haematological - journals and probably through my work on the Committee on the Safety of Medicines and the Commission on Human Medicines.

98. The Department of Health in 1998 decided not to inform potentially exposed transfusion recipients about the possible risk of exposure to vCJD. Did you, or your colleagues at the RIOE agree with this decision?

98.1 Yes - but a letter was written saying that it was a possibility and whether they would like to know more.

99. In February of 2001 you co-authored a letter informing patients that a donor had recently been found to have vCJD who had donated plasma that had been used to make Replenate, BPL 8Y, Replenine-VF and ATIII [LOTH0000057_016]. The letter indicates that the risk of transmission of vCJD in blood products is theoretical. Did you share this view at the time? Do you still hold this view? If not, how did your knowledge and understanding develop over time?

99.1 The risk was theoretical as no patient with haemophilia had developed nvCJD dementia. In 2008, variant CJD infection was found in the spleen of a neurologically asymptomatic UK adult patient with haemophilia. The conclusion

was that it was most likely route of infection was receipt of blood products. As far as I am aware, there have been no other confirmed or suspected cases. In a systematic review of 32,441 persons in the UK who had appendicectomies showed that asymptomatic abnormal prions in the appendix tissue were found in 1 in 2,000. Therefore, the risk of infection from blood products received by patients with haemophilia is still theoretical.

100. Did you have any other involvement in decisions as to what information to provide to patients about vCJD? If so please answer the following questions:

100.1 I can't remember - children not really part of this.

a. What steps were taken to put in place a process at the RIOE for informing patients about possible exposure to vCJD?

100a.1 All UK patients with bleeding disorders treated with any UK-sourced pooled factor concentrates between 1980 and 2001 were informed that they may be at an increased risk of infection with variant Creutzfeldt-Jakob disease (vCJD)

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

100b.1 Letters were written.

c. What steps were taken to provide information to patients about the risks of vCJD?

100c.1 Letters were written.

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

100d.1 Counselling was available on request - this was offered in the letters. Counselling was from Haemophilia Centre staff.

101. What measures were put in place at the RIOE, from a public health perspective, in relation to the care and treatment of patients?

101.1 I know that there were policies regarding gastro investigations for example use of-gastroscopes. Precautions were also advised with dental instruments and dental care

Section 8: The financial support schemes

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

102.1 I had no involvement with any of the trusts or funds as I cared solely for children and young people <18 years of age.

103. To what extent, during your time at the RIOE, did staff (including you) Inform patients about the different trusts or funds?

103.1 I did not inform any patient about the funds as I had no patients under my care who were eligible. I was aware that other staff did speak to patients but have no knowledge of the details

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

104.1 I do not know specifically but assume that there was a policy and/or guidance.

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

105.1 I do not know.

106. Did the RIOE, 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.

106.1 I do not know.

107. Was the RIOE 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.

107.1 I do not know.

108. Based on your own dealings with any of the trusts or funds and/or based on your knowledge of the experiences of your patients i n 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?

108.1 I have had no dealing with the trusts or funds.

Section 9: Other Issues

109. 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.

109.1 None.

110. 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.

110.1 No other matters.

Statement of Truth

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

Signed GRO-C

Dated 12 March 2021

Table of exhibits:

Date	Notes/ Description	Exhibit number
2003	UKHCDO, Guidelines on the selection and use of therapeutic products to treat haemophilia and other hereditary bleeding disorders, Haemophilia (2003), 9, 1–23	WITN4741002
1998	C. Prowse, et al., Human parvovirus B19 infection in persons with haemophilia, (1998) Thromb Haemostas 80:351.	WITN4741003
1999	P. Simmonds, et.al., TT virus - part of the normal flora? (1999) J Infect Dis 180: 1748-1750.	WITN4741004
2000	C.A. Ludlam, et al. (On behalf of haemophilia directors of Scotland), Haemophilia care in Scotland 1980-1994. (2000) Demographic characteristics, hospital admissions and causes of death. Haemophilia 6: 494-503	WITN4741005
2017	K. Khair, S. Ranta, A. Thomas, K. Lindvall, The impact of nursing practice on the outcome of central venous access devices in children with haemophilia. (2017) Haemophilia 23: e276-e281	WITN4741006

2015	A. Nijdam, et al., Bleeding before prophylaxis in severe haemophilia; paradigm shift over 2 decades, (2015) Haematologica 100: e84-e8	WITN4741007
2013	S.C. Gouw, et al. FVIII Product Brands and Inhibitors in Children with Severe Hemophilia, 2013). N Engl J Med 368: 231-239	WITN4741008
2007	E.A. Chalmers, et al., Early factor VIII exposure and subsequent inhibitor development in children with severe haemophilia. (2007) Haemophilia 13(2) 149-155	WITN4741009
2005	E.A. Chalmers, et al., The Paediatric Working Party of UKHCDO (2005) Management of neonates with inherited bleeding disorders--a survey of current UK practice. Haemophilia 11(2): 186-187	WITN4741010
20042	A.E. Thomas & E. Chalmers, The neonate with haemophilia' in Textbook of Haemophilia, editors Lee, Berntorp, Hoots, publishers Blackwells; 1st edition 2004	WITN4741011
2010	A.E. Thomas & E. Chalmers, The neonate with haemophilia' in Textbook of Haemophilia, editors Lee, Berntorp, Hoots, publishers Blackwells; 2nd edition 2010	WITN4741012
2014	A.E. Thomas & E. Chalmers, The neonate with haemophilia' in Textbook of Haemophilia, editors Lee, Berntorp, Hoots, publishers Blackwells; 3rd edition 2014	WITN4741013
2016	P. Colins, et al. The use of enhanced half-life coagulation factor concentrates in routine clinical practice: guidance from UKHCDO' published Haemophilia 2016 Jul;22	WITN4741014