Witness Name: Professor Charles Richard Morris Hay
Statement No.: WITN3289039
Exhibits: WITN3289040 to WITN3289170
Dated: 07/10/2020

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF PROFESSOR CHARLES RICHARD MORRIS HAY

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 3 July 2020

I, Professor Charles Richard Morris Hay, will say as follows: -

Section 1: Introduction

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

1.1.Professor Charles RM Hay MD FRCP FRCPath

1.2.DOB GRO-C 52

1.3.Clinical Professor of Haemostasis and Thrombosis, Consultant Haematologist

1.4.University Dept. of Haematology,
Manchester Royal Infirmary.
Oxford Road,
Manchester M13 9WL

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.*

Employment History: (in reverse chronological order):-

2.1. ***December 1994 to date.*** Consultant Haematologist and Haemophilia Centre Director, Manchester Royal Infirmary. Honorary Senior Lecturer in Medicine and then Professor of Haemostasis and Thrombosis.

2.1.1. Managing the adult Haemophilia Centre. Head of the Dept. of Haematology 2007-2011 approx. Multidisciplinary day to day clinical management of Thrombosis and Haemostasis and some General Haematology for inpatients and outpatients. Ward rounds, MDTs, Clinics. Joint Clinics with Orthopaedics, HIV, Obstetrics and Paediatric Haematology. Teaching and training of junior staff and clinical research.

2.2. ***May 1987-November 1994***. Senior Lecturer in Haematology, University of Liverpool. Honorary Consultant Haematologist. Director Mersey Region Haemophilia Centre. Royal Liverpool University Hospital Trust. Prescott St. Liverpool, L7 3BX.

2.2.1. I was a Senior Lecturer in Haematology (University of Liverpool) and Honorary Consultant Haematologist (Royal Liverpool University Hospital) with sole charge of the Haemophilia Centre. Consultant colleagues would cover holidays but had no other involvement in the Haemophilia Service. I also took a third of the malignant Haematology and bone marrow transplantation between 1987-93, at which point we were joined by a fourth colleague and I was permitted to specialise completely in Thrombosis and Haemostasis.

2.2.2. Throughout this time, I adopted a 1 in 3 rota for Consultant responsibility for the Haematology inpatients in three-month blocks (mostly haematological malignancy and bone marrow transplantation) all ward rounds, the Haematology Service for the rest of the hospital and the lab

service for all Haematology patients and the hospital as a whole. I conducted several outpatient clinics every week whether on call or not. I was also involved with undergraduate and postgraduate teaching and training of Haematology junior staff. I was also expected to conduct research, publish and present at scientific meetings and to undertake undergraduate and postgraduate teaching. I also had responsibility for the RLH Anticoagulant Service and for providing a Haematology Service for Liverpool Woman's Hospital.

2.2.3. When I started in this post in Liverpool there was no Haemophilia Comprehensive Care system. There were no joint clinics or multidisciplinary care, no physiotherapy, social work, nursing or orthopaedic input. I had to justify and arrange for this to be built up from scratch. Within 18 months, I had established a joint orthopaedic service and arranged physiotherapy input. Liverpool's first Haemophilia Nurse Specialist and Haematology Social Worker followed. I also developed close working relationships with Hepatology and STD (Sexually Transmitted Disease, who also managed HIV). During that time I would have a rotating Senior Registrar in Haematology attached for training in Thrombosis and Haemostasis...

2.3.***Aug. 1982-May 1987*** Rotating Senior Registrar in Haematology, Hon. Clinical Tutor. Sheffield University Hospitals. Prof FE Preston, Dr DA Winfield, Dr JS Lillyman.

2.3.1. This was a rotational training post. As far as I can recollect, I rotated as follows:-

2.3.1.1. *August 1982-April 1983 Blood Transfusion Service (BTS), Sheffield Longley Lane.*

2.3.1.1.1. My time at BTS, shared with Dr Katie Foreman, also Senior Registrar in Haematology, involved many training practicals and tutorials in all the sub-departments of BTS.

We rotated from department to department for training purposes. We fielded clinical enquiries by phone from hospitals around the region and screened requests for specific services or products. We were supervised by several consultants (Dr Bill Wagstaff, Dr Virge James and Dr Bob Sokol).

2.3.1.2. *April 1983 to August1984: Senior Registrar in Haematology Royal Hallamshire Hospital.*

2.3.1.2.1. Since the Clinical Assistant in Haemophilia had just left and I was going to be attached to the unit for longer than the other juniors, I was given day to day responsibility for the Haemophilia Service under the supervision of Professor Eric Preston, Consultant Haematologist and Dr Mike Greaves, Senior Lecturer in Haematology. I also shared responsibility for the malignant haematology, lab service and general haematology with another rotating senior registrar and two junior registrars under the supervision of Dr David Winfield and Dr Harold Swann. Apart from day to day ward management and outpatient clinics we also had responsibility for the lab (mainly microscopy).

2.3.1.2.2. When I arrived, there was very good laboratory and consultant support but multidisciplinary comprehensive care had not been established. During my time there, I facilitated the development of comprehensive care, establishing a joint orthopaedic clinic, arranging physiotherapy input and facilitating the appointment of Sheffield's first Haemophilia Nurse Specialist (Sr. Joy Farnsworth). We had one Haemophilia follow-up clinic per week, which gradually evolved into a multidisciplinary clinic.

2.3.1.3. *August 1984 to April1985 Senior Registrar in Haematology, Sheffield Children's Hospital.*

2.3.1.3.1. Under the supervision of Dr John Lilleyman, I was responsible for day to day management of the entire range of paediatric Haematology and paediatric solid tumours. This responsibility was shared with a junior registrar in Paediatrics rotating through Haematology. This included the day to day management of children with bleeding disorders and outpatient management of the whole range of paediatric haematology.

2.3.1.4. *April 1985 to August 1986. Senior Registrar Royal Hallamshire Hospital.*

2.3.1.4.1. As above.

2.3.1.5. *August 1986 to April 1987 Senior Registrar in Haematology, Sheffield Chidren's Hospital.*

2.3.1.5.1. April to May 1987,

2.3.1.5.2. Duties as in my first rotation to this hospital.

2.3.1.6. *April 1987:*

2.3.1.6.1. My recollection is that I rotated back to the Northern General Hospital for a short while prior to taking up post in Liverpool. My duties were as they had been as a junior registrar except at a higher level.

2.4.***Aug 1979-AUG 1982*** Junior Registrar in Haematology, Northern General Hospital (T), Sheffield. Dr ACK Lawrence, Dr MJ Brown.

2.4.1. This post involved day to day management of general Haematology and malignant haematology patients and also outpatient clinics. It also involved providing a general Haematology service for the remainder of the hospital and laboratory work (Microscopy interpreting blood tests etc). I was also involved in teaching undergraduates and postgraduates. I was supervised by a rotating Senior Registrar in Haematology and the two Consultant Haematologists listed. Although this hospital had a number of academic units, it did no specialist thrombosis and Haemostasis, since this was all based in the Royal Hallamshire Hospital and Sheffield Children's Hospital.

2.5.***Aug 1978- Aug 1979*** Junior Medical Registrar, St Mary's Hospital London W9. Dr R Elkeles, Dr H Tunstall-Pedoe.

2.5.1. This was a junior Registrar post in General Medicine and Diabetes. It involved General Medical outpatient clinics and an anticoagulant clinic. It also involved day to day management of inpatients with daily ward rounds and emergency admissions "on take". and a one in three on call rota. I was also involved in teaching of undergraduates.

2.6.***Aug 1977-Aug 1978*** Senior House Physician, Royal Hospital, Sheffield. Dr J J Daly, Dr D Cullen.

2.6.1. This involved mostly clinical duties, including ward rounds and clinics in general medicine, diabetes and endocrinology and day-to-day clinical management and investigation in general medicine and endocrinology. It also involved emergency admissions "on take" and a one in 3 on-call.

2.7.***March 1977-Aug 1977*** House Physician, Haematology and General Medicine, Sheffield Royal Infirmary. Prof EK Blackburn, Dr FE Preston, Dr D Holdsworth, Dr JD Ward.

2.7.1. This was a new rotational post. I was the first post-holder. This involved 3 months as Haematology Houseman and three months as General

Medicine Houseman covering patients of Dr D Holdsworth (General Haematology and Gastroenterology, and Dr JD Ward, General Medicine and Diabetes). There was a one in two on-call rota covering both Haematology and General Medicine.

2.7.2. During the day, we conducted ward rounds, minor procedures and general inpatient management supervised by the listed consultants and more senior junior staff. .

2.8.***Aug 1976-March 1977***, House Surgeon, University Dept. of Surgery, Royal Infirmary, Sheffield._Prof H L Duthie

2.8.1. House Surgeon General Surgery. This involved ward rounds, occasional clinics and minor procedures, assisting in theatre, and day to day management of inpatients undergoing general surgery. We were also involved with emergency admissions "on-take" and a one in two on-call rota.

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.**Local Committees:**

Chairman, North West Non-Malignant Haematology Speciality Group of the **NIHR (CRN) (National Institute of Health Research (Clinical Research Network).**

3.2.**National Committees:**

Clinical Lead; DH National Procurement Team, UK Coagulation Factor Procurement 2005/6 and 2009/10 (seconded part time to DOH 1/9/09-1/9/10).

Member of the Advisory Group, and reporting to, the Health Protection Agency and DH Blood Policy Unit on vCJD 2009-2011

Northern Representative. **Haemophilia Clinical Reference Group** advising the **National Commissioning Board** since 2011.

North West Representative on the National Non-Malignant Haematology Speciality Group of the **NIHR (CRN)** 2011-2018.

Member of the Advisory Group to the Dept. of Health on support for individuals infected with hepatitis C or HIV by blood transfusion or blood products 2008.

Secretary Haemophilia Alliance 1999-2002.

Fellow and external examiner of the Royal College of Pathologists since 1993.

3.3. **UKHCDO (UK Haemophilia Centre Directors Organisation changed to UK Haemophilia Centre *Doctors* organisation in 1992)**

Chairman UK Haemophilia Centre Doctors Organisation **(UKHCDO)** 2005-2011.

Director, of the **UK National Haemophilia Database (NHD)** since 2002.

Vice-Chairman UKHCDO 1997-2005.

Treasurer of the UK Haemophilia Centre Directors Organisation (UKHCDO) 1992-97.

Trustee of UKHCDO 1992-2011.

Director **UKHCDO Ltd** since its inception in 2003.

Chairman: UKHCDO Inhibitor Working Party 1993-2005 (member since).

Chairman, UKHCDO Data Management Group 1998-2005 (member since).

Member of the Committee of Regional Haemophilia Centre Directors of the UK 1987

Member Therapeutic Guidelines Taskforce of UKHCDO 1996.

Member Information Technology Working Party of UKHCDO 1996-98.

Member of the UKHCDO Paediatric Working Party 1993-2005.

Member of the UKHCDO Von Willebrand Working Party 1996-2000.

3.4. **International Committees:**

Member of the Scientific Committee of the World Federation of Haemophilia since 1993-96

International Advisory Committee of the International Society on Thrombosis and Haemostasis (ISTH).

Steering Committee member European Haemophilia Adverse Event System (EUHAS).

Co-Chair of Factor VIII and IX Scientific Standardisation Subcommittee of the ISTH 2007-11.

Member of the advisory group to the Journal of Thrombosis and Haemostasis, The Journal of ISTH 2007-11.

Member of the International Immune Tolerance Study Group since 1996.

Founder Member of the Editorial Board of "Haemophilia" the Journal of the World Federation of Haemophilia (Wiley-Blackwell) since 1993.

3.5. **Professional Affiliations:**

Fellow of the Royal College of Physicians (1994).

Fellow of the Royal College of Pathologists (1996)

Member British Society of Thrombosis and Haemostasis since 1986.

Member British Society of Haematologists since1987.

Member International Society of Thrombosis and Haemostasis (ISTH) since 1987.

Member of the American Society of Haematology since 2000.

Co-Chair ISTH Factor VIII and IX Scientific Standardisation Sub-Committee 2007-11.

3.6. **I have reviewed regularly for the following journals: -**

The British Journal of Haematology.

Blood Coagulation and Fibrinolysis.

The Journal of Thrombosis and Haemostasis,

Blood, the Journal of the American Society of Haematology.

Haemophilia, the Journal of the World Federation of Haemophilia.

The British Journal of Anaesthesia,

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 (other than those which are enclosed with this letter).*

4.1. I was not invited to give evidence to the non-statutory, independent, Archer Inquiry.

4.2.I gave written and oral evidence to the Penrose Inquiry, firstly in my capacity as Director of the UK National Haemophilia Database, to clarify issues surrounding statistical data requested by the Inquiry and secondly to provide background evidence in relation to the development of knowledge about blood-borne viruses and to discuss the findings in my MD thesis, which was submitted in evidence.

4.3.I acted as an expert witness, retained by the Defence, in the Hepatitis C Class action of 1998-2000. Unusually, this action, which focussed on three test-cases, was brought under consumer protection legislation. My reports in this action comprise: -

a. Haemophilia And Hepatitis C 10/3/98
b. BW001A v Portsmouth 28/9/99
c. Medical Report to answer questions for the purpose of clarification of my previous report RE: BW001A –v- Portsmouth HA. 23/11/99.
d. WK001A. 206/99
e. GRO-A (Deceased) 15/10/95.
f. GRO-A (deceased) 21/7/99.
g. Supplementary report: DMS 14A and the risk of contracting hepatitis C from Blood Products in the early nineteen-eighties.

4.4.I have also provided reports to my employing Trust and the GMC in relation to complaints, and have provided reports to the Coroner. I have occasionally acted as an expert witness in such cases over the years, acting for the complainant or the defence and/or provided reports at the request of the coroner or reports to the Trust as part of their investigations of a complaint. These are listed below.

4.4.1. In Relation to my own Patients: -

4.4.1.1. GRO-A response to allegations of Mrs GRO-A. 2/7/1996

4.4.1.2. GRO-A Report for the Trust in response to allegations from Mr GRO-A 's widow. 2/8/01

4.4.1.3. GRO-A Trust Complaint Correspondence. 14/8/02

4.4.1.4. GRO-A Response to the GMC. 9/6/03

4.4.1.5. GRO-A Complaints Correspondence. 14/02/06

4.4.1.6. GRO-A Report to the Coroner. 24/10/09

4.4.1.7. GRO-A report to the Coroner. 4/9/19

4.4.2. Reports as an expert Witness in relation to hepatitis C

4.4.2.1. GRO-A (for the defendant) 22/7/01

4.4.2.2. GRO-A (for the defendant) 4/11/01

4.4.2.3. GRO-A (for the defendant) 20/5/02

4.4.2.4. GRO-A (for the Defendant) 4/8/02

4.4.2.5. GRO-A (for the complainant) 30/12/04

4.4.2.6. GRO-A (for the Complainant) 10/1/08

4.4.2.7. GRO-A (for the Defendant) 21/1/11

4.4.2.8. GRO-A (for the defence) 26/1/11

4.4.2.9. GRO-A (Joint report for Complainant and Defendant) 25/8/12

4.4.2.10. GRO-A (for the defendant) 27/12/12

5. *Please consider the evidence which you gave to the Penrose Inquiry which is attached to this letter [PRSE0000480; PRSE0002297; PRSE0006008: PRSE0006083; PRSE0002287 and PRSE0001940]. Please confirm whether the contents of the written and oral evidence you gave to the Penrose Inquiry are true and accurate. If there are any matters contained within the written statements or in the oral evidence you provided that you do not consider to be true and accurate, please explain what they are.*

5.1. I consider my evidence to the Penrose Inquiry to be true and accurate.

Section 2: Decisions and actions of the Centres at Sheffield, Liverpool and Manchester and your decisions and actions

6. *The questions below focus, as appropriate, on your time as a Senior Registrar in Haematology at Sheffield University Hospitals ("Sheffield") between 1982 and 1987, as Director of the Liverpool Haemophilia Centre ("the Liverpool Centre") between 1987 and 1994 and as Director of the Manchester Haemophilia Centre ("the Manchester Centre") from December 1994 onwards. Some questions focus on Sheffield and/or Liverpool, but if you have information concerning Manchester relevant to the period or issue to which the question relates, please include that in your response. Insofar as your earlier experiences in Sheffield and/or St Mary's are relevant to the questions asked, please include reference to these too.*

1.

7. *In relation to your work in Sheffield as Senior Registrar in Haematology please:*

a. *describe your role and responsibilities and how they changed over time;*

7.1. Senior Registrar was a sort of sub-consultant grade, which no longer exists. Senior Registrars did not make Unit Policy decisions or participate in hospital administration but had a greater degree of clinical independence than the current Specialist Registrar (SpR) grade. In that way, when I was at the Royal Hallamshire

Hospital, I had day to day clinical responsibility for the Haemophilia Centre and would deal with patients dropping in to the centre with clinical problems but discuss these with either Prof Eric Preston or Dr Mike Greaves, if they were complex. Inpatients were also discussed on the Ward rounds. This did not change with time. Clinical management changed gradually in that we started joint Orthopaedic clinics, obtained physiotherapy input and appointed a Haemophilia Nurse Specialist during my time there. Liaison with hepatology was always close but not formalised around a joint clinic.

7.2. I also shared the responsibility for all the other Haematology patients, mostly with haematological malignancy, and attended all the Haematology clinics of which the Haemophilia follow up clinic was but one. I also participated in clinical investigation of all Haematological conditions. This work was pooled between the consultants, two senior registrars, of whom I was one, and two junior registrars.

7.3. The organisation at the Children's Hospital and my duties there were similar.

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

7.4. I reviewed patients with bleeding disorders in outpatient clinics and *ad hoc* when they presented to the Haemophilia Centre (which was a clinical room on Ward P2) or when they were outpatients. Patients with non-A non-B hepatitis were seen every six months and had their liver function tests conducted each time and an abdominal ultrasound every two years or so and in some cases also liver biopsy, since there was no non-invasive method of determining the severity of the liver disease at that time. Hepatitis would be discussed with them in clinic and also the very uncertain and emerging AIDS situation. However, Prof Preston also had larger meetings with the patients to discuss the emerging state of knowledge of AIDS. I recall that when a test became available in late 1984, this was discussed with them individually and they were tested and Prof Preston saw them all individually in his office with Sr Joy Farnsworth, the Haemophilia Nurse Specialist

to tell them the result of the test and the implications of the test result as far as that was known at the time..

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

7.5. The Senior Consultants in Charge of the adults with bleeding disorders at the Royal Hallamshire Hospital were Professor Eric Preston and Dr Mike Greaves. The consultant in charge at Sheffield Children's Hospital was Dr John S Lilleyman.

8. In relation to your work at the Liverpool Centre please:

a. *describe the facilities, organisation, roles, functions and responsibilities of the Liverpool Centre during the time that you worked there and how they changed over time, and provide (if you can) an account of the history of the Liverpool Centre, its establishment and its activities during this time.*

8.1. In May 1987, when I took up post in Liverpool, the Haemophilia Centre was an examination room in the middle of the ground floor Laboratory in the Duncan Building of the Royal Liverpool Hospital. Patients could also come to the Haematology Ward (7Y), on the 7th floor. Historically, The Royal Liverpool Hospital had looked after patients with Haemophilia for decades. Originally they went to the "Tropics Ward" of the old Royal Liverpool Infirmary (RLI), which also served The Liverpool School of Tropical Medicine, until the RLI closed in the 1970s. I was supported by clerical staff, laboratory staff and a rotating Senior Registrar but no comprehensive care system was in place. The development of the centre is well summarised in my article published in the Bulletin March 1990 (HCDO0000276_001) detailing how the availability of "AIDS Money" enabled us to acquire a Haemophilia Nurse Specialist (Alison Jones) and a full time social worker (Miriam Waite) and a Nurse Counsellor (Helen Rogers). We also set up a joint Orthopaedic service with Professor Leslie Klennerman and his Senior Lecturer John Walsh. As the Speciality of HIV Physician developed, I also

increasingly collaborated with Dr Peter Carey, Consultant in STD. From early on, I also developed a close working relationship with Professor Ian Gilmour, Consultant Hepatologist and later President of the Royal College of Physicians, whose clinic ran next door to my own.

b. describe your role and responsibilities and how they changed over time;

8.2. I had sole consultant responsibility for all aspects of Thrombosis and Haemostasis in the hospital and provided a tertiary referral service for Mersey Region. I was responsible for the coagulation lab and the Haematology lab in the Liverpool Woman's Hospital.

8.3. The consultant staff in the Department included Professor JC Cawley and Dr John Davies (also a Senior Lecturer). I shared with them a one in three rota (three months on and six months off) for Consultant responsibility for all laboratory and inpatient Haematology and a third of all the malignant haematology outpatients. They had no consultant responsibility for outpatient Thrombosis and Haemostasis. This continued until 1993, when we were joined by Dr Patrick Chu, Consultant Haematologist, at which point I was permitted to give up malignant haematology.

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

8.4. The patients had been HIV tested before I arrived in Liverpool and informed of their results by letter and without much psychological support or explanation, as far as I could determine. This had understandably engendered considerable anger and resentment amongst the patients, which had to be addressed as far as it was possible for me to do so. No treatment for HIV or non-A Non-B hepatitis was available in the beginning and the outlook for those patients with HIV was extremely uncertain. Uncertainty is very difficult to deal with psychologically. I had to deal with this on my own to start with by speaking with the patients and arranging patient meetings and then built up a multidisciplinary team as fast as I could.

8.5. HIV physicians did not exist as a sub-speciality at that time. When HIV was discovered it was dealt with by the physician to whom the patient presented. Drug addicts and sex workers presented generally to STD (Sexually Transmitted Diseases) doctors, people with bleeding disorders to the Haematologist and the rest to infectious disease doctors. In the beginning, each of these groups of physicians knew as much or as little as each other about the treatment and natural history of HIV but Haematologists did have the advantage over the others that they were very experienced in the management of immunocompromised patients and the diagnosis and management of infections caused by opportunist pathogens. As time went by and more treatments became available, particularly after 1995 with the advent of triple therapy, HIV Physicians crystallised out as a subspecialty, drawn mainly from STD Medicine but in some areas from Infectious Diseases and it became increasingly common to conduct HIV Clinics Jointly.

8.6. Liver disease was managed between Haematology, Hepatology/Gastroenterology and General Surgery. Uncomplicated patients with mild liver disease were managed largely by Haematology in consultation with Hepatology. I monitored their liver disease using ultrasound, LFTs and alfa fetoprotein and talked to the patients about their non-A non B hepatitis when they were reviewed. Thus, when the HCV antibody test became available, this was viewed by the managing clinicians as just an extension to their previous investigation, and they would be told they were being tested and, if their liver function test were abnormal, warned that the test would probably be positive. At the next clinic visit, the result would be discussed. Those with serious liver disease were always jointly managed with Prof Gilmour and Prof Shields, Professor of Surgery. Once Interferon and subsequent treatments for HCV became licensed, the use of these was shared between Haematology and Hepatology, both selecting patients for treatment using similar criteria passed down by Hepatology.

d. Identify senior colleagues involved in the care of patients with bleeding disorders and/or patients infected with hepatitis and/or HIV in consequence of blood or blood products, and their roles and responsibilities during the time that you worked there.

8.7. My two consultant colleagues would manage patients with bleeding disorders on

call and when managing the ward, but often following my advice.

8.8. I had a close working relationship with Prof Klennerman, Professor of Orthopaedics, who operated on many patients since there was a backlog of orthopaedic problems when I arrived. I had a close working relationship with Prof Gilmour and Professor Shields, Professor of Surgery, who helped manage those of my patients with serious liver disease. Although the specialism of HIV physician was very much in its infancy, I had increasing dealings with Dr Peter Carey, Consultant STD Physician. We would ask each other for second opinions and sometimes I would also obtain a second opinion from Infectious Diseases, based in Fazakerly Hospital.

9. In relation to your work at the Manchester Centre please:

a. *describe the facilities, organisation, roles, functions and responsibilities of the Manchester Centre during the time that you worked there and how they changed over time, and provide (if you can) an account of the history of the Manchester Centre, its establishment and its activities during this time;*

9.1. There was a small dedicated Haemophilia Centre based in the laboratory comprising a store-room, office and two clinical rooms. There were three Haemophilia Nurse Specialists one of whom was a nurse-counsellor. We had a part time Clinical Assistant but no other junior medical support. There was no physio input but we had help from a shared social worker. There was one Haemophilia Clinic a week attended only by me. There were no joint clinics, although the centre had good historic links with hepatology. The factor VIII budget was unusually small (per patient factor usage the lowest in the UK, at 25,000 units/year). This was, in terms of patient numbers, the second largest Haemophilia Centre in the UK.

9.2. The hospital has been rebuilt and both inpatient facilities and the Haemophilia Centre are now in the new building. We now have four nurses and four consultants and rotating junior staff and research fellows. We have help from a team of three

physiotherapists and shared social worker. We have weekly joint antenatal clinics, monthly joint HIV clinics, bimonthly Joint Orthopaedic Clinics and bimonthly adolescent Clinics held jointly with Paediatric Haematology Colleagues. We have a very close working relationship with Hepatology who have managed all our anti-HCV and anti HBV treatment for a number of years now.

b. *describe your role and responsibilities and how they changed over time;*

9.3. I had consultant responsibility for all Thrombosis and Haemostasis in the Trust and provided a tertiary referral service for a region from Stafford to Carlisle. This included responsibility for the Anticoagulant Service and the coagulation laboratory. In the beginning, I was on call all the time except when on leave, when my malignant colleagues would cross-cover. From 1998 I began to acquire additional colleagues, finally increasing from 3 to 4 specialists in Thrombosis and Haemostasis in 2019. With each additional member of consultant staff, we divided the patients between us and one colleague adopted responsibility for the Anticoagulant Service. In 2000 Dr Bolton, our clinical assistant retired and was not replaced. I have retained responsibility for the HIV-infected cohort of patients joint-managed with the HIV Physicians.

c. *describe your work insofar as it involved the care of patients with bleeding disorders and/or patients infected with hepatitis and/or HIV in consequence of blood or blood products;*

9.4. In 1994, most haemophilia doctors managed their own HIV. Treatment options were limited. This continued with the advent of triple therapy in 1995. However as the number of treatment options and potential drug interactions increased and the technology became available to predict drug sensitivity based on a genotypic analysis of the HIV virus itself, the management became more complex and the sub-speciality of HIV Physician emerged. For that reason, from about 1997 all the HIV patients were seen in a joint HIV clinic by me and an HIV Physician, first Dr Deb Mandel and then Dr Ashish Sukthanker.

9.5. Treatment of HCV was sometimes managed jointly with hepatology and

sometimes by us but with the passage of time and the increase from one to three consultant Hepatologist and increasing complexity of the treatment regimens available they have increasingly managed all anti-HCV treatment for the past five to ten years.

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

9.6.**Hepatology:**

9.6.1. Dr TW Warnes Consultant Hepatologist gave advice and sometimes joint management from 1994 until his retirement in the early noughties. He had been involved with our cohort of patients for many years and had co-authored the Report from Manchester in 1991 entitled "NANB hepatitis in Haemophilia, an overstated problem".

9.6.2. Dr Harry; Consultant Hepatologist joined us for a few years in the late 2000s. Dr Martin Prince and Dr Campbell another doctor (recently replaced) have provided advice and management of antiviral therapy for the past ten years or so. Through a systematic campaign following the introduction of a new generation of treatments, we have eliminated HCV from all but the handful of our patients who refuse treatment.

9.7.**HIV:**

9.7.1. Our Joint Clinics were run with Dr Deb Mandal for about three years and subsequently with Dr Ashish Sukthanker cross-covered by his colleagues. One or two patients attend an HIV clinic in Infectious Diseases in North Manchester.

10.Approximately how many patients with bleeding disorders were under the care of (a)

Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre when you began your work there, and over the years that followed? (If you are able to give exact rather than approximate figures, please do so).

10.1. The following data was obtained from the National Haemophilia Database and therefore gives the number of *registrations* with the database rather than the number of patients attending the centres in question. Whilst this is the best that I can do, the Inquiry should recognise that although all patients with bleeding disorders were supposed to be registered with the database, it was a voluntary database and in the days before UK Haemophilia Centres acquired their current staffing infrastructure, there was considerable under-reporting. This is evidenced by the fact that when the National Haemophilia Database moved to Manchester it had 16,000 registrants but now has approaching 30,000.

Sheffield:	1983	166 registrants
	1987	218 "
Liverpool	1987	162
	1994	332
Manchester	1994	525
	2020	2248

11. *To the best of your knowledge, what policies were formulated at (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre regarding the selection, purchase and use of blood products (in particular factor concentrates) during the time that you worked there? What if any involvement did you have in the formulation and application of these policies?*

11.1. **Sheffield:**

11.1.1. As a registrar I did not make any of these decisions but my limited recollections, made without access to any documentation but with the benefit of additional data from the National Haemophilia Database

(WITN3289040), are as follows: -

11.1.1.1. The concentrates in use were from Bioproducts Limited (BPL: UK NHS manufacture) Immuno (Vienna), and Armour (US Manufacture). I recall that BPL products were initially provided free of charge and also recall that the amount provided to the Centre was on a *pro-rata* basis according to how much plasma the local transfusion centre sent to BPL for fractionation. I do not remember how long this arrangement persisted but at some point BPL charged and supplied in the same way as commercial suppliers. I recall that the BPL product supplied was sufficient for almost all Haemophilia B patients but only about 40% of Haemophilia A patients. Treatment policy would have been influenced by UKHCDO Guidance issued on 24/6/83 and December 1994 (WITN3289041 and WITN3289042 UKHCDO Guidelines 1983 and 1984). Heat-treated Alphanate, which had previously been used in the centre in clinical trials, was used for about 50% of the patients from very late 1984. I think this product was used for HIV negative patients. There was not enough supply to use it for all patients. By the end of 1995, all factor VIII concentrate and factor IX concentrate in use in the centre was virally attenuated by heat treatment.

11.2.**Liverpool:**

11.2.1. We did not have a written policy. My policy was to treat the patient with a product that was virologically safe and to use the best product that I had available to me. Within those constraints, I also ensured that the patient was always supplied with their designated brand and not treated on occasion with some other brand. If it was necessary or desirable to change brands, this would be discussed with the patient. When I took up post in 1987, all the products in use in the centre were virally attenuated to an acceptable degree. When high purity products became available later in the decade, I was able to switch my HIV positive patients to high-purity

immunopurified concentrates, despite the considerable increase in cost. These were still the state-of-the-art products in 1994 when I left Liverpool. I also maintained 2-3 different suppliers at all times to maintain security of supply, so that I would never be too dependent on a single supplier.

11.3.**Manchester:**

11.3.1. My policy in Manchester was the same as the policy I had adopted in Liverpool. If we needed to change products, we would write to patients describing the change, and the relative merits of their existing and proposed future product and offering to discuss this with them further if they so wished. They were also offered the option to continue to use their previous product, if that was possible.

12. *Who had responsibility at (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre for the selection and purchase of blood products, and what decisions were taken at each as to which products to purchase and use? In addressing this issue, please answer the following questions:*

12.1.**Sheffield:** Prof Preston made the purchasing decisions.

12.2.**Liverpool**: I made the purchasing decisions.

12.3.**Manchester**: Initially, I would make the purchasing decisions. As we increased the number of Thrombosis and Haemostasis Consultants, we would make these policy decisions collectively by consensus and also involve managers and Commissioners.

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?*

12.4.There was little to choose between different concentrates in the late seventies and early eighties in terms of purity, efficacy and safety. The suspicion that American

concentrates were less safe than UK ones was not born out in relation to HCV but persisted in relation to AIDS and is reflected to some degree in the UKHCDO Guidance of 1983 and 1984 (WITN3289041 and WITN3289042).

12.5. In Sheffield, because there was some very soft (and with hindsight, probably incorrect) evidence that patients might contract a different strain of non-A non-B hepatitis when treated with concentrates of different geographical origin, we ensured that patients were treated with a single brand of concentrate for as long as possible and did not, therefore treat the concentrate as a generic product. This also facilitates product tracing in the event of a product recall. This is a policy that I adopted in both Liverpool and Manchester. Where this policy was adopted, it had the unforeseen benefit that the cohort of patients treated exclusively with UK products, whilst equally likely to contract HCV, were significantly less likely to contract HIV.

12.6. In 1983 and 1984 and 1985, the choice of product (WITN32890340) was determined by UKHCDO Guidance from 1983 and late 1984 (WITN3289041 and WITN3289042) and both the advent of HIV testing and the emerging availability of heat treated factor concentrates.

12.7. Changes in brand were sometimes inevitable, because there were sometimes interruptions in supply and old products were superseded by newer, purer and safer products. The Sheffield Centre participated in some early clinical trials of heat-treated concentrates with both Armour and Alpha products. Early attempts by Armour to virally attenuate the concentrate by heat treatment were unsuccessful in preventing NANB. The Alpha trial was far more successful. Conducted across the Centres in Sheffield, The Royal Free, St Thomas' and Canterbury, this product appeared to prevent transmission of non-A, non-B hepatitis in 24/27 patients, as I recall. When it became apparent, I think in late 1984, and based on data using model viruses, that the AIDS virus might be heat-labile, the centres participating in this trial (Sheffield, Royal Free, St Thomas' and Canterbury) changed many of their patients to Alphanate to minimise the risk of both HCV and AIDS transmission. I do not think the product was fully licensed at the time and am not sure when it gained a product license. Supplies were limited and I do not think any

other centres were able to switch to this product until some time later

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

12.8. Product safety was always the first consideration. Prior to the advent of viral attenuation techniques there was very little to differentiate the products in terms of viral safety. There is no evidence that there was any difference in risk of non-A-non-B hepatitis between different clotting factor concentrates and the risk of HIV was unknown until a test became available in 1985. Eventually, once a test became available, it became apparent that UK products transmitted less HIV than US products because HIV spread earlier in the US donor population but by the time this was known, virally attenuated products were becoming available. Different methods of viral attenuation were used and some appeared likely to be more effective than others. For example, dry heat treatment, whilst adequate for HIV, might be considered potentially less effective than solvent detergent plus ultrafiltration or plus heat treatment for some other viruses. However, the margin of safety of all of these products appeared adequate to prevent HIV transmission and, other than early products marketed as "hepatitis reduced", appeared completely free from the risk of HCV transmission. Consequently, differences in viral safety could not be demonstrated between licenced virally attenuated products.

12.9. Theoretical increments in safety were still considered, and we would use the products that appeared likely to be safest. Viral safety was the main driver influencing the campaign to switch to Recombinant factor VIII and IX, which was UKHCDO Policy from 1996, when recombinant factor VIII first gained a product licence and 1998, when recombinant factor IX gained a license.

12.10. Considerations of security of supply led most larger and medium-sized centres to prescribe several different brands of factor concentrate because interruptions in supply were common well into the 2000s and no centre wished to be overly dependent on any single supplier. This is a policy that I have always followed. An

example of such an interruption in supply was the Kogenate (Bayer Recombinant factor VIII) supply problem of 2000-2002. The supply of Kogenate stopped world-wide following a regulatory inspection of their Berkley plant, reducing the supply of recombinant factor VIII to the UK and the world by half overnight and leaving some centres that only used that brand without any supply of recombinant factor VIII. I, as Vice Chair of UKHCDO, organised a voluntary national scheme to redistribute the remaining supply of recombinant factor VIII so we could at least keep the younger children using recombinant factor VIII whilst older patients had to switch temporarily back to plasma-derived products.

12.11. Clotting factor cost was not a major deciding consideration until the advent of high-purity immunopurified clotting factor concentrates. These cost twice as much as earlier products and their advantages were disputed, not least by commissioners. I was fortunate in that I was able to switch all my HIV positive patients to these products without significant delay but other centres were not able to switch because the commissioners would not pay. This issue is explored in the in later sections. Finance delayed the introduction of recombinant factor VIII for years. The initial unit price of recombinant VIII/IX was very high, compounded by 20% VAT, which was levied on recombinant but not plasma-derived products. This rendered recombinant products at least twice the unit cost of the plasma-derived alternatives. The DoH would not accept that recombinant products were safer than the plasma-derived alternatives available at that time. We were initially unable to prescribe recombinant factor VIII because the commissioners would not fund them. This will be fully explored elsewhere. Suffice it to say, that once DH policy changed, and particularly since the advent of national procurement of factor VIII concentrates, cost is no longer a significant deciding consideration.

12.12. Patient preference was also taken into account. Patients sometimes prefer one product over another. The strongest patient preference, however, is for biosynthetic rather than plasma-derived products. When changing a patient's product, it has long been my practice to write to them, and or speak to them describing the change and offering them the opportunity to discuss the matter further and the right not to switch products. Changes in the class of product to be

used e.g. to extended half-life products or to Emicizumab are discussed with the patient in person, since they may choose not to change.

12.13. It should also be born in mind that the number of suppliers has been very limited. In the 1980s, suppliers of factor VIII/IX to the UK were Immuno, Alpha Therapeutic, Armour and its successor companies, Cutter and Bioproducts Ltd (BPL). Cutter subsequently disappeared. Immuno merged with Baxter. With the advent of recombinant products, Bayer, Baxter and Sobi became major suppliers of Kogenate, Recombinate and ReFacto and their successor products. These three suppliers supplied all the UK's recombinant factor VIII/IX (other than clinical trial products) until the last two years, when Novo entered the VIII/IX market.

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

12.14. The products were sourced direct from manufacturer's UK affiliate by the Haemophilia Centre or pharmacy. The products are usually stored in the Haemophilia Centre itself and/or the hospital blood bank. .

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

12.15. I don't remember commercial considerations playing a significant role in 1984/5. Additional funding had to be found but that did not involve me and I was unaware if that caused problems. Financial considerations delayed the introduction of more expensive products, e.g. Ultra-high purity plasma derived products in the early nineties and recombinant products in the late nineties and early noughties and extended half-life products after 2015 but these were problems with Commissioners across entire product classes and not problems related to a single brand and therefore did not influence us to use one brand in preference to another.

e. What involvement did you have?

12.16. Please, see above.

13. *What products were used for treating patients at (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre, over what period of time and for which categories of patients? How were decisions taken, at (a) Sheffield, (b) Liverpool and (c) Manchester, as to which products to use for individual patients? What involvement did you have in such decisions?*

13.1. An excel spreadsheet of data obtained from the National Haemophilia Database is attached which shows what products were being used in each of the centres that I worked in from 1983 until 2020 (WITN3289040). This shows Sheffield changing from unheated products to all heated products in stages during the course of 1985.

13.2. Liverpool was already on all heat-treated products when I joined in 1987. It shows that I was introducing high purity products (Monoclate P) in Liverpool in 1994 and conducting clinical trials of Recombinant factor VIII (rFVIIISQ, ReFacto) in 1994. The return to the National Database for my first two years in Liverpool (1987 and 1988) is incomplete. Comparison with products issued to patients showed that Liverpool used approximately 45% Alphanate, 10% Koate HT and 45% BPL 8Y during those years.

13.3. It also shows a wholesale change from intermediate purity products to high-purity plasma-derived products for all patients with haemophilia A and B during the course of 1995, within months of me taking up post in Manchester. By late 1995 we were also participating in clinical trials with two recombinant products RVIIISQ and Kogenate. Participation in clinical trials was the only way in which patients could gain access to recombinant products at that time because they were not licensed.

14. *What was the relationship between (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre, and the pharmaceutical companies manufacturing/supplying blood products? What influence did that relationship have on the decisions and actions referred to above?*

14.1. Company representatives would visit from time to time to discuss technical developments, supply issues and centre requirements etc. Manufacturers would also sponsor scientific meetings and attendance at scientific meetings not funded by the hospital. This sponsorship is explored elsewhere.

14.2. I do not think these influenced purchasing decisions at all, since such decisions were based on objective safety and efficacy criteria and the need for security of supply and, since the advent of the National Procurement scheme in 2005, have been reached on a national basis.

15. In the enclosed letter dated 19 June 1987 [BAYP0000010_128] from you to a sales manager at Cutter Laboratories, there is a handwritten note "Peter has arranged with Dr Hay a free sample system as before". Please provide details of the "free sample system" that had been arranged between you and Cutter.

15.1. I have no memory of this exchange, which took place six weeks after I became a consultant 33 years ago. I assume that this was some sort of discount scheme on a sort of buy one get one free basis, benefitting the hospital and set up by my predecessor.

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

16.1. I am unable to address this question in relation to the Sheffield Centre.

16.2. Whilst the choice of product to be used nominally lay with the managing clinician(s), Commissioners became involved if that choice incurred significantly increased cost and that cost then had to be negotiated. Our negotiations in relation to the introduction of high purity products were ultimately locally successful in Liverpool and Manchester causing only a short delay in introducing these products.

However, the cost of recombinant products delayed their introduction for up to a decade, depending on patient's age.

16.3. National Procurement of clotting factor concentrates started with "*recombinant for all"* in 2005-6 and the National Haemophilia Database had to calculate the financial uplift necessary for each centre to permit them to change to the recombinant products of their choice. This was complex because at that time each centre was paying a different unit price for each product and through this process we would establish a national price for each brand of recombinant product for the first time, the recombinant products themselves varied in price. This is described in Hay CRM; Purchasing factor concentrates in the 21st century through competitive tendering. ***Haemophilia*** 2013, 19, 660-667. (WITN3289043).

16.4. Although in each subsequent round of national procurement, we have tried to preserve some degree of prescribing freedom, prescribing freedom has been reduced and financial considerations have come into play to some degree. In financial terms, repeated rounds of national procurement have been enormously successful, reducing unit price of factor VIII, for example by 90% to the lowest unit price since the 1970s. These products are sold for more than ten times the unit price in some European countries. However NHS England very effectively discouraged us from changing more patients to much more expensive long-acting factor VIII.

17. *What alternative treatments to factor concentrates were available for people with bleeding disorders? In answering this question please describe the involvement with early treatments with DDAVP referred to in your oral evidence to the Penrose Inquiry [PRSE0006008 and PRSE0006083].*

17.1. The use of DDAVP for the treatment of mild haemophilia and von Willebrand's disease was first described in the Lancet in 1977, when I was a houseman. DDAVP was not licensed until 1982 for this indication, as I recall. This was discussed as a strategy for minimising risks associated with blood product therapy amongst the patients who might respond to DDAVP.

17.2. I can remember administering probably the first dose of DDAVP we had used in Sheffield for this indication in 1977 to correct von Willebrand's disease prior to a minor procedure. The patient went bright red and complained of a headache.

17.3. During the late seventies and early eighties, centres explored and learned how to use DDAVP and learned its strengths and limitations. Its use was well established in Sheffield when I joined in 1983 and it was used wherever the response was considered adequate.

17.4. Once licensed, its use became more widespread and UKHCDO recommended that it be used in preference to blood products wherever the haemostatic response was considered adequate and the patient was able to tolerate the product (WITN3289041, WITN3289042 and WITN3289044).

18. *What were, in your view, the advantages and disadvantages of those alternative treatments? What use was made of them at (a) Sheffield and at (b) the Liverpool 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?*

1.1. The advantage of DDAVP is that it was synthetic and did not confer any risk of infection with blood borne infection.

18.1. The disadvantages were: -

18.1.1. Tachyphylaxis, (reducing response with each subsequent dose) especially with Haemophilia A and more severe von Willebrand's disease.

18.1.2. Poor response: 10% of mild VWD and a higher proportion of more severe haemophilia A with a baseline <15% FVIII had a very poor response. Bleeding disorders other than Haemophilia and VWD and some platelet disorders did not respond.

18.1.3. Unsustained response/short half-life of action in many patients: Thus a

trial of DDAVP is necessary to establish how each individual will respond and how sustained the response is and for which procedures it would be appropriate to use it.

18.2. Treatment side effects: DDAVP has an antidiuretic effect requiring fluid restriction for 24 hrs after each dose and electrolyte monitoring to avoid water overload and epileptic fits. Facial flushing and headache. Some patients are unable to tolerate the product.

19. What was the policy and approach at Sheffield and at the Liverpool 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?

19.1. **Sheffield: 1977:** I recall there was still limited use of cryoprecipitate in patients with Haemophilia A and von Willebrand's disease. However, the vast majority of severely or moderately affected patients were already on home-therapy and that required concentrate, since cryoprecipitate needed to be stored at -40^{0}C. It was being phased out also for other reasons, including the very frequent and often severe transfusion reactions associated with the cryoprecipitate and relative haemostatic inefficiency. Twelve bags (a big dose) was equivalent to a single 1000 units vial of factor VIII, whereas the standard dose for prophylaxis is 2000 units and surgery requires on average 4000 units pre-op and 2000 units twice daily for 7 days. Cryo became increasingly impractical as a replacement therapy.

19.2. **Sheffield 1983-87:** I don't think cryoprecipitate was used for congenital bleeding disorders except in very limited circumstances as outlined in the UKHCDO Guidance of 1983 and1984 (WITN3289041 and WITN3289042). Table 1 of the 1986 UKHCDO Annual Report shows that the use of Cryoprecipitate across the UK reduced to almost nothing between 1982 and 1985 (WITN3289045).

19.3. **Liverpool 1987-94**: I do not recall Cryoprecipitate being used for congenital bleeding disorders and it was recommended that it *not* be used for congenital

bleeding disorders by UKHCDO in 1988 (WITN3289044).

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

19.4. Once virally attenuated concentrates became available, it was recommended by UKHCDO in 1988 (WITN3289044) that we no longer use cryoprecipitate or plasma for any congenital bleeding disorder for which there was a concentrate available since plasma and cryoprecipitate, whilst tested for HIV were still not screened for hepatitis C until September 1991 and were not virally attenuated and were therefore considered less safe than virally attenuated factor concentrates at that point in time.

20. What was the policy and approach at (a) Sheffield and at (b) the Liverpool Centre in relation to home treatment? Did the policy and approach change over time and if so how?

20.1. The policy approach in Sheffield and Liverpool in the nineteen eighties was that all patients with severe haemophilia A and B and those with moderate Haemophilia with a severe bleeding phenotype should be trained to self-inject so that they could be on home therapy. The process of establishing patients on home-therapy had been largely completed by the late seventies and early eighties. The advantages of home therapy were obvious. It improved life expectancy and minimised joint damage. Most of the bleeds treated at home will be joint bleeds. However, it is important that patients come in for more severe bleeds and consult the Haemophilia Centre when necessary. A common rule is that if the patient feels the need to treat a bleed more than twice they should seek advice from the Haemophilia Centre and they should come to the centre for all muscle bleeds. This policy has not changed since the nineteen seventies. Patients with milder bleeding disorders who bleed infrequently are not established on home therapy because they lack the experience to know when it is appropriate to treat themselves.

21. What was the policy and approach at (a) Sheffield and at (b) the Liverpool Centre in

relation to prophylactic treatment? Did the policy and approach change over time and if so how?

21.1. **Sheffield:** 1983-87: Patients were treated on-demand. Some prophylaxis was being introduced in Children towards the end of this time, I think.

21.2. **Liverpool**: 1987-94: I looked after adults. Patients were generally treated on-demand throughout this time. Some children at Alder Hey began to use prophylaxis I think.

21.3. **Manchester:** 1994-2000 When I arrived all patients were managed on-demand and the budget for factor concentrates was surprisingly small and constrained. I changed the contractual structure and treatment intensity increased rapidly year on year and I switched all patients with Haemophilia to high-purity products. Prophylaxis for all children but not adults became UKHCDO Policy in 1996. All the clinical studies of prophylaxis were conducted in children and the evidence for efficacy of prophylaxis in adults was weak. The objectives of prophylaxis in adults were more limited because adult patient already had established arthropathy whereas early prophylaxis in children could prevent arthropathy from developing

Nevertheless, opinion slowly shifted over the years so that prophylaxis for all patients with Haemophilia became a widespread aspiration. This was resisted by commissioners because this more than doubled treatment cost I began introducing prophylaxis for more frequent bleeders in the second half of the nineties and this has progressed as a "creeping development" so that by about 2010 I would estimate that about 80% of patients with severe haemophilia A and B used prophylaxis.

21.4. Our ambition has also changed over the years so that at first we hoped just to dramatically reduce the number of joint bleeds using prophylaxis, whereas now, we wish all the patients to be bleed-free, an aspiration previously considered unrealistic. This involved personalising the patient's prophylaxis regimen, pharmacokinetically optimised and increasing treatment intensity. To give some measure of this, the average UK patient with severe haemophilia used 120,000

units of factor VIII in 2004 and the average now is about 300,000 units (UKHCDO figures). Further progress is being made as we switch our patients with severe haemophilia A from factor VIII prophylaxis to Emicizumab (Hemlibra, Roche) a factor VIII-mimetic monoclonal antibody with a half-life of 33 days. Not only is its weekly subcutaneous administration far more acceptable to the patient, but it has rendered almost all of them completely bleed-free and with far less joint pain. This is huge step forwards and the patients treated with this agent have been delighted.

21.5. It should also be noted that one of the barriers to the introduction of prophylaxis in adults comes from the patients themselves. The patient has to understand what one is trying to achieve with prophylaxis and buy into it. This involves a long conversation and explanation of the pharmacokinetics of factor VIII and IX and one's current understanding of the development of haemophilic arthropathy so that the patient understands the underlying principles and the objectives of the treatment. When you talk to patients with Haemophilia you discover that, whilst they may not complain about it unless asked directly, many really dislike giving themselves intravenous factor VIII. They dislike the injections and the hassle and their veins may also be poor. Some also harbour residual concerns about product safety. Patients brought up treating their bleeds on-demand also sometimes have difficulty accepting the principle of preventative treatment involving far more frequent injections up to 3-7 times a week. From about 2010 almost all my remaining on-demand patients were older patients, some uncompliant patients, and patients who tried prophylaxis but just couldn't keep it going and who had poor venous access or just hated injecting themselves. The advent of extended half-life factor VIII/IX products and then Emicizumab has been very useful for these patients because treatment compliance and patient acceptability are much better.

22. *What was the policy and approach at (a) Sheffield and at (b) the Liverpool Centre in relation to the use of factor concentrates for children? Did the policy and approach change over time and if so how?*

22.1. I cannot answer this question. I was attached to Sheffield Children's Hospital for two periods of six months as a senior registrar about 35 years ago. I was not

responsible for such policy decisions and I cannot recall what they were.

22.2. In Liverpool, I was responsible for Adult Haematology and I did not have a contract with Alder Hey Hospital. Whilst I did some joint clinics for a little while with Dr Paula Bolton Maggs at Alder Hey to help out, those ceased when Dr Lynne Ball was appointed Consultant Haematologist at Alder Hey in late 1988. Previously, the Haemophilia Unit had been the responsibility of Dr John Martin, Consultant Paediatric Oncologist. I never had consultant responsibility at Alder Hey and have no knowledge of their policies.

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

23.1. The only conditions that respond adequately to DDAVP are most cases of mild von Willebrand's disease type 1, mild Haemophilia A, generally with a baseline factor VIII significantly in excess of 15%, and some platelet disorders. All other conditions will not respond and will be treated with blood products, either concentrates, or plasma (factor V) or Cryoprecipitate (Going out of use in the seventies and early eighties).

23.2. DDAVP treatment of bleeding disorders was first described by PM Mannucci in a letter to the Lancet in 1977. However, was not licensed for treatment of bleeding disorders until 1982.

23.3. Prior to 1982 some centres (and certainly Sheffield) used DDAVP on a "named patient" basis. That is a system whereby a clinician may use an unlicensed product on his own responsibility. That is to say, if something goes wrong the responsibility lies with him and not the manufacturer. Prior to the advent of DDAVP, there was no alternative to blood products to correct the haemostatic defect of patients with bleeding disorders and for most bleeding disorders that remained the case.

24. What viruses or infections, other than HIV, HCV and HBV, were transmitted to patients at (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre in

consequence of the use of blood products?

24.1. In the early 1990s, there was a minor outbreak of hepatitis A in relation to concentrates not used in my centres. None of my patients were affected. Hepatitis A does not cause chronic liver disease and consequently is not traditionally considered a transfusion hazard. Nevertheless, patients have been vaccinated against hepatitis A since that time.

Section 3: Knowledge of, and response to, risk

General

25. When you began work as a Senior Registrar in Haematology at Sheffield, 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?

25.1. At that point, in early 1983, I was aware of Prof Preston's 1978 Lancet paper. I was aware of non-A, non-B hepatitis and the assumption that this was transmitted by blood or blood products. I was also aware that no causative virus had been identified and that it was defined by abnormal liver biochemistry in the absence of serological markers for hepatitis B and A. I was also aware that the international consensus of scientific opinion amongst haematologists at the time was that NANB was generally benign and non-progressive. One Professor of Haematology described it to me in conversation as "a biochemical curiosity". I was also aware that hepatitis B had been transmitted by blood and blood products. However, this was a numerically relatively small problem because 90-95% of patients cleared hepatitis B spontaneously and so relatively few patients with bleeding disorders had chronic liver disease secondary to hepatitis B. Furthermore, in 1982, a synthetic hepatitis B vaccine had been introduced and all patients with bleeding disorders lacking immunity to hepatitis B were subsequently vaccinated.

26. What advisory and decision-making structures were in place, or were put in place at

(a) Sheffield and at (b) the Liverpool Centre, to consider and assess the risks of infection associated with the use of blood and/or blood products?

26.1. In Sheffield, these decisions were made by Professor Preston and Dr Michael Greaves, as the consultants in charge. Whilst I cannot remember the details, it was very clear that in deciding policy, they were very much guided by national and international opinion from the Literature, UKHCDO discussions and policy statements from the Haemophilia Society and the World Federation of Haemophilia. This was discussed in the journal club and the main weekly pre-Ward-round discussion. It was, for example, speculated at one point in the literature that we should revert wholesale to treatment with cryoprecipitate to minimise the number of donors to which the patients were exposed. This was universally rejected across the globe for reasons which I will explore further in answer to Question number 43 (below).

26.2. I do not remember whether Sheffield had a Transfusion Committee at that time. I was certainly not involved with one.

26.3. In Liverpool, I decided which treatments were to be used for patients with bleeding disorders. We were only using virally attenuated products and I used DDAVP wherever the patient could be shown to obtain a haemostatically adequate response. I did not use cryoprecipitate for congenital bleeding disorders because it was not virally attenuated and it was recommended not to use it for congenital bleeding disorders in the 1988 UKHCDO Guidance (WITN3289044).

26.4. There was a Transfusion Committee, of which I was a member but, given that I left Liverpool a quarter of a century ago, I have very little memory of it and have retained no minutes from it.

27. 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?

27.1. It was apparent from shortly after taking up post as senior registrar in Sheffield that

there was no difference in the risk of Non-A, Non-B hepatitis between commercial and BPL concentrates (Craske, Pavier Trowell et al BMJ Oct 23rd 1983 (WITN3289046).

27.2. The relative risk of transmission of the virus responsible for AIDS was unknown until after a test became available in 1984. Since AIDS had been reported throughout the world, one would have assumed that patients would be potentially at risk from blood and blood products from all geographic locations but since only a single UK patient with a bleeding disorder had developed AIDS in 1983 and only 3 by late 1984, (UKHCDO Guidance 1983 and 84 WITN3289041 and WITN3289042) at that time it did not appear the serious problem it would ultimately become. Furthermore the cause of AIDS and the extent of that risk and the natural history of the condition were completely unknown in the early eighties. By 1985 we had been in the fortunate position in Sheffield that we had been able to change many of our patients to Alpha Prophilate, a virally attenuated product, and by late 1985 all Sheffield patients with Haemophilia A and B were treated with virally attenuated products. .

28. What decisions and actions were taken at (a) Sheffield and at (b) the Liverpool Centre and/or by you to minimise or reduce exposure to infection?

28.1. We used DDAVP when we could in those patients whose haemostatic response to the drug was adequate. This appeared to be well established in Sheffield in 1983, when I joined the staff as senior registrar, by which time DDAVP was licensed for this indication.

28.2. We took care to avoid switching brands so that patients were only treated with their allocated brand for as long as possible.

28.3. We switched to virally attenuated products at the first opportunity in late 1984 and during the course of 1985, as suitable products became available and based on theoretical, model virus, data. I cannot remember the regulatory basis for this change because I suspect that the product (Alpha Profilate) may not have been

fully licensed at that time. It may have been prescribed on a "named patient" basis. Few centres were in a position to change products so soon because supplies were very limited.

28.4. By the time I took up post in Liverpool in May 1987, only virally attenuated concentrates were in use.

Hepatitis

29. *When you began work as a Senior Registrar in Haematology at Sheffield, what was your knowledge and understanding of the risks of the transmission of hepatitis (including hepatitis B and NANB hepatitis) from blood and blood products? What were the sources of your knowledge? How did that knowledge and understanding develop over time?*

29.1. I was aware that Hepatitis B and NANB could be transmitted by blood and blood products but that risk had not been quantified and at that point in time was not perceived to be a major hazard. In contrast, the enormous improvement that such treatments had brought, in terms of improved life expectancy (from a pre-treatment life expectancy of 10-15 years to apparently near normal (WITN3289047: and WITN3289052) were very obvious. The sources of my knowledge were the literature and my Blood Transfusion training in Sheffield BTS between August 1982 and March 1983.

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

30.1. I kept abreast of the literature and developed a significant interest in viral liver disease. See my MD thesis HCDO0000661 . I have, from the early 1980s had a close working relationship with Hepatology.

31. What, if any, actions did you, or the Centres at which you worked, take to reduce the risk to patients of being infected with hepatitis (of any kind)?

31.1. Virally attenuated concentrates were used when they became available and DDAVP used when an adequate haemostatic response could be obtained. We campaigned for recombinant factor concentrates and changed to these products as soon as we were permitted to do so. This was UKHCDO Policy from 1996 (WITN3289048: UKHCDO Therapeutic Guidelines 1997). The use of cryoprecipitate was abandoned as soon as virally attenuated concentrates became available because cryoprecipitate was not virally inactivated (WITN3289044).

31.2. Patients lacking immunity were vaccinated against hepatitis B and chronic carriers of this virus advised to use barrier contraception. Whether to advise barrier contraception for patients with HCV remained controversial, and no consensus emerged. It became clear that HCV was not as readily transmitted sexually as HBV. Patients were also vaccinated against hepatitis A from 1991.

32. What liver function tests and/or other forms of monitoring were undertaken at (a) Sheffield, at (b) the Liverpool Centre and at (c) the Manchester Centre and how did that change over time? What was the purpose of such testing and monitoring?

32.1. During my time in Sheffield, Liverpool and Manchester, patients with severe bleeding disorders were reviewed every 6 months and those with mild bleeding disorders every year unless they failed to attend and became lost to follow up, a common situation in patients with mild bleeding disorders the world over. This led to delays in testing some patients who were poor attenders.

32.2. When I took up post In in Manchester in 1994, I found that patients with mild bleeding disorders had open access to the service but were not followed up systematically. This was a common pattern for patients with mild bleeding disorders at that time because such patients require medical attention so infrequently. I did not think that this was acceptable not least because some

needed HCV antibody testing and so I started to follow these patients up annually, but discovered that we no longer had a current address for about a third of them. It therefore took years to get them all back to clinic.

32.3. Those known to have liver disease had liver function tests at each visit and usually also alpha fetoprotein (a marker for hepatocellular carcinoma). An abdominal ultrasound was arranged every two years or so, to look for signs of splenomegaly, portal hypertension and cirrhosis. Patients suspected to have cirrhosis would also have either a barium swallow in the early years and from the late eighties onwards endoscopy to assess for the presence and size of oesophageal varices (varicose veins in the gullet). Varices could be treated through an endoscope to prevent them from bleeding, initially by sclerotherapy and subsequently by the insertion of TIPS. Patients would be examined for physical signs of liver disease.

32.4. In the early years, many centres conducted liver biopsy, as the only means of assessing the severity of underlying liver disease since neither the degree of abnormality of liver function tests nor physical examination gave any indication of the severity of the liver disease until obvious clinical signs of cirrhosis developed. From the late Eighties, liver biopsy was reserved for more selected patients where some diagnostic difficulty was present. This has from the early 2000s been almost completely supplanted by the recently available Fibroscan, a quantitative ultrasound technique, which quantifies the extent of hepatic fibrosis and which is capable of detecting hepatic fibrosis/early cirrhosis and which has been deployed for all our patients with liver disease.

32.5. When hepatitis antibody testing became available in 1992, we tested all available patients who had had some treatment during the period of risk for hepatitis C (pre-1986 for concentrate and pre late 1991 for blood products) at the first opportunity. This told us who had been previously exposed to HCV but did not tell us who was still actively infected. When a HCV PCR test (polymerase chain reaction- a test for circulating hepatitis C virus) became available, antibody positive patients and untested patients were tested. This told us who was actively infected. Many of those patients had normal liver function tests and would not have been identified

by liver function testing alone. After the introduction of virally attenuated concentrates, we continued to test for HCV for a number of years in uninfected patients, monitoring for any failure of viral attenuation. When HCV genotyping became available, patients with chronic HCV were tested since the HCV genotype informed one's choice of treatment and its duration and gave information on the likely response-rate which was useful to manage patient expectations.

32.6. The purpose of this monitoring was to monitor for the emergence of more serious liver disease, which would require more active multidisciplinary management. We were also monitoring for the development of hepatocellular carcinoma in those patients with cirrhosis. As treatment for HCV emerged and developed, such monitoring was used in various ways to select patients for treatment, to select the best treatment regimen and to inform the patient of the likely response-rate. One other important function of monitoring is obviously to inform discussion with the patient about the condition of their liver and to inform treatment discussions and the patient's decisions.

33. 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?

33.1. Hepatitis A is common infectious hepatitis. It commonly causes a flu-like illness and not always jaundice so that the some 35% of the population who get it in their lifetime may be unaware that they have been exposed. It is commonly spread by food and, since it resolves completely without causing a chronic carrier state or chronic hepatitis it was not considered a transfusion hazard. It is caused by a protein coated virus now thought to be resistant to some of the early viral attenuation techniques such as dry heat treatment or solvent-detergent treatment but not pasteurisation. Consequently, when there was a small outbreak of hepatitis A associated with a single brand of concentrate, many concentrates moved to dual viral attenuation methods. There has not been a recurrence of hepatitis A transmission, since that time. Patients with bleeding disorders have, since then, been recommended to be vaccinated against hepatitis A.

33.2. Hepatitis B, historically known as "serum hepatitis", was recognised from at least the Second World War when large outbreaks amongst GIs were attributed to the use of non-sterilised needles for mass vaccination. The causative virus was identified in 1967.and I believe blood transfusions were tested for it from the late sixties. Interestingly, this led to the cessation of blood donor sessions in British Prisons, because most of the positive tests were coming from prison inmates and they realised that prisoners were a high-risk group (or so I was told by the Head of Virology in Sheffield BTS during my training). Acute hepatitis B could be a severe illness with a small but significant mortality rate. However, it became apparent (see my MD thesis) that many patients had been exposed to hepatitis B and had developed serological markers of past exposure to the virus without developing jaundice or an acute illness. When I looked at the Sheffield population, I found that 80% of patients with severe haemophilia and 40% of these I looked at with non-severe haemophilia had markers of past exposure to hepatitis B but few gave a history of jaundice.

33.3. The virus could be spread parenterally and there was significant sexual spread so sexual partners of carriers should be vaccinated and /or barrier contraception used. A synthetic vaccine was introduced in 1982.

33.4. 5-10% of patients infected with hepatitis B become chronic carriers and these patients may develop chronic hepatitis, cirrhosis and hepatocellular carcinoma. This provided the model for NANB hepatitis, which it was at first assumed, would follow a similar course.

33.5. NANB hepatitis was first described in 1974 but the causative virus was not described until 1989. Acute NANB was usually asymptomatic and relatively few patients developed a severe acute illness with jaundice and the mortality rate from acute NANB hepatitis was very low. It was clear from relatively early on (Preston et al 1978, PRSE0003622) that a much higher proportion of patients exposed to the causative agent for NANB developed a chronic carrier state, compared to those with HBV, as judged by the proportion of patients with haemophilia who developed persistent abnormalities of liver biochemistry during the course of the

1970s. However, a number of liver biopsy studies published as late as 1982 reported generally mild histological abnormalities and consequently the consensus of opinion was that this was a mild and non-progressive condition. During the course of the nineteen-eighties, Liver biopsy studies in the UK (Hay et al 1985 PRSE0004229, Hay et al 1987 WITN3289050) and the US (Aledort et al 1985 WITN3289049) showed that although most patients had mild liver disease, a significant minority had progressive liver disease. Once the virus had been isolated and a test for HCV became available, it also became apparent that most patients with "cryptogenic cirrhosis", cirrhosis of previously unknown cause, had markers of chronic hepatitis C, which was presumably the cause of their cirrhosis. This led to a more measured assessment of chronic HCV in which most patients chronically infected had mild liver disease and indeed some chronic carriers have normal LFTs but a minority progress, often slowly and over decades, to severe liver disease. Severe liver disease was much commoner amongst patients who drank alcohol moderately or heavily and amongst those who were immunosuppressed for any reason.

34. *You were involved in an 8 year study of 79 patients with haemophilia, which was discussed in an article (enclosed, [PRSE0004229]) published in The Lancet in June 1985 entitled "Progressive Liver Disease in Haemophilia: An Understated Problem?".*

a. *Why was this study undertaken?*

34.1. I observed, in an outpatient clinic, that a patient who had previously had a liver biopsy showing mild hepatitis had progressed to cirrhosis. I drew Professor Preston's and Dr Trigger's (Consultant Hepatologist) attention to this observation because I understood that this form of hepatitis was thought at that time to be benign and non-progressive based on previous liver biopsy studies. We agreed that we needed to investigate the patient group more closely to determine whether their liver disease was progressing or not. Since there were no non-invasive methods of investigating this, it involved liver biopsy, a standard approach to the investigation of any liver disease at that time.

b. *What did the study involve?*

34.2. It involved repeat liver biopsies in those who had already had an earlier liver biopsy and a first liver biopsy in patients with abnormal liver function tests. We also continued to monitor liver function tests and ultrasound as before and conducted tests (barium swallow or endoscopy for oesophageal varices in patients found to have serious liver disease. Oesophageal varices need active management to avoid or minimise the risk of catastrophic bleeding.

c. *Were the 79 patients aware that they were the subject of this study?*

34.3. This was an observational study. Dr Trigger and Professor Preston considered that the liver biopsies were indicated for clinical management since this was the established approach to the investigation of liver disease at that time. Either I or Dr Trigger (who conducted all the biopsies) took consent from the patients for liver biopsy as one would for any invasive diagnostic procedure.

d. *What conclusions did you reach as a result of the study?*

34.4. We concluded that: -

34.4.1. The natural history of HCV differed from that of HBV.

34.4.2. That the degree of inflammation of the liver in HCV often waxed and waned.

34.4.3. For that reason, the histological appearance of mild hepatitis did not reliably predict a benign subsequent course.

34.4.4. That a significant minority (15% of our cohort) had developed progressive liver disease (chronic active hepatitis or cirrhosis) and one might expect an unknown proportion to develop serious liver disease in the future.

34.4.5. The majority of patients either did not have liver disease or had mild,

hepatitis. Whilst one might expect the majority to have a good prognosis (as indeed proved to be the case) there was nevertheless uncertainty about the future and this underlined the importance of close monitoring of the liver disease in the future and the importance of finding antiviral treatments to eliminate the hepatitis if possible.

e. *What was the response amongst clinicians to your presentation of the findings of the study to the AGM of the British Society of Haematology in March 1985?*

34.5. Professor Arthur Bloom, who chaired the session, described the findings as "sobering". I don't think the findings were fully accepted until confirmed by other groups, however.

f. *What was the response amongst clinicians to the study following the publication in The Lancet?*

34.6. International Authorities, especially Mannucci, who had published on this subject as recently as 1982, disputed our findings and speculated that there was something peculiar about our patient population. This dispute played out in the letters page of the Lancet (WITN3289051) and our findings continued to be disputed until a similar report appeared from the United States (LM Aledort et al Blood 1985, WITN3289049). With the wisdom of hindsight, early studies had observed mostly mild liver disease because they were investigating a patient population who had contracted HCV a relatively short time before. When we investigated our patients in the early eighties the natural history of HCV had had longer to unfold and more serious liver disease was seen.

35. Please describe your involvement in the investigations of NANB hepatitis which resulted in the publication of results by Professor Preston et al in 1978 [PRSE0003622].

35.1. My only involvement in this that I remember was to administer the replacement therapy to one or two of the patients undergoing liver biopsy during my three months as their Haematology houseman. I think Dr Trigger took consent.

36. You wrote to the Haemophilia Society on 7 October 1991 about hepatitis C (letter enclosed, [HSOC0003297]).

a. *What was the factual/evidential basis for the description in your letter of chronic persistent hepatitis as "a mild and usually non-progressive form of liver disease unlikely to give problems"?*

36.1. This comment is taken out of context. It appeared true in 1991 insofar as most of these patients had not been shown to progress but the remainder of the paragraph goes on to say that we had shown 15% of our patients to have cirrhosis and gives various reasons for suspecting that this was an underestimate and that perhaps up to 25% might have cirrhosis. The paragraph after that deals with my suspicion that deaths due to liver disease may, for various reasons, have been underestimated.

b. *What was the factual/evidential basis for the assertion in your letter that the majority (80-85%) of older patients "will never suffer any problems from liver disease"?*

36.2. This alludes to the fact that the natural history of HCV, as known in 1991, was one of spontaneous resolution in an unknown proportion, stability without progression or slow progression. Therefore most of the patients who were already old in 1991 would die from an unrelated cause before they had time to develop complications from HCV. This was correct in 1991 and should not be confused with the course of HCV in patients who were young in 1991 but who subsequently developed complications of HCV after having HCV for 30 or 40 years. .

c. *What was the factual/evidential basis for the assertion in your letter that "very few patients who are HIV seronegative will actually die from liver disease"?*

36.3. This was obviously speculation, but at the time and for several years until Triple therapy for HIV came along, 75% of liver deaths in patients with bleeding disorders

occurred in patients with full blown AIDS. There were very few liver deaths in HIV negative patients and we were cautiously optimistic, probably too optimistic as it turned out, about the emergence of effective viral elimination treatment for HCV. The number of patients with bleeding disorders who have died from liver disease has probably been underestimated but of the more than 36,000 patients registered with the National Haemophilia database over its 52 year history, 294 (0.8%) have been reported to have died from liver disease (UKHCDO Annual Report 2019).

d. *What was the factual/evidential basis for your assertion that there were "only minimal side effects" from interferon?*

36.4. In 1991 Interferon was only being used in clinical trials and was only being used on its own for the relatively short durations of six months. It was not in general use and I was not participating in those trials but reports indicated that interferon alone was relatively well tolerated. Frankly, there was little experience of this approach at that time. Subsequent personal experience showed me that many patients did tolerate interferon monotherapy reasonably well though most suffered fatigue and a variety of other side-effects. The addition of Ribavirin and the use of Ribavirin and Peginterferon increased side effects considerably.

e. *Why did you advise that the Society should be "very wary about making too much of a fuss about it and giving it too high a profile"?*

36.5. Again, this comment is taken out of context. This is a paragraph about the communication strategy of the Haemophilia Society to its members about hepatitis and how high a profile this should be given. I was advocating, in a clumsily expressed sentence, a medium profile strategy rather than a high profile splash because I was concerned about causing undue alarm in an already traumatised group of patients going through almost the worst phase of the HIV era, when treatment was failing and many patients were dying, often in the most distressing circumstances of their third or fourth AIDS-defining illness. AIDS was a clinically defined diagnosis based on the occurrence of opportunist infections and the development of unusual secondary malignancies. I felt that this group, most of

whom expected to die soon and who required a lot of psychological support, had enough on their plate.

f. *What is your current view of the accuracy of each of the statements set out in sub-paragraphs a. to d. above?*

36.6. I still think the number of deaths attributable or partly attributable to HCV may be underestimated. Subsequent experience showed us that interferon therapy was generally not well tolerated, particularly when used in combination with other drugs. I have already described this elsewhere in this report. Any optimism about the efficacy of antiviral treatment for HCV was subsequently dashed, response rates remaining very disappointing until the introduction of a new generation of drugs in the past few years. We have now eradicated HCV from almost all of our patients except the handful who refuse treatment.

37. *In your oral evidence to the Penrose Inquiry (on 12 January 2012 [PRSE0006083]) you stated (at pp.78-79) that "the natural history of chronic persistent hepatitis at that time was largely based on a paper by Chadwick et al, which looked at chronic persistent hepatitis in patients with Hepatitis B. And with hindsight perhaps we shouldn't have expected that it would pursue the same natural history with a different virus." Why did clinicians expect or assume that the natural history with NANB hepatitis would be the same or similar to the natural history with hepatitis B? Should clinicians have recognised, or at least suspected, earlier that NANB hepatitis might lead to significant liver disease? On what basis was it considered to be "a benign and non-progressive disease"?*

37.1. What the author of this question may be missing in the Chadwick comparison is that it is a comparison of the natural history of a specific histological appearance of "chronic persistent hepatitis" between the two viruses rather than an overall comparison of the two viral illnesses. This appearance down the microscope is very common in both conditions and in HBV is associated with a non-progressive course. The general assumption that the same would be true for NANB was not just a leap of faith but was also backed up by early liver biopsy studies showing

very little progressive liver disease.

37.2. Our knowledge of the natural history of NANB in the early 80s was based on a number of liver biopsy studies from various groups, which showed very little severe liver disease. Against that background, it was not unreasonable to consider it likely that the natural history of NANB would be similar to chronic HBV since evidence to the contrary had not yet emerged. This was a newly discovered disease. It is common for it to be assumed that newly discovered diseases will behave similarly to other similar but not identical diseases (e.g. SARS and Covid-19, - both caused by COVID viruses) and it takes time to discover in what way the diseases are similar and in what way different. Both HCV and HBV can cause cirrhosis and hepatocellular carcinoma, for example.

38. A memo dated 7 September 1987 (enclosed [BAYP0000010_161]) regarding a report, by your predecessor at Liverpool, of NANB hepatitis in a patient receiving a particular batch of Koate records you expressing "surprise that any report had been made at all as non-A, non-B hepatitis is not unexpected in recipients of factor VIII concentrate". Does that accurately reflect your view at that time? Did you routinely inform your patients to expect that they might become infected with NANB hepatitis if they received factor VIII?

38.1. I suspect I am being misquoted here because this memo, between two people I neither know nor remember, is internally contradictory and does not reflect views I have ever held. It relates to a report made by my predecessor, Dr Mackie, to Cutter of a suspected case of hepatitis transmitted possibly by Koate HT in relation to a patient managed in Alder Hey hospital who presumably developed jaundice. Far from being "expected" this was very unexpected since this product was virally attenuated and would NOT be expected to transmit hepatitis. In the end it turned out the patient had infectious hepatitis, hepatitis A. Since this does not cause a chronic carrier state, it was not regarded as a transfusion hazard, which is fortunate since 35% of us contract it at one time or another. The hepatitis therefore probably had nothing to do with treatment with Koate HT.

38.2. I did not routinely warn people that they might contract HCV after the advent of effective viral attenuation though we did continue to monitor for it just in case. .

HIV and AIDS

39. 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 Sheffield? How did your knowledge and understanding develop over time?

39.1. As far as I can remember, in early 1983, AIDS had been defined clinically and the risk groups for the condition had been defined. Donor screening was introduced, reducing the risk of HIV and HCV from blood transfusion and blood components probably by 90%. It was clear that AIDS was probably caused by an, as yet unknown, virus and since isolated cases of HIV had been reported in patients with bleeding disorders it was assumed that some blood transmission had taken place. We had no idea in 1983 how many patients would be infected or the relative risk from UK or Commercial clotting factor concentrates. In 1983 only one case had been in reported in an UK person with Haemophilia and by late 1984 that total had risen to only 3 (WITN3289041 and WITN3289042). It was assumed, based on what had already been reported, that few HIV-infected patients would develop AIDS because almost none had, at that point. This view persisted into the late eighties to some extent. The natural history of HIV was unknown and indeed it was not until well into the 1990s or even the 2000s that we would conclude that all HIV positive patients would eventually develop AIDS, if left untreated because some of our patients had preserved stable CD4 cell counts for 20 years without treatment only for their counts to decline after all of that time.

39.2. In late 1984, a test for HIV (then known as HTLV-3) antibody became available. All our patients with bleeding disorders were tested and it became apparent that about 50% of potentially exposed patients had become infected but most remained well

40. How and when did you first become aware that there might be an association between

AIDS and the use of blood products?

40.1. It was apparent from the early 1980s, based on reports in the literature. Very few cases of AIDS were seen in UK Haemophiliacs until 1985/6 (one in 1983 and 3 in toto by 1984 (WITN3289041 and WITN3289042)

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

41.1. We all followed the literature.

41.2. Professor Preston, in particular, also went to UKHCDO and various working parties (of which I was never a member) and reported back current opinion (much of it, in the absence of hard evidence, being very speculative and subsequently disproven by events). Two guidelines from 1983 and 84 are attached and discussed below (WITN3289041 and WITN3289042)

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

42.1. Patients were kept to a single brand of concentrate. The reasoning for this related to NANB, as described above.

42.2. We changed over some patients to a virally attenuated product in December 1984 based on experimental evidence that showed that a model virus thought to be similar the causative agent for AIDS was heat labile. This concentrate (Alpha Profilate, Alpha Therapeutic Corporation, US) may not have been fully licensed at the time; I am not sure. It was not known in late 1984 to be AIDS-free and the method of viral attenuation was not completely effective against NANB and had not been shown to be effective against HIV (though it subsequently proved to be so). On the other hand, there was no reason to think that this change of product would harm the patients and it seemed likely to be a big step in the right direction.

Supplies of this product were initially limited and it was only possible to change half the Sheffield patients to the product at first and only the four centres who had participated in the trial were able to obtain supplies of this product at that time. It became more widely available during the course of 1985, when other "hepatitis reduced" products came into use. Fortunately HIV proved easier to inactivate than hepatitis viruses.

42.3. Unheated concentrate was returned to the manufacturer in early 1985 and BPL heat treated those vials and reissued them. This product was insoluble and not used. BPL was producing 8Y, a heat-treated factor VIII concentrate and 9A a heat treated factor IX concentrate by mid-1985. I am uncertain of the precise date. By the end of 1985 all concentrates in use in Sheffield were virally attenuated.

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

43.1. I did not make the policy, though I think it was correct, particularly given the state of knowledge at the time. I was also led to understand that the policy we were following had been endorsed by UKHCDO and is encompassed in the UKHCDO Guidance of 24/6/83 and December 1984 (WITN3289041 and WITN3289042), The Haemophilia Society and the World Federation of Haemophilia. We continued to use concentrate for the following reasons: -

43.1.1. Changing wholesale to cryoprecipitate would not obviate viral risk since Cryoprecipitate was not tested for HIV until 1985 and not tested for HCV until 1991 and was not virally attenuated.

43.1.2. Changing to Cryoprecipitate or no-treatment would dramatically increase the risk of haemorrhagic death, decrease life expectancy dramatically and lead to more rapid deterioration of haemophilic arthropathy.

43.1.3. Changing to Cryoprecipitate would be incompatible with home-therapy, which would have had to be abandoned because the product has to be stored at between -40 and -60 degrees.

43.1.4. There is no acceptable alternative treatment for patients with Haemophilia B, who will respond to neither DDAVP nor Cryoprecipitate. One litre of plasma will only raise the factor IX level by 15% and carries a significant risk of transfusion reactions in multi-transfused individuals.

43.1.5. The risk of continuing concentrate was unknown but thought to be relatively small. In the guidance of 24/6/83, it is mentioned that there had only been one patient with Haemophilia in the UK with Aids. In the 1984 guidance, this number had risen to 3 with only 102 cased in the general population. In late 1994 tests for HTLVIII (HIV) antibody had become available from PHLS Colindale and the Middlesex Hospital and patients were beginning to be tested in large numbers. Whilst the significance of those test results would still have been very uncertain, widespread testing led to a rapid re-evaluation of the situation.

Response to risk

44.Did you take steps to ensure that patients were informed and educated about the risks of hepatitis and (in relation to Sheffield) HIV? If so, what steps?

44.1.I spoke to the patients in clinic. Prof Preston held regular meetings with groups of patients to inform them of the development of knowledge of HIV. Naturally, the patients were and continued to be hungry for information but so much was unknown or speculation. An example of this was the consensus in about 1985/6, after the test had become available, that "if you haven't got AIDS after two years, you won't get it". The following year the same statement was being made in relation to a period of three years. We now know both statements to be incorrect. One thing I learned from all of this was that however well-meaning it may be to share with patients current thinking about a condition, it is sometimes better to admit what is not known and not to speculate.

45.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?

45.1. Please see above.

45.2. We used heat treated or otherwise virally attenuated products for all patients for whom such products were available who were unlikely to respond to DDAVP. This included patients with HIV or HCV on the grounds that there might be other undiscovered viruses for which the viral attenuation might offer some protection. We used these products subject to availability. There were delays of several months in the supply of a usable UK manufactured virally attenuated factor VIII and IX concentrate. I recall that there was no access to virally attenuated factor IX until late 1985, for example.

46. *Please consider the enclosed correspondence between you and Armour Pharmaceutical Co Ltd from May to June 1985 regarding a batch of factor concentrate potentially contaminated with HTLVIII (Factorate HT Batch No. Y69402) [ARMO0000380; ARMO0000389; ARMO0000410 and ARMO0000395]. Please set out what you can recall about this matter. How did you become aware of the contaminated batch? What was done with any unused product from this batch? Were patients who received a contaminated batch informed that they were at risk of being infected (and if not, why not?) Did you provide the requested information to Armour? What, if anything, did you tell your patients about this request and your response to it?*

46.1. I have no recollection of this correspondence from 35 years ago. However, it is clear from the correspondence that I was able to account for all 50 vials of the product received and return the unused vials to the manufacturer. The remainder had been administered to a single patient who, testing of stored samples revealed to have been HIV positive at least a year or so before this batch was administered. One could not, therefore, draw any conclusions about the efficacy of their heat-treatment regimen for HIV-eradication from this case, since he was already infected with the virus. I cannot remember which patient was involved or whether we discussed it.

47.In the letter from Armour Pharmaceutical Co Ltd to you dated 17 June 1985 [ARMO0000410] reference is made to "your letter of June 6th". If available, please provide a copy of your letter dated 6 June 1985 to the Inquiry.

47.1.I do not have access to this letter. Bear in mind also that we were still using mechanical typewriters and were not computerised at that time.

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

48.1.I don't think this question is well framed, since it is phrased in such a way as to suggest that the questioner believes that it might have been possible to start using heat-treated products sooner. Heat-treated products were made available as soon as they *were* available and as the volume of supply permitted, as far as I know. None were licensed in the UK in 1984, as far as I am aware.

48.2.I think it is unfortunate that virally attenuated concentrates did not *become* available earlier but the path to viral attenuation was not an easy one. All early attempts at heat treatment reduced the factor VIII activity of the concentrate significantly and several did not appear to inactivate the NANB agent either or, as in the case of Alpha Profilate and Koate HT appeared, initially at least, to be only partially effective in eradicating HCV and were described as "hepatitis reduced" concentrates. BPL's first attempt to produce a heat-treated UK sourced concentrate in early 1985 was an abject failure, since the product was so badly denatured by heat that it would not go into solution. This product was rapidly withdrawn. Some clinical trials conducted abroad, were protracted.

48.3.In any case, direct evidence that HIV was heat labile did not emerge until the virus was isolated and a test became available in 1985. It was therefore not evident until 1985 that viral attenuation techniques developed to inactivate NANB, and only partially effective against that agent, would inactivate the newly described HIV virus. In fact it turned out that HIV was more easily inactivated than hepatitis viruses but this was not known at the time.

48.4. In the absence of alternative supplies of virally attenuated products, most Haemophilia Centres were obliged to continue to use some untreated concentrates until some time in 1985.

49. Did you revert to treatment with cryoprecipitate for some or all of your 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?

49.1. Sheffield, in common with all other centres here and abroad that I know of, did not revert wholesale to the use of cryoprecipitate because cryoprecipitate was also not tested or virally attenuated and was not as haemostatically effective. Table 1 from the 1986 Annual Report (WITN3289045) shows that Cryoprecipitate use declined from a very low level to more or less zero in the period 1982-85. Reverting to cryoprecipitate wholesale was not recommended, though its use for PUPS (previously untreated patients) and infrequently treated patients was endorsed in the UKHCDO 1983 guidance (WITN3289041) would have resulted in abandonment of home-therapy, delay in treating bleeding which would, again become hospital based, and an expected increase in damage to joints and a reduction in life expectancy to pre-concentrate levels (average about 35 yrs. (WITN3289047 and WITN3289052). Cryoprecipitate treatment of severe haemophilia involves administration of hundreds of units and many of the older patients who were treated with this product prior to the advent of concentrates contracted their hepatitis C from Cryoprecipitate rather than concentrate. Cryoprecipitate also had a high incidence of transfusion reactions, which could be severe.

49.2. Furthermore, changing back to Cryoprecipitate wholesale would have achieved little unless instituted as early as 1980-81, since most patients were infected with HIV in 1982-84 and most patients were infected with HCV in the nineteen seventies. It would have to be acknowledged however that a relatively small group of patients were infected with concentrate in the mid-eighties.

50. *Do you consider that your decisions and actions, and the steps taken at (a) Sheffield and/or (b) the Liverpool 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.*

50.1. Yes, given the state of knowledge current at the time, the products available at the time and weighing up the relative risks that appeared to be attached to the therapeutic alternatives available at the time, I think that our actions in Sheffield were reasonable and in some respects we were ahead of the curve. For explanations of "why?" see above.

50.2. I have very limited knowledge of policy and actions in Liverpool prior to taking up post there. No psychological support was available for these patents because there was no haemophilia team prior to 1988. This reflected a lack of resources for most Haemophilia Centres outside London, which was not resolved until "AIDS Money" was made available

50.3. By the time I took up post in Liverpool in May of 1987, all factor VIIII and IX concentrates were virally attenuated.

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

51.1. Please see above

52. *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?*

52.1. I don't have specific knowledge of centres that I did not work in from this early period of the seventies and eighties.

53. 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?

53.1. This is a period before I was involved in the management of hereditary bleeding disorders. However, from my knowledge of the history of this area and my knowledge of drug discovery and development, I would make the following comments, which will hopefully provide some context.

53.2. It typically takes a drug ten years or more for a drug to get through the development process. We have recently started using Emicizumab, a factor VIII-mimetic bispecific monoclonal antibody as an alternative to factor VIII prophylaxis. This took 20 years to bring to market. Four Years ago, Octapharma launched their recombinant factor VIII which had been 15 years in gestation.

53.3. Drug companies started to work on viral attenuation in the seventies, even before it became apparent that NANB could be more progressive than initially thought. My impression was that BPL and PFC, the UK NHS fractionators were *not* at the forefront of these efforts and did not begin to even look into this until 1984/5 and their first heated product was more or less insoluble. Armour, Hyland, Alpha and Behring (and maybe others were all making efforts to produce a virally attenuated product in the early eighties and Behring started in 1979 (Haemate-P) Most of the early products failed to prevent transmission of NANB and had to go through lengthy trials to obtain a license in any case. (Farugia review WITN3289053).

Section 4: Treatment of patients

Provision of information to patients

54. What information did you provide or cause to be provided (or was, to your knowledge, provided by others) to patients at (a) Sheffield, (b) the Liverpool Centre and (c) the

Manchester 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.

54.1.**Sheffield:** I do not have a clear recollection. Please see previous answer.

54.2.**Liverpool:**

1.2.

54.2.1. All products in use were heat treated but still described as "hepatitis reduced". We were reasonably confident that this was adequate to eliminate HIV, which turned out to be more heat-labile than hepatitis viruses. One or two isolated cases of hepatitis transmission were still being reported internationally though investigation of cases in the UK invariably showed they were old cases and not new infections. Longer follow up would show that the products we were using at that time did not transmit HBV or HCV or HIV but at the time we had not got long follow-up and did not have the confidence to describe them as completely safe. Frankly, this was not an issue for patients who had had lots of treatment over the years. However, for the occasional adult patients who had had little or no treatment in the past and who would not respond to DDAVP, we would describe to them the donor selection, the testing of all donors for HIV and hepatitis B and the viral attenuation techniques and tell them that we thought the products were probably safe from that perspective but that we continued to monitor.

54.2.2. As my period in Liverpool continued, we had growing confidence in the products that we were using and switched to products that were increasingly pure and virally attenuated with more and more rigorous methods. Furthermore longer follow-up, without observing virological breakthrough, provided a greater degree of confidence in the methods being used to virally attenuate the concentrates.

54.2.3. Although evidence of an isolated outbreak of hepatitis A (HAV) in 1991 and evidence of transmission of parvovirus provided concern about the

adequacy of virological attenuation for protein coated viruses (HIV, HBV and HCV are all lipid-coated) and caused the introduction of new methods of viral attenuation, HAV and parvovirus were not a concern in themselves because parvovirus is a common childhood illness affecting about 90% of us and HAV does not cause chronic liver disease and affects about 35% of the general population.

54.3. **Manchester**: By 1994, there was a high level of confidence that the concentrates were not transmitting viruses. Patients who were infrequently treated would nevertheless harbour concerns and we reassured them that the donors were tested for HAV, HBV, HCV and HIV and underwent donor section prior to donation and that the viral attenuation processes appeared effective. Within months of taking up post in Manchester I had switched all the patients to high-purity products and I recruited patients to clinical trials of recombinant factor VIII at the first opportunity. We would have told patients switching to recombinant factor VIII that since those products were biosynthetic that they should be free from all viral risk.

55. *In light of the study of progressive liver disease that you were involved in, what information, if any, did you provide to your patients about the risks of chronic and/or serious liver disease?*

55.1. What I would tell them depended on an assessment of their liver disease.

55.2. If they had cleared the virus and had normal liver function tests and did not have cirrhosis, I would tell them that they had been exposed to HCV but had cleared the virus permanently and this would not be a problem for them in the future and that they had no more likelihood of developing liver disease than anyone else.

55.3. If they had cleared the virus through successful anti-viral treatment, but still had cirrhosis, I would warn them that the cirrhosis might improve but would not go away and would require ongoing monitoring (by a Hepatologist as well as a haematologist). This monitoring and potential treatment would be explained to them. They would also be warned that successful viral eradication, whilst it

reduces the risk of hepatocellular carcinoma does not eliminate it. We have, in fact, seen a number of patients who have developed hepatocellular carcinoma (HCC) sometimes many years after successful viral elimination. HCC is a complication of all causes of cirrhosis.

55.4. For patients with chronic HCV viraemia but normal liver function tests we would offer relative reassurance that their outlook was generally very good and that HCV would probably not cause them problems but that we nevertheless needed to keep an eye on it in case it became more active and the liver disease would be monitored every 6-12 months.

55.5. If liver function tests were intermittently or persistently abnormal, but the patient did not have cirrhosis or hepatic fibrosis, patients would be told what their current assessment was and offered whatever degree of relative reassurance that seemed appropriate. They would all be warned that there was uncertainty about the future and that their liver disease could progress to cirrhosis and hepatocellular carcinoma at some stage in the future and provided with the statistics as known.

55.6. Patients with severe liver disease who were still viraemic would be warned of the risk of liver failure and cancer and strongly encouraged to accept treatment. They would be joint-managed with a Hepatologist.

55.7. All patients with active liver disease would be asked to moderate their alcohol intake. All patients with severe liver disease and many of the others would be joint-managed with a Hepatologist. All viraemic patients were offered antiviral treatment at some point according to the availability of treatment and the treatment selection criteria operated by the Hepatologists at the time. This obviously varied over the years.

55.8. Whether patients with HCV should use barrier contraception was controversial and no consensus was ever reached because sexual transmission is not prominent and sexual partners have a low risk of contracting the virus. This contrasts with HIV and chronic HBV where we always recommend barrier contraception. We would offer testing for wives. We would reassure patients that transmission within

families was not a significant problem, children of patients with HCV having little more than the background risk of contracting HCV. We would also tell them that no more than normal domestic infection control precautions were required, e.g. hand washing before food preparation and after using the toilet.

56. *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.*

56.1. Throughout my time in Sheffield and later, we would use DDAVP where we could obtain an adequate response. Almost all the remainder were previously treated patients (PTPs) for whom this conversation was generally not needed. PUPs or their parents would require a discussion of relative risks. In the early 1980s, some of these may have been offered cryoprecipitate or preferentially treated with UK sourced products or once they had become available heat treated products in line with UKHCDO Guidance in 1983 and 1984 (WITN3289041, WITN3289042 and WITN3289044)

57. *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?*

57.1. I assume this to mean what information would you have provided when patients were about to be treated with concentrate for the first time?

57.2. I saw very few patients just starting home therapy since all the adults had already started home therapy and home therapy usually started in early childhood. Patients starting home therapy have already been treated in hospital and so this would not be their first treatment.

HIV

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

58.1. Some time in 1983 when I became a Senior Registrar in Sheffield. AIDS had been described and was being reported in US patients with bleeding disorders. The first case in a UK patient with haemophilia was described in 1983. Patients were beginning to ask about it.

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

59.1. When they were tested first for HTLV-III in late 1984 and early 1985, as far as I can remember.

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

60.1. As far as I can remember, Professor Preston and Sr. Joy Farnworth saw them for a pre-test chat in his office in which he would discuss the state of opinion about the test and the test result and then Sr Farnsworth would take the blood sample.

60.2. This was not universal practice, though I have limited insight into what happened in other centres. The idea of pre-test counselling had not been established in 1984/5 and, given that so very little was known, it could have been a relatively brief conversation. I think that patients were usually told they were being tested (invariably in Sheffield) but not necessarily fully "counselled" as is currently understood. Whilst the practice of providing pre-test counselling for HIV testing became universal, in the 1984/5 that was not so. Pre-test counselling involves, the likelihood of a positive test to be explained and the implications of a positive test to be explained including implications for insurance and health and treatment. Back in 1984/5, none of this was known and the content of such a conversation would be largely speculative (and possibly incorrect as events would subsequently show).

60.3. The main fact to transmit in 1984/5 was that a positive test did not equate to AIDS and they would be told of the need for ongoing monitoring and that we hoped there would soon be treatment. Sexual transmission would be described and the need for barrier contraception also discussed since sexual transmission was already

established and patients would have been recommended to use barrier contraception even before a test became available. They would be reassured that there was no evidence of transmission to other family members.

60.4. I would say that pre-test counselling became universal quite quickly, by 1986/7 and was certainly the norm when I took up post in Liverpool in 1987. By that stage, the implications of the test were becoming much clearer. It is worth reflecting, however, that this is no longer the norm. It has become routine to automatically test all pregnant women, all potential transplant recipients and many admissions to hospital without seeking consent or providing pre-test counselling.

61. 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?

61.1. In Sheffield Professor Preston saw them individually or with their partner in his office with Sr Farnsworth and discussed the result and its implications. I was not directly involved in this process but naturally both HIV and NANB came up during consultations in clinic both before and after a test became available and I would discuss it with them.

61.2. By the time I took up post in Liverpool and subsequently in Manchester the patients had already been informed of their HIV status and I was therefore not involved in that. It is my understanding that in those centres they were informed of their result by post. Subsequently I saw them to discuss their condition individually, only holding larger meetings to discuss more general issues like the establishment of the Macfarlane trust or vCJD.

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

62.1. I was not in the room when they were told the test result but based on knowledge at the time and talking to Professor Preston, I suspect they were told that a positive test did not mean that they had AIDS or that they would develop AIDS and that

very few patients with HIV and a bleeding disorder had developed AIDS (3 in the UK at the time testing first became available). It was not known how many people would develop AIDS but opinion at the time was that it would probably be a low percentage. There was no treatment at the time but it was hoped there soon would be. They would also be told that there was evidence of sexual transmission, that they should use barrier contraception (which we provided) and that we would like to test their sexual partner. The need for ongoing monitoring would be discussed and the uncertainty about the future. They would be told that as information developed they would be kept informed.

62.2. In all three centres, the patients and their partners were kept regularly informed in their consultations as knowledge of HIV and its treatment developed.

62.3. The natural history of HIV had not had time to unfold and reveal itself in 1984/5.

62.4. Patients were not told to keep their HIV a secret in Sheffield, Liverpool or Manchester but were advised to be circumspect in whom they told. Some patients even chose to keep their haemophilia secret because people assumed that they had HIV even if they did not. There was unquestionably a stigma attached to HIV positivity during the 1980s and into the 1990s. Many patients were further traumatised by the excessive and very visible infection control measures adopted by those hospital staff who were not usually involved in their management and who did not realise that such measures were not required. .

63. 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?

63.1. Partners were offered HIV tests from the beginning. Other family members such as children were not offered testing unless their mother was HIV-positive and likely to have been during gestation.

64. 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?

64.1. We strongly advised patients to bring their partners to clinic so that they both got the same information and both had the opportunity to ask questions. Problems could arise with some patients who never brought their partners with them to clinic. This left me with the concern that their partners might not be fully informed. We rapidly learned, when patients did bring their partners with them to clinic that the partners were far more likely to be open about the degree to which the patients were complying with safe sexual practice advice (using condoms etc.). Many couples just stopped having sex altogether and I had some young male patients who avoided romantic attachments altogether because of the complications involved with HIV. They were all advised to use barrier contraception and to inform partners of their HIV status. This could be difficult if, for example, a new partner was already using the contraceptive pill. How do you explain the need for barrier contraception in such a situation without discussing HIV?

64.2. We reassured them that there was no significant risk of transmission of HIV to other family members.

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

65.1. In Sheffield patients were seen individually by Prof Preston and the result discussed. The implication would be discussed repeatedly in clinic thereafter. In common with almost all Haemophilia centres at that time, we had no significant access to clinical psychology that I can remember and the same applied in Liverpool.

65.2. From 1988, we had a counsellor in Liverpool who would see patients in their homes and in the department, to provide further psychological support. We would also tell the patients and their partners of any new development in knowledge of HIV and its treatment when they came to clinic or the department.

65.3. In Manchester we had a nurse counsellor who would also see patients in their homes and in the department to provide further

66.How many patients at a) Sheffield, b) Liverpool and c) Manchester were infected with HIV?

66.1.24 had HIV of which 1 was under the age of 18. I am unable to give a breakdown by disease type or severity.

66.2.In Liverpool 43 patients had HIV, of whom 4 were under the age of 18.

66.3.In Manchester 83 were HIV positive, of which 10 were under the age of 18 years.

66.4.Most HIV positive patients had severe haemophilia A. The incidence of HIV amongst patients with haemophilia B was lower than in Haemophilia A, probably because haemophilia B is rarer than Haemophilia A and we were largely self-sufficient in factor IX

67.Was work undertaken at Sheffield to establish the time period during which patients seroconverted? If so, please describe what work was done and what if any conclusions were reached. If you are able to provide the same information for the Liverpool Centre and/or for the Manchester Centre, please do so.

67.1.Some stored samples were available in Sheffield from some but not all patients, which enabled the approximate date of the initial infection to be determined. I recall that most had been infected in 1982-84. Similar data was available to me in Manchester but not in Liverpool.

Hepatitis B

68.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?

68.1. Bearing in mind that all blood donations had been tested for this virus since probably the early nineteen seventies and hepatitis B vaccination had been introduced in 1982, we saw no new infections with hepatitis B during my time as senior registrar or as a consultant so I never had to have that conversation. However, all the patients chronically infected with hepatitis B had been informed, knew they had hepatitis. B and we would discuss it in clinic visits.

69. How many patients at Sheffield were infected with HBV?

69.1. I do not know. I can remember two such patients.

NANB Hepatitis/Hepatitis C

70. 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?

70.1. Patients with Haemophilia had their liver function tests checked at every clinic attendance from the late nineteen seventies onwards in all three Haemophilia Centres I worked in. In my practice, if these tests were intermittently or persistently abnormal the patients would be informed and told that they probably had NANB. They were examined for signs of severe liver disease. This involved an abdominal examination, looking at their tongue and palms and skin, none of which would be part of the routine for an uninfected patient with Haemophilia. Abdominal ultrasound would be arranged every two years or so. The need for these tests and their results would be explained to the patient in clinic. They would be told current knowledge of NANB. As far as I can determine, this was also the practice of my predecessors in Manchester, Dr Richard Wensley and Dr Guy Lucas.

71. 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?

71.1. A reliable, second generation, HCV antibody test became available in 1992. This showed which patients had been exposed to HCV but did not establish who was still actively infected since about a third of antibody positive patients would have cleared the virus spontaneously. Bearing in mind that these patients had already been monitored for NANB from about 1980, the patients were tested for HCV when they attended for their routine Haemophilia Clinic review, mostly during the course of 1992/3. It was my practice to tell them that I was testing for this and they would be informed of the result face to face at the next review appointment. We wrote to the GP after every clinic appointment. This is what I did in Liverpool and, as far as I can determine, this is what was also done in Manchester by my predecessor Dr Guy Lucas.

71.2. Patients with a past history of blood product therapy would be told before testing that the result of the HCV-antibody test would probably be positive. For patients with NANB as evidenced by abnormal liver function tests, this was just a confirmatory test.

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

72.1. This was not a major intellectual watershed. We just had a test for the causative virus for NANB, which had been studied already for 17 years at that point and had finally been given a proper name. That did not change what we had already learned about the condition's natural history. The new label did provide a focus for discussion with patients and their relatives, some of whom seemed to have believed that they had contracted a new disease, but that was not the case for most of them. The exceptions to this were patients who had not been regularly monitored for some reason, such as being lost to follow-up or being followed in a peripheral hospital by non-specialists.

73. *How many patients at the Liverpool Centre and at the Manchester Centre were infected with HCV?*

73.1. I am unable to answer for the Liverpool Centre since I do not have access to accurate figures.

73.2. For the Manchester Centre we have records of 186 patients who were exposed to HCV at some time, of which approximately 30% would have cleared the virus spontaneously and almost all the remainder have had their HCV eradicated through treatment or have died at some point since testing was introduced in 1992 (from all causes of death). Six patients remain untreated. Half of these have consistently refused treatment over many years and half have some medical contraindication to treatment.

Delay/public health/other information

74. *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.*

74.1. In Sheffield, patients were brought in specially one at a time for HIV testing and an appointment made a few days later to discuss their result. I cannot comment on Liverpool and Manchester because I was not there. However, I believe that the patients in those centres were informed of their results by letter. I would not regard that as acceptable way to communicate the result but I do not believe that it incurred significant delay.

74.2. As a generality, patients were tested for HCV when they came to clinic and the result would be discussed at the next clinic visit. Testing and/or communicating the result was delayed in some individuals because they were uncompliant with follow-up i.e. did not keep appointments. They were tested at the first opportunity.

75. *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?*

75.1. For HIV and HBV, we attempted to trace and test sexual partners and offered safe sex advice which was regularly reinforced and supplied a range of condoms, femidoms and dental dams free of charge. We strongly encouraged outpatient attendance of sexual partners so that we could offer them advice testing and safe sex instruction. They were far more inclined to comply with this for obvious reasons. We also offered vaccination for partners of HBV carriers and post-exposure antiviral treatment to partners who had had unprotected sex with one of our HIV-positive patients (often through a burst condom) to minimise the risk of virus transmission. Consequently, pregnancy was either discouraged or viral transmission minimisation strategies employed to permit pregnancies to occur for determined couples. This involved the use of a predictor kit so that the couple only had unprotected sex during the period of ovulation. In the case of a successful (and occasionally unplanned) pregnancy, the mother would be tested repeatedly for seroconversion during pregnancy, because seroconversion could be delayed for up to three months after exposure. If she was or became HIV positive, the baby would be tested for up to six months after birth.

75.2. The public health implications of HCV were discussed in UKHCDO committees but no consensus was reached about the use of barrier contraception since sexual transmission is not prominent in this condition. Testing would be offered to spouses but few contracted the condition.

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

76.1. If patients with HIV had a CD4 count (T-helper cells, the cells damaged by the HIV virus) of ≤ 200 they would be given antibiotics to prevent Pneumocystis pneumonia (PCP) and warned about other opportunist pathogens and the open access arrangements to the service would be emphasised to them.

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

77.1. Please see above. This was repeatedly reinforced in clinic.

78. What actions or decisions were taken at any of the hospitals at which you worked to

trace patients who may have been infected through the use of blood or blood products?

78.1. See above. In case of any difficulty and with occasional casual sexual encounters of our patients, we would and still do enlist the assistance of the STD department whose staff were far more experienced than we were in "trace and test".

79. At the 19th meeting of the UKHCDO Executive Committee on 5 June 2000 (minutes enclosed, [HCDO0000474]), there was a discussion about HIV and HCV testing following which "it was agreed to continue to test for HIV and HCV at least annually". Was it intended that all patients would be tested at least annually for HIV and HCV? What was the purpose of the continued, routine testing? What information was provided to patients about it?

79.1. My recollection of this and of our practice at the time was that patients whose tests had been negative for these viruses continued to be tested for several years after their first negative test in case there was any failure of the viral attenuation techniques. This was explained to the patients at the time. It naturally engendered some anxiety amongst them but most seemed to appreciate the reassurance that a continued negative test gave.

Consent

80. How often were blood samples taken from patients attending (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester 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?

80.1. Blood samples were taken at every clinic visit. These clinic reviews generally took place every six months but from 1985 until about 2015 HIV positive patients were seen every three months. This has been extended to six-monthly for all HIV risk-groups because anti-retroviral therapy has improved and the patients are very

stable, requiring very infrequent changes in therapy.

80.2. The blood samples taken from the patients vary, depending on whether they are virologically naïve or have active HCV or HIV. Very few patients still have HCV, this having been eradicated from almost all of them. Blood samples commonly taken, depending on the patient's status and current clinical situation may include some or all of the following:-

80.2.1. **Full blood count.**

80.2.2. **Liver biochemistry and electrolytes.**

80.2.2.1. To monitor hepatic and renal function

80.2.3. **Alpha fetoprotein:** a marker for hepatocellular carcinoma.

80.2.3.1. Ultrasound would also be arranged every couple of years and, in recent years, a *fibroscan*.

80.2.4. **Factor VIII/IX level.**

80.2.4.1. To monitor and optimised prophylaxis.

80.2.5. **Factor VIII inhibitor screen.**

80.2.5.1. To screen for emergence of factor VIII inhibitors.

80.2.6. **Factor VIII/IX/VWF genotype (only ever done once!)**

80.2.6.1. As a marker for family studies, antenatal testing, carrier testing and in some cases to establish severity and the risk of developing a factor VIII/IX inhibitor.

80.2.7. **HCV antibody/antigen/viral load/ HCV-genotype**

80.2.7.1. To establish HCV infection status, to estimate likely response to treatment and to select the most appropriate treatment regimen and to monitor the response to treatment.

80.2.8. **HIV antibody/antigen/viral load/HIV-genotypic analysis.**

80.2.8.1. To establish HIV status and monitor response to treatment and need for any change in treatments and to monitor for the emergence of anti-retroviral drug resistance.

80.2.9. **CD4 count (T-helper cells).**

80.2.9.1. To estimate the degree of damage (or post-treatment recovery) of the immune system by HIV and to estimate the need for PCP prophylaxis. This was also used at one time to select patients for anti-retroviral therapy in the early days when the emergence of drug resistance was a big problem which would discourage one from starting everyone on treatment.

80.3. One did not ask for consent to take blood samples. I think it is assumed that the patient has consented because they go along and allow the phlebotomist to take the sample. It is not normal to take verbal or written consent for blood sampling other than for the purpose of research.

80.4. If one is testing for something new, one would discuss this with the patient, probably only in outline. Results would be discussed in the next consultation, if abnormal or if the result affected their management. HIV-positive patients would routinely ask what their CD4 count and viral load were when they came to clinic and often made a note of the result. The results are often discussed in detail. In more recent years, detailed HIV-genotyping linked with computer-assisted analysis for drug resistance mutations provides a detailed assessment of HIV drug resistance and informs the choice of treatment regimen. For HCV, viral load testing is the mainstay for assessment of the response to treatment and HCV-genotyping

is necessary to provide the patient with an estimate of the likely response-rate and for the clinician to select the best drug regimen.

80.5. I refer to the Human Tissues Acts of 2004 and 2019. Plasma samples are not covered by these Acts. It is not necessary to obtain consent for the storage of plasma except for the specific purpose of research. Any research involving ***additional*** blood samples or sample storage would require consent and ethical approval. It is, and has been for many years, a routine for virology labs to store all their plasma samples for 3 years in case they need retesting or further investigation. Cellular blood samples are covered by the Human Tissues Act but are not stored by Haemophilia Centres except for research purposes.

80.6. DNA samples are stored long term but specific consent for this is obtained using a nationally agreed consent form and patient information leaflet (WITN3289054 and WITN3289055) and one copy of the consent form is filed in the notes and one in the lab where the sample is analysed and stored. Analysis only starts when the consent form is received by the lab.

80.7. It has not been my practice, either in Manchester or in Liverpool, to store blood or plasma samples.

81. 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?

81.1. Written consent to use factor concentrates would only be obtained if this was part of a clinical trial, in which case a copy of the consent should be filed in the notes. It is not normal practice to obtain written consent to use any fully licensed medicinal product in a routine manner for the licensed indication for that product.

81.2. If the patient was changing products, we would write to them to tell them of the proposed change and outline the relative characteristics of the two products and offer them the opportunity to discuss the change or to refuse to change (if

possible). If we were considering a change of class of product e.g. plasma-derived to recombinant or standard half-life to extended half-life or factor VIII to Emicizumab, then we would discuss this change face to face, sometimes over several consultations, copy them into the correspondence with the GP and often provide them with product leaflets, examples of which I attach as WITN3289073 and WITN3289074.

82. *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?*

82.1. Please, see answers above.

PUPS

83. *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).*

83.1. As an adult treater rather than a Paediatric Haematologist I very seldom come across a PUP, since almost all are children. If I did and it was necessary to treat them for the first time, I would explain the pros and cons of treatment with them (or their parent).

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

84. *How was the care and treatment of patients with HIV/AIDS managed at (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre? In particular:*

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

84.1. In all three centres there was very close liaison with Hepatology throughout this period. In all three centres, hepatology took a special interest in our cohort of patients even though this was not formalised around a joint clinic. In both Liverpool

and Manchester, the Liver clinic was adjacent to the Haemophilia clinic and patients would often come on the same afternoon to see both Haematology and Hepatology and many joint consultations, some ad-hoc, were conducted. Throughout that time, we (Haematology and Hepatology) would consult to determine which patients Hepatology thought they should see and treat. This evolved with time across the whole country partly as treatment options advanced and partly as the sub-discipline of Hepatology expanded massively. In Sheffiield and Liverpool, there was only one Hepatologist during my time there. This was also the situation in Manchester for the first few years more recently increasing to three Hepatologists on our hospital site. Throughout that time (1983-2020) Hepatology would provide a lead or take over the management of severe liver disease and patients with cirrhosis and varices and/or liver disease or hepatocellular carcinoma were managed primarily by Hepatology or joint managed. In Sheffield and Liverpool, Hepatology (Drs David Trigger, and Prof Ian Gilmore, respectively) were very available but tended to offer advice and send the patient back to the managing clinician unless they had severe liver disease. In the early days in Manchester, our Hepatologist, Dr TW Warnes, would similarly offer advice even on therapy and leave the treatment of HCV for us to complete. Some treatments were joint-managed. As the number of Hepatologists increased, however, they took over all antiviral therapy for HBV and HCV. In recent years, as the new generation of Interferon-free regimens were rolled out, we had frequent meetings for them to update us on the rapidly changing NHSE criteria for patient selection so that we methodically worked our way through all remaining patients, who had either failed previous treatment or refused treatment, to eradicate their HCV. This treatment was initially very, very expensive and this limited availability to severe liver disease. However, as drug costs tumbled and funding was made available, not least to expand the hepatology team, the criteria were fairly quickly expanded, eventually to anyone with HCV viraemia, even in the absence of obvious hepatic inflammation.

84.2. Patients with severe liver disease were considered for hepatic transplantation, either in Leeds or Birmingham. The initial assessment was made by our local Hepatology colleagues and all such referrals were made by Hepatology and not Haematology. In general, we (Hepatology and Haematology) made these referrals

before the patient needed transplantation and the transplant unit would keep the patient independently under review and decide when to transplant because if referred late, they might not be fit for transplantation. Prior to the advent of effective anti-retroviral treatment of HIV there was considerable resistance from transplant surgeons to transplanting HIV positive patients because most HIV positive patients with liver failure were severely immunosuppressed and did quite extraordinarily badly, if transplanted. The only patient I had who managed to persuade Leeds to transplant him, against their better judgement, died 6 months after his transplant from cirrhosis and liver failure in his transplanted liver (WITN3289023).

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

84.3. During my time in Sheffield there was no treatment for HIV and the patients were managed by Haematology.

84.4. As HIV monotherapy and dual therapy developed in the late 1980s and early nineties, patients were managed by the physician to whom they presented; Drug addicts, sex workers and homosexuals were managed by Sexually Transmitted Disease (STD) Doctors. Patients with bleeding disorders were managed by Haematologists and assorted patients went to Infectious Diseases Physicians. For a number of years, each group knew as much as each other about HIV and its treatment, which was limited, but Haematologists had an advantage in that we were very much more experienced than the others in managing immunosuppressed patients and opportunist infections, because these are central problems in the management of haematological malignancy.

84.5. As treatment options multiplied and the management of drug resistance became more complex, computer assisted and based on HIV genotypic analysis the sub-speciality of HIV Physician developed. These physicians were usually STD doctors but in some cases Infectious Diseases doctors. In Sheffield, Liverpool and Manchester Infectious Diseases were based in other hospitals miles away from the Haemophilia Centre, whereas in Liverpool and Manchester we had STD departments on site. For that reason, in Sheffield, I would sometimes consult Dr Peter Carey (STD) and he would sometimes consult me. In Manchester, similar

consultation became increasingly frequent and led to the establishment of a monthly Joint HIV clinic, first with Dr Deb Mandal and then with Dr Ashish Sukthanker, starting in the late nineties. Although we have four Thrombosis and Haemostasis consultants in Manchester, the HIV positive patients have remained under my care and with Dr Sukthanker to maintain continuity of care.

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

84.6. When patients were started on treatment for HIV or HCV or their treatment was changed, the drug side effects were discussed in detail and, indeed often discussed on a number of occasions before any treatment was started. Side effects would also be reviewed at each follow-up discussion. Treatment side-effects were also much discussed amongst patients and in self-help groups leading in many cases to marked reluctance from the patient to start treatment and undesirable delays in initiating treatment (e.g. WITN0145003 and WITN3114001).

84.7. Many patients were extremely reluctant to start treatment because of side effects. Others were reluctant because they were dealing with the uncertainty surrounding HIV by "denial". Whilst this is a very useful psychological mechanism for dealing with uncertainty, essentially putting the condition to the back of their mind as much as possible, denial could not be maintained whilst taking pills every 4 hours, which was what the early Zidovudine regimen involved. Many patients had considerable and very understandable psychological difficulties surrounding the initiation of treatment for HIV and in some cases delayed starting for years, contrary to medical advice or alternatively defaulted from clinic for periods of years.

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

84.8. They were reviewed every three months until recently and have always had open access to the service.

85. 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?*

85.1. As for HCV, except since we had far fewer of these patients. and the treatment was different from HCV, we always deferred treatment to the Hepatologists. All patients with chronic HBV were referred to hepatology. .

b. *What treatment options were offered over the years?*

85.2. This was directed by hepatology and is described in more detail below in Q86.

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

85.3. These were discussed with them by hepatology once hepatology had taken over treatment of HCV. Prior to that, I would speak to them at length about treatment side effects, the likely response-rate and the consequences of no treatment, preferably with their partner present and often over the course of several consultations. This was a major undertaking for the patient and their family and was never clinically urgent and so was approached with care and a lot of consultation.

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

85.4. Followed up as per HCV.

86. How was the care and treatment of patients with NANB hepatitis managed at (a) Sheffield and (b) the Liverpool Centre? In particular:

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

86.1. Patients were referred to Hepatology if we wished to consider antiviral therapy, if we suspected serious liver disease, if the patient requested it or if we had a

diagnostic difficulty or wished a second opinion on treatment. For many years now all patients who continued to have active HCV were referred for the Hepatologists to conduct the anti-viral treatment.

b. *What treatment options were offered over the years?*

86.2.In chronological order and as treatment evolved: -

86.2.1. Alpha Interferon for three months.

86.2.2. Alpha interferon for 6-12 mths. depending on HCV Genotype.

86.2.3. Alpha Interferon plus Ribavirin for 6 or 12 months, depending on HCV Genotype.

86.2.4. Peginterferon plus Ribavirin for 6-12 months depending on HCV Genotype. (sometimes provided by hepatology)

86.2.5. Interferon-based triple therapy (provided exclusively by hepatology)

86.2.6. New Interferon-free multiple regimens including the new generation of drugs varying according to the HCV genotype.

86.3.Other treatments include sclerotherapy or TIPS for oesophageal varices and hepatic transplantation provided by hepatology or surgery. In Liverpool management of oesophageal varices was primarily provided by Professor Shields, Professor of Surgery, for example,

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

86.4.This was usually extensively discussed, sometimes on several occasions and sometimes over a period of years in patients reluctant to undergo treatment. It was my practice to request that patients bring their partners to clinic so that I could discuss treatment side effects and the clinical outlook with both of them at length because the side effects of interferon based regimens had to be endured by the entire family for up to a year..

d. What follow-up and/or ongoing monitoring was arranged in respect of patients who

were infected with NANB hepatitis?

86.5. These patients were seen every three to six months in clinic and had open access to the service.

87. How was the care and treatment of patients with HCV managed at (a) the Liverpool Centre and (b) the Manchester Centre? In particular:

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

87.1. See above.

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

87.2. See above for treatment regimens offered.

87.3. We started to offer Interferon alone in the late nineties. We did not participate in clinical trials of treatments for HCV and so started to offer interferon therapy and all the other therapies, as they emerged once they were licensed and funded. We had a different funding stream from the Hepatologists for treatment such that we were actually in a position to offer Peginterferon and Ribavirin before it became available to Hepatology.

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

87.4. Patients were told the likely response-rate, taking the HCV genotype and treatment regimen into account. Many patients refused treatment on that basis, because treatment was not clinically urgent and they preferred to wait for something better to come along, which was perfectly reasonable. The side effects of fatigue, malaise, depression, tetchiness, and blood count abnormalities etc. would be discussed in detail (and amongst patients) and many patients deferred treatment because of that also.

87.5. The side effect profile of current treatments is very much better and I know of nobody who has refused treatment on those grounds. In my experience, about 50% have some medical reason for not being offered treatment such as advanced old age +/- dementia and the remainder do not have any contraindication to treatment but refuse to contemplate treatment without any plausible medical reason.

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

87.6. I take this to mean patients who are no longer infected with HCV? If so, these patients are generally discharged from hepatology once they have been shown to have cleared the virus and assuming they do not have serious liver disease. They continue under haematological supervision with a review clinic every 6-12 months depending on the severity of their bleeding disorder. If they have cirrhosis, they continue under joint Hepatology/Haematology supervision and are monitored for the development of hepatocellular carcinoma and their liver disease and/or oesophageal varices in monitored and treated as necessary.

88. 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?

88.1. I have not managed children since 1987 and so cannot answer this question.

89. What if any involvement did you and/or colleagues at (a) the Liverpool Centre and/or (b) the Manchester Centre have with any clinical trials in relation to treatments for HIV and HCV? Please provide details (including the "early clinical trials with antiretroviral drugs" that you refer to in your oral evidence to Penrose – transcript, 12 January 2012, p. 80 [PRSE0006083]).

89.1. I participated in a multicentre clinical trial of antiretroviral monotherapy back in the late eighties or early nineties. To be honest, I can't remember very much about it

and in Manchester I don't think I participated in any HIV research other than our report on the abnormal bleeding associated with the use of protease inhibitors.

89.2. I did not participate in clinical trials of treatments for HCV.

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

90.1. I provided as much support as I could in clinic to both the patient and their family. Support was also provided by our social worker, counsellor and Nurse Specialists in both Liverpool, and Manchester and once these members of staff were in post (by 1988). It would be fair to say, that in 1985, 86 and 87, despite my best personal efforts, support was lacking because the support infrastructure was basically just me. I am sure that was a common situation across the country. It was an extremely difficult time for the patients because there was no treatment and, for a wide range of their reasonable and intelligent questions about the future, no answers either. Neither the natural history nor the therapeutic future of HIV was properly known in the mid-1980s.

91. *Did any of the centres at which you worked 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?*

91.1. We obtained funding through the Regional Commissioners, I think, and employed a counsellor and social worker and Haemophilia Nurse Specialist from 1988.

92. *What (if any) difficulties did you encounter in obtaining sufficient funding for the treatment of people who had been infected with HIV and/or hepatitis C? (You may wish to consider when answering this question the enclosed letter you wrote dated 7 September 1995 to Dr Rejman at the Department of Health concerning problems with funding for interferon [BART0000735]; and the minutes of the Haemophilia Society's Health Sub Committee on 4 July 2001 which recorded reports that it was proving difficult to secure funding for interferon ribavirin [BART0002004]).*

92.1. As Centre Director in Liverpool and Manchester it was always my habit, until Andrew Lansley reorganised the Health Service, to meet regularly with the Commissioners. This raised the profile of my patient group with the Commissioners and provided an opportunity to review the performance of our contracts, to advocate for changes in treatment and service provision and finally to horizon scan new and expensive products on the way. I thought that, if warned, Commissioners would include such future financial pressures in their plans, thus reducing any delays in introducing new and improved treatments. Unfortunately, Health Commissioners are always short of money with competing demands on their resources and are therefore always focussed on the bottom line at the end of the year.

92.2. Consequently, whenever a new treatment was introduced requiring a financial uplift they never had the money available and only then incorporated the additional cost into their plans, unless they considered the request unreasonable and would not fund it at all. HCV treatment was always relatively expensive (£14,000 for a course of Peginterferon and Ribavirin, for example) and when the new generation of products such as Sofosbuvir were introduced they were extremely expensive. Consequently there were usually initial delays until commissioners were funded and we had set up a mechanism which became fairly automatic to request "permission to pay" on an individual patient basis.

93. 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.

93.1. See Q 89, above. I had a little involvement in HIV therapeutic research (see below) and no involvement in trials of treatment of HCV.

93.1.1. (WITN3289056) Wilde JT, McKernan AM, Hay CRM. DDI treatment of haemophilic patients infected with HIV. Haemophilia, 1995, 1; 122-125.

High Purity products

94.Please set out your involvement in the debate about the need for and/or use of high purity products for HIV positive patients, including details of the study that you undertook. You may wish to consider the following enclosed documents: letter dated 11 November 1992 to Mr David Watters of the Haemophilia Society and the report from Dr Jill Meara [HSOC0002578]; an article in 'The Independent' dated 9 April 1991 [HSOC0002632]; an article in the Health Service Journal dated 12 November 1992 [HSOC0002582]; and an article in 'The Bulletin' (No. 4, 1992) [HSOC0023004].

94.1.My own patients were in a good position because I had switched my HIV positive patients to high-purity products in 1992 and my local commissioners never seriously threatened to reverse this decision, probably because I made my own representations to them and the patient group was politically charged. I also lobbied, with the Haemophilia Society and UKHCDO, for the change. At the same time there was a widespread (international) feeling in medical circles that the manufacturer had increased the price excessively (doubling) when they introduced high-purity products, leaving us with an unnecessary contractual problem. We therefore lobbied Industry to reduce their price. Meanwhile, in 1994, BPL started to introduce Replinate and Replinine, high purity products, similar to Monoclate and Mononine (Armour), manufactured using the Baxter Haemophil method-M methodology under license. This competition led to price reductions and it then became much easier to change all patients.

94.2.I also published several papers investigating the effect of factor VIII concentrate on the immune system (WITN3289057 and WITN3289058): -

94.2.1. Hay CRM, McEvoy P, Duggan-Keen M, Inhibition of lymphocyte IL2-receptor expression by factor VII concentrate: a possible cause of immunosuppression in haemophiliacs. *B.J. Haem* 1990 75; (2): 278-81.

94.2.2. Hay CRM, Ludlam CA, Lowe GDO, Mayne EE, RC Lee, RC Prescot, Lee CA. The effect of monoclonal or ion-exchange purified factor VIII concentrate on immune function: a multicentre cohort study. B J Haematol 1998, 108, 632-637.

95.At the 12th meeting of UK Haemophilia Centre Directors Regional Representatives on

10 December 1992 (minutes enclosed [HCDO0000447]) there was a discussion about "the use of AIDS money for purchasing Factor VIII concentrates for HIV positive haemophiliac patients".

a. What was meant by "AIDS money"?

95.1. It was recognised in 1987 that most haemophilia centres outside London, were not adequately resourced in terms of staffing, skill-mix and other infrastructure to deal adequately with the needs of their patients with HIV and hepatitis. Many large haemophilia centres had few or no staff members from the professions allied to medicine such as Nurse Specialists, Counsellors or Clinical Psychologists. Social work provision was often inadequate and based in local authorities rather than in the hospital. There was no additional drug funding. My staffing in Liverpool in 1987, for example was me, a junior doctor, a secretary, a lab and access to a pool of hospital social workers.

95.2. NHS England or DoH made money available across the country ("AIDS money") to develop an appropriate supportive infrastructure and enabled us to employ a social worker, counsellor and nurse and to obtain greater physio input.

95.3. The consensus was that to use AIDS money for high-purity concentrate would be a mis-use and that it should be funded in some other way, which it was.

b. Did you consider that there was sufficient evidence to support the need for high purity products for HIV positive patients?

95.4. The evidence that high-purity concentrates conferred clinical benefit to patients infected with HIV was not strong and the evidence was conflicting, but we wanted to get the best products possible for our patients and so we employed those arguments to obtain the necessary funding.

c. Did you use high purity products for the HIV positive patients under the care of the Liverpool and/or Manchester Centre?

95.5. Yes I did (see list of products used broken down by year, above (WITN3289041). I encountered less difficulty obtaining funding than some centres and was able to switch all my HIV positive patients in Liverpool to high-purity products (Monoclate and Mononine, Armour Pharmaceuticals, King of Prussia, US). in 1993/4. These products were not in use in Manchester when I took up post there in December 1994, but by changing the contractual structure, in collaboration with our very helpful Contracts Manager and through representations to the commissioners, I was able to change all of our patients (HIV_+ve and –ve) with Haemophilia A and B to high-purity products within months (Replinate and Replinine (BPL, Elstree) and. Monoclate and Mononine (Armour)).

d. These minutes also indicate that you wrote a letter in reply to Dr Jill Meara's report. If available, please provide a copy of your reply to the Inquiry.

95.6. Unfortunately, I do not have a copy of that letter. I did campaign, where the opportunity arose, for both high-purity and then recombinant products.

96. At the meeting of the Council of the Haemophilia Society on 27 February 1993 you gave a lecture on High Purity Blood Products (minutes enclosed [HSOC0010425]). If available, please provide a copy of your lecture to the Inquiry.

96.1. Sadly, I no longer have a copy of that lecture in a format that my computers can read.

Recombinant

97. Please provide (to the extent that you are able to from your own knowledge) a chronological account of the introduction of recombinant products in the UK. (You may be assisted by consideration of the various UKHCDO minutes enclosed with this letter).

97.1. It would be logical to take Q97 and Q98 together.

98. Please explain your involvement, and that of UKHCDO, with efforts to obtain

recombinant blood products for patients with haemophilia. What difficulties were encountered and why?

98.1.I recruited patients both in Liverpool and Manchester into phase 3 clinical trials of Kogenate (Bayer) and ReFacto (Pharmacia) recombinant factor VIII from 1993 till 1995. These trials were very popular with the patients because this was, at the time, the only way that they could access recombinant products, since they were not licensed at that time. I recall that at one time I had 16 Manchester patients in those trials, the largest number of patients I have ever entered into an interventional study.

98.2.I co-authored the UKHCDO therapeutic Guideline which recommended recombinant for all as UKHCDO Policy from 1996 (WITN3289048): -

98.2.1. CA Ludlam, BT Colvin, CRM Hay, CA Lee, G Dolan. The UKHCDO Therapeutics Guidelines Task-Force on behalf of the UKHCDO Executive Committee. Guidelines on the use of therapeutic products to treat haemophilia and other hereditary coagulation disorders (2nd edition). Haemophilia 1997, 3, 63-77.

98.3.Collaborating informally with the Haemophilia Society UKHCDO and I campaigned for Recombinant for all and the patients and particularly parents of children with haemophilia campaigned very vigorously for this. I can remember parents chaining themselves to the hospital railings at Manchester Children's Hospital as a protest.

98.4.Professor Hill and I, as Chair and Vice Chair of UKHCDO and representatives of the Haemophilia Society met with Lord Hunt (Junior Health Minister) and various DH officials at Richmond House to make representations on behalf of the patients to obtain recombinant factor VIII.

98.5.The problem was that recombinant factor VIII was initially relatively expensive to manufacture, attracting a commercial premium and VAT. Blood products, through some tax anomaly, were tax-free. In consequence, recombinant factor VIII was twice the price of plasma-derived factor VIII at 55-60p+ per unit and the average

patient with severe haemophilia was then using 120,000 units a year. That is to say that the change to recombinant factor VIII would have cost an average of £40,000 per patient per year bringing their average treatment cost up to £80-£90,000 per patient per year. Commissioners were not funded for this and refused to pay. This required a ministerial decision.

98.6. The position adopted by the DH, which has never changed, incidentally, was that they did not accept that recombinant factor VIII/XI was safer than plasma-derived factor VIII/XI, because an increment in viral safety could not be demonstrated and the plasma derived products were all virally attenuated with a ten year history of being, in their view, acceptably safe. We (UKHCDO) argued that there had been an outbreak of HAV, that there was evidence of parvovirus transmission and there were concerns about prions (vCJD) and we knew that whilst HAV and parvovirus were merely relatively resistant to viral attenuation and of little clinical concern, other unknown pathogens resistant to viral attenuation might emerge and we knew that prions were unaffected by all practical methods of viral attenuation. DH never conceded this argument but the government eventually made a political decision to grant recombinant factor VIII to children (patients aged <18 years) in 1998 "to relieve the anxiety of their parents". Recombinant factor IX became available the same year and so it was possible to change children with both haemophilia A and B at the same time. When these children grew older, they remained on recombinant products and so by the time recombinant for all started to roll out, all the patients aged 23 and under were already using recombinant factor VIII or IX unless there was some specific reason to remain on plasma derived products (patient choice or, in the case of factor IX, lack of efficacy in 5-10% of patients).

98.7. In 2003. A further ministerial decision released money to switch those patients who wished to (almost all) to switch to recombinant factor VIII/IX. This process is described in the various minutes letters and reports and excel spreadsheets attached (WITN3289060-WITN3289068. We planned this in a DH Task force (WITN3289060, WITN3289061, WITN3289062), which involved: -

98.7.1. The DH Commercial Directorate CD)

98.7.2. Health Protection

98.7.3. PASA (The Purchasing and Supply Authority, a branch of DH later renamed CMU or the Central Medicines Unit)

98.7.4. UKHCDO (represented by me, Professor Hill and Dr G Dolan .

98.8.This was an immensely complicated process for the following reasons: -

98.8.1. Funding was staged over three years so that it was impossible to start all the patients at the same time.

98.8.2. They therefore had to prioritise some patients over others and DH/UKHCDO decided that although there were pros and cons to various forms of prioritisation that the most equitable was to prioritise by age. This was ultimately challenged in court by the Birchgrove Group who felt that HIV positive patients should be prioritised. Whilst this challenge was unsuccessful it did delay the beginning of the rollout.

98.8.3. It was decided, for logistic reasons related to the calculation of the financial uplift which each centre would require, that the recombinant product should be purchased through a national framework contract. This would yield, for the first time, a single price for each product across the UK. Previously centres negotiated the price individually leading to very variable pricing.

98.8.4. In order to finalise the modelling and calculate how much money was to be allocated to each centre, we needed to complete the national tendering exercise, facilitated by PASA, so that we knew how much each product would cost and then we (UKHCDO and the National Haemophilia Database (NHD)) needed to ask centres which patients they wished to change to which of the four recombinant products available and to tell us how much factor VIII they used each year and what the unit price of their

current plasma-derived product was. Thus the NHD calculated the financial uplift of an individual basis. Knowing how much each patient would cost and how much money we had available in each year, we were able to work out which patients and which age range could switch each year. The process was completed in three years.

98.9. As Vice Chair and then Chairman of UKHCDO and as the Director of the Database from 2002, I was central to this process throughout, working closely with DH and PASA. Further details of the process may be gleaned from WITN3289062 - WITN3289068).

98.10. It should also be mentioned that switching the children to recombinant products in 1998 was slowed up by supply considerations. Manufacturing capacity for recombinant products was limited in the late 1980s and it was not possible to switch all the children immediately because we couldn't get the product into the country.

98.11. Furthermore, in 2000, when we only had two suppliers of recombinant factor VIII (Baxter and Bayer); Bayer stopped supplying for two years. This caused an acute world shortage of recombinant factor VIII and deprived some centres that only used Bayer products of all their supply. I, as Vice chairman of UKHCDO, organised a voluntary system whereby centres and their suppliers agreed contract swaps to redirect some of their supplies of Baxter Recombinate to centres with no alternative supply so that we would be able at least to maintain patients who had never been treated with plasma-derived concentrates and those under age 10 on recombinant products. This was a labour-intensive but remarkably successful national collaborative effort that had to run for two years, during which time other suppliers were able to increase their supply to some degree.

98.12. Towards the end of the recombinant rollout to adults, it became apparent that funding might not be secure. Representations were made to DH to leave them in no doubt about the anguish, which would have been caused to the entire Haemophilia Community should funding not be maintained. DH agreed to continue funding but also wished to contract nationally, since the first national contract had

been successful in reducing unit price to a limited degree. A working group was established between UKHCDO, PASA, Delloite and Commercial Directorate to plan and implement this (WITN3289069).

98.13. I was clinical lead for the introduction of National Procurement and the first two rounds of procurement. I was seconded one day a week to DH for a year to assist with the second round of national procurement. Subsequent rounds of procurement have been managed by PASA/CMU and a group from UKHCDO including me. National procurement of clotting factor concentrates, conducted jointly by PASA and its successor organisation, CMU, and UKHCDO has been financially enormously successful, reducing drug unit price by 90% since 2005, yielding the lowest factor prices in the world whilst firmly securing ongoing patient access to recombinant products. .

98.14. The background and details of the process of the first two rounds of procurement are described in WITN3289043: -

98.14.1. Hay CRM. Purchasing factor concentrates in the 21st century through competitive tendering. ***Haemophilia*** 2013 Sept; 19(5):660-7.

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

99.1. Yes. It was UKHCDO policy that we wished to treat all our patients with recombinant factor VIII from 1996 (WITN3289048), and for Haemophilia B from 1998 when recombinant factor VIII and then recombinant factor IX became available. We wanted to give the patients the benefit of the doubt about safety based on the "unknown virus hypothesis". Having been at least thrice bitten by previously unknown viral pathogens and knowing that some pathogens were difficult (protein coated viruses such as parvovirus and HAV) or impossible (prions – the cause of vCJD and classical CJD) to inactivate. We wished to treat the patients with a product that should theoretically be free from all human pathogens.

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

100.1. About 16 of my patients were able to use recombinant factor VIII from 1995 through their participation in phase 3 clinical trials of Kogenate and ReFacto. Otherwise my, exclusively adult, patients were not able to access recombinant products until the recombinant rollout in 2005 onwards. Paediatric patients were treated with recombinant products from 1998, as described above.

Research

101. Please list all research studies that you were involved with during your time at Sheffield, Liverpool and Manchester. 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.

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

c. Explain what your involvement was.

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

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

f. State the number of patients involved.

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

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

101.1. For convenience, I have taken all subsections of this question together.

101.2. Given that I have published in excess of 200 papers, chapters, guidelines and reviews over the course of the past 38 years and conducted my first investigator-led interventional clinical trial in 1982, it is impossible for me to comply in full with this request. My list of publications is appended. I do not have a list of every study that I have been involved in. My involvement in such studies was sometimes peripheral and I have not always been included in the authorship. I don't think I can even remember all of them.

101.3. I am aware that witnesses have claimed that they were experimented on without consent. Whilst many of my patients certainly have been used as research subjects, this has not been without an appropriate level of consent.

101.4. The following generalities may be helpful. Research is divided into interventional and observational research. **Interventional studies** involve changing the patient's treatment either to an unlicensed new product or a new mode of administration or a new treatment regimen for the express purpose of investigating the outcome of this intervention. **Observational research** involves observing patients to determine the natural history of their condition, the frequency of disease complications or treatment side-effects and the clinical outcomes of their treatment but *without* changing their treatment for the purpose of research. This would include post-licensure pharmacovigilance of routine and fully licensed treatments and comparison of old routine treatments or treatment regimens with new ones.

101.5. Both interventional and non-interventional research use anonymised data only and I will go into this in more detail below. Interventional research requires a much higher level of informed consent than observational research and has done since the 1940s and the introduction of the Nuremberg code. The level of consent required for observational research has changed over the years and will be discussed in detail below.

101.6. The conduct of interventional research has been highly regulated for many years using a complex European-wide system known as Good Clinical Practice (GCP). This system has its origins in the Nuremberg Laws, which emerged from the Nuremberg Trials after the Second World War, the 1972 Treaty of Helsinki and

regular revisions since. Because the details of GCP change with time, all personnel involved in clinical research have to be trained in GCP and certified as having completed successfully a GCP refresher course every 2 years. If one's GCP training lapses, one is not permitted to conduct clinical research. This is monitored both by the hospital and by the sponsor of any interventional study.

101.7. The protocol and patient information leaflets and consent process have to be reviewed to and approved by a local and commonly a national ethics committee and the Hospital R&D Committee before the study is permitted to start. The process of obtaining all these consents and complying with GCP during the conduct of such studies is so involved and time consuming that I have employed a research coordinator and 1-2 research nurses to deal with it since the late 1990s.

101.8. During the conduct of such a study a GCP trained monitor known as a CRA or Clinical Research Assistant will visit to examine all the paperwork and monitor compliance with GCP, verify the data to ensure against research fraud and audit the site file. All the patient data is anonymised and the patient is identified only by a study number. The study files are stored for a minimum of 15 years.

101.9. The consent process is also highly regulated. The patient information leaflet and consent form are reviewed by the ethics committee who will often suggest modifications which have to be completed before the study is permitted to start. Patients cannot even be approached for participation in a study until it is fully approved and set up. Obtaining consent is a multi-stage process, which involves approaching the patient, sounding them out and if they express interest, giving them the written patient information about the study, which often runs to a number of pages and sending them away to think about it. An important detail is that it is made clear to the patient that refusal to participate is acceptable and will not jeopardise future treatment. This is explicitly stated in all patient information sheets. If they are still interested to participate, they will be seen by the study team including the investigator or sub-investigator (a clinical research doctor such as myself); the study explained in more detail and they will have the opportunity to have their questions answered. They will then sign the patient information and consent documentation in duplicate. One copy is kept in the site file and the

second copy is filed in the patient's case notes. Other than the introduction of a "cooling off" period between being given patient information and obtaining consent, the process of obtaining consent for interventional research has not changed much in 40 years.

101.10. The conduct of observational research is discussed in section 5 UKHCDO.

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.

101.11. Observational Research using anonymised data collected for other reasons and not involving any blood samples or procedures that would not be required except for research did not require explicit written informed consent. The position in relation to consent for observational research has evolved over the years, however, and is described and discussed more fully in relation to UKHCDO and the National Haemophilia Database in section 5.

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

102.1. No. an appropriate level of consent was obtained according to the standards of consent that pertained at the time and was considered appropriate and which has been reviewed at intervals (see above Q101 and section 5).

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?

103.1. Please see answers above and section 5 where it is discussed in detail. .

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?

104.1.This is discussed in detail in section 5.

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

105.1.My publications are listed as an appendix at the end of this section.

Your reports to the Penrose Inquiry on hepatitis - "Re Communication to Patients about Hepatitis 1974-1995" ("Communication report") [PRSE0000480] and "Commentary on the report to the Penrose Inquiry from Professor Vivienne Nathanson" ("Commentary report") [PRSE0002297]

106.In your Communication report at para. 52, you stated that many, perhaps most, centres did not monitor liver function tests systematically in patients until about 1980 and that from the late 1970s onwards most regularly reviewed patients would have had liver function tests conducted. What was the practice with regard to liver function tests at the Centres at which you worked?

106.1.This was the practice in all the Haemophilia Centres in which I worked. My commentary reflected that practice.

107.In your Communication report at para. 52 and para. 53, you stated that "most regularly reviewed patients would have liver function tests conducted and I would expect most of those affected to have been told that they had non-A, non-B hepatitis but that it was probably nothing to worry about" and that "In the late 1970s and early 1980s patients should have been told what was known about this type of hepatitis at the time". What information did you actually provide to patients during this period?

107.1.I have already answered this question in my response to Q 71-4

108.In your Communication report at para. 54 you claim that "If they were counselled about hepatitis in the context of a consultation also about AIDS they would often "deny" hepatitis C and deny that it had been discussed … I have found that patients commonly

deny that they have been counselled about hepatitis C even when such counselling has been documented in the notes". You say further in para. 59 that "Many patients in my experience appear to have genuinely no recollection of documented conversations about liver disease that took place during that time".

a. *What do you mean by being "counselled about hepatitis C"?*

108.1. I mean if during a consultation in clinic or the Haemophilia Centre hepatitis C was discussed at the same time as discussing HIV/AIDS. When I say that they would "deny" it, I do not mean to imply anything other than that HIV would have been so much greater a concern that other, and at that time lesser, issues would fade into the background of their memory. It is common for patients to deny, in all sincerity, ever having discussions which were documented at the time but which they have forgotten over the past 30-50 years. The Inquiry evidence includes examples of such denials.

108.2. They would have been informed of the results of hepatitis blood tests and ultrasound tests and the prognosis discussed. Treatment would have been discussed in general or specific terms as appropriate.

b. *Did you always have such discussions*?

108.3. In the late eighties and early nineties we would often but not invariably have such discussions. We were monitoring their liver disease at every visit with LFTs and alpha fetoprotein and bi-annual ultrasound and abdominal physical examination. Those results would be discussed. Since most did not have serious liver disease they would generally be offered qualified reassurance about the *current* state of their liver. Especially in the context of HIV, which engendered a high level of anxiety, this would often be forgotten

c. *Did you always document such discussions?*

108.4. Not invariably, especially if there were other clinical problems requiring action. At the time (late eighties and early nineties) HIV dominated the consciousness and

concerns of both doctors and patients and there would also have been a constant background of haemophilic orthopaedic problems requiring attention.

d. *What information regarding the discussion of hepatitis C and liver disease would you typically record in patients' notes?*

108.5. A brief summary, results of blood tests and ultrasound. The prognosis and any discussion of treatment.

109. In your Communication report at para. 60, you state that in the mid-1980s "most affected patients will have been told" that they had NANB hepatitis and you set out the information that you say "would" have been given to them.

a. *Does this reflect your clinical practice at the time?*

109.1. Yes, that was my practice.

b. *Would you expect this information, if given to patients, to be recorded in their notes?*

109.2. Not necessarily and sometimes only indirectly. The standard of note keeping in the past was not always as good even as it is now and back in the seventies it was not invariably the case that a letter was generated to the GP for every visit as it is now. Letters tend to focus on the main problems being addressed during the consultation, often orthopaedic in severe haemophilia, and the NANB may not be directly mentioned even though it was being monitored by physical examination, ultrasound and six-monthly biochemistry.

c. *What is the factual basis for your statement that "most" patients would have been given this information? Please explain how you are in a position to know what patients other than those under your care or under the care of the Centre(s) at which you worked were told.*

109.3. I have worked in three Haemophilia Centres and have audited a number of others

including Great Ormond Street, The Royal Free Hospital, St Thomas' Hospital (twice), The Royal London Hospital, Leicester Royal Infirmary, Glasgow Royal Infirmary and Glasgow Royal Hospital for Sick Children. These audits include a detailed patient questionnaire and review of notes and clinical practices. I believe that this has given me some insight into the practice of my colleagues around the country.

110. What did you mean by the statement in paragraph 64 of the Communication report that "there has never been a specific consent process attached to hepatitis C testing"?

110.1. This statement seems fairly self-explanatory.

110.2. Unlike HIV, which almost uniquely requires pre-test counselling during the eighties 1990s and until fairly recently, because of the wider ramifications associated with the diagnosis, it has never been customary, in any branch of the health service, to provide pre-test counselling or obtain specific consent for hepatitis C testing, hepatitis A testing or hepatitis B testing. My colleagues in Hepatology inform me that if they see a patient with abnormal liver function tests (in 2020) they would arrange a battery of blood tests which would include test for a range of viruses including HCV test for biochemical and autoimmune disorders and tell the patient they were doing "a few test including tests for viruses" and the results would be discussed at the next consultation.

111. In your Commentary report at para. 8, you assert that "most haemophilia centres counselled patients both at the time of HIV testing, in 1985, and when they communicated the result in a face-to-face interview".

a. What do you mean by "counselling" in this context?

111.1. I meant that the haemophilia staff, usually one of the doctors, would have discussed the test result and its implications with the patient. I do not mean that they saw a counsellor or clinical psychologist since such a person was not available in almost all centres at that time.

b. What is the factual/evidential basis for your statement that "most" haemophilia centres counselled patients in the way you describe? Please explain how you are in a position to know what was said to patients not under your care and/or by centres other than those at which you worked at the relevant time.

111.2. Obviously, I have limited insight into the way in which this was handled in different centres in which I did not work. However this issue has been much discussed over the years by Haemophilia Centre Directors and the Haemophilia Society and in Haemophilia Centre Audits, as described above. Any insights that I have obtained come from speaking to patients and colleagues, examining notes and patient questionnaires. .

112. In your Commentary report at para. 10, you suggest that in 1992/3 "treatment was available and the prognosis even without treatment for HCV was regarded as generally very good".

a. What treatment are you referring to (bearing in mind that in para. 28 of the Communication report you state that alpha-interferon was not widely used outside clinical trials until 1996 and was successful only in about 10% of this group in the late 1990s)?

112.1. I was referring to the early availability, admittedly in the context of clinical trials at that time, of Interferon.

b. What is the factual/evidential basis for your suggestion that the prognosis even without treatment was regarded as very good?

112.2. The prognosis of HCV was generally good, even though a minority developed serious liver disease. As a generality, it was and is correct.

113. In the Commentary report at para. 12, you state that "haematologists tend always to tell the patient they are testing for HCV and to discuss the condition prior to testing. Certainly, that is my invariable practice".

a. *Has this always been your invariable practice or is this something that has changed over time?*

113.1. It was almost my invariable practice. It would generally be a short conversation, especially in patients known already to have liver disease. In patients with normal liver function tests and no liver disease one would have to discuss things in more detail. I can't remember deviating from this practice. Not all the tests were arranged by me, of course. Some may have been arranged by my senior registrar if they saw the patient in my clinic at that particular time.

b. *Apart from your own practice, what is the factual basis for your suggestion that this is something that haematologists "tend always" to do? (You may wish to consider your acceptance in your oral evidence to the Penrose Inquiry on 12 January 2012, transcript [PRSE0006083] p. 126, that "some of my colleagues may well have tested, you know, without actually mentioning what the test was" and that "in many places the patients would have been tested without it being specifically discussed", transcript p. 127).*

113.2. I obviously have limited insight into what happened in other departments, but I had the impression is, that since HCV antibody testing was just seen as a continuation of hepatitis monitoring that had already been going on for 12 years or more that in some cases it would just have been added to the list of blood tests without much being said.. That would be normal practice amongst Hepatologist in 2020. The idea that specific consent should be sought before testing for HCV is not one that our Hepatologists recognised when I recently put it to them.

114. What did you mean in para. 17 of the Commentary report by "special arrangements" being made with a patient's GP?

114.1. Occasional patients requested that we *not* send clinic letters including HIV data to their GP. This was their right but potentially created problems. We would explain to the patient that the GP practice needed to know this sort of thing in case they

had to see them. In one case, the patient explained to me that he lived in a small village and his next door neighbour was his Doctor's receptionist and he was worried about confidentiality. This seemed an entirely reasonable concern. I therefore phoned the GP, with the patient's permission, and we agreed a compromise, which was agreeable to all parties, that the GP would keep his medical records stored securely at his home and that I would write to the GP at his home address marked "private and confidential". This was a unique solution, which is why I remember it so well.

115.What did you mean by "implied consent" in paragraph 24 of the Commentary report?

115.1.Implied consent is given when a patient is made aware of the general use to which their data or blood sample is used and has not raised any objection. This is discussed more fully in section 5 with exhibits.

116.In your oral evidence to the Penrose Inquiry your view appears to have been that there was not a stigma, alternatively not much of a stigma, associated with Hepatitis C (transcript, 12 January 2012 [PRSE0006083] p. 150-151). Does that remain your view and if so why?

116.1.This remains my view. This is partly because, in contrast with HIV, there is little public awareness and very limited reporting on HCV in the media. In contrast, there was a massive, high profile, public health publicity campaign in the 1980s ("Don't die of ignorance!") about HIV which made it clear that it was associated with intravenous drug abuse, homosexuality and sex, which assumed a very high profile in public awareness.

116.2.Nothing similar has occurred in relation to HCV, even though possibly as many as half a million of the population are or have been infected with this agent.

Transfusion

117.The questions above have focused on the care and treatment of patients with bleeding

disorders. In your report prepared at the request of the defendants' solicitors in the Hepatitis C litigation ("The Risks of Transfusion of Blood and Blood Products with particular Reference to Hepatitis C", [NHBT0000033_036]) at paragraphs 60-62 you stated that you spoke to many patients and to colleagues about the risks of blood transfusion during the period 1988-1991 in your capacity as hospital haematologist responsible for the blood bank and because you were responsible for patients with haematological malignancy.

a. *Over what period of time were you the hospital haematologist responsible for the blood bank and/or responsible for patients with haematological malignancy?*

117.1. As stated above, I was responsible for the Blood Bank in Liverpool up to 1991 when Dr Chu took up post and responsible for a third of the Haematological Malignancy during that time.

b. *How frequently (approximately) did you speak to patients about the risks of blood transfusion and/or the risks of blood products (other than products used in the treatment of patients with bleeding disorders) and in what kinds of circumstances?*

117.2. It was a very long time ago and I can't remember how frequently this occurred. It was not the job of the clinician with responsibility for the blood bank to discuss the risks of transfusion with every recipient of blood. That would not have been practical and would have been the responsibility of the prescriber of the blood. However, Haematology, especially the malignant side, consumed half the blood used in the hospital so there was a lot of transfusion going on within the department and particularly during the AIDS era, many patients were quite anxious about transfusion and would sometimes refuse blood. One would have a conversation with these patients and try to put the risks into context. Patients having a blood transfusion for the first time would be given a leaflet, which had been produced by the Transfusion Service with the aim of putting the risks into context. I attach a scan of the only example that I have, which dates from the nineteen nineties and obviously post-dates the introduction of HCV testing of all blood donations in 1991 (WITN3289070; Transfusion Patient leaflet.).

c. *What (if any) information did you typically provide to patients about the risks of infection from transfusion?*

117.3. Please see above.

117.4. Prior to the advent of HIV and HCV testing of blood donations, one was not in a position to put these viral risks into context because they had not been well quantified. Retrospective analysis suggests that donor screening alone reduced the risk of HCV by 90% even before the introduction of HCV testing of donations in 1991. The availability of testing and the increasing number of people with AIDS and public health campaigns in the second half of the Eighties raised the profile of HIV in such a way that although all donations were tested from 1985 and the risk had been enormously reduced, there was much more anxiety about blood transfusion after 1985 than before.

d. *What (if any) information did you typically provide to patients about the risks of infection from blood products (other than products used in the treatment of patients with bleeding disorders)?*

117.5. I assume you mean red cells and blood components. See above, as for whole blood.

e. *What discussions did you have with colleagues about the risks of transfusion?*

117.6. This was discussed in the Transfusion Committee. I now have no recollection of those discussions.

f. *Who was responsible for providing information to patients about the risks of infection from transfusion – the treating clinicians, you as the haematologist responsible for the blood bank or some other person?*

117.7. The treating clinician.

Records

118. What was the policy at (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre as regards to recording information on death certificates when a patient had been infected with HIV or hepatitis? (You may wish to consider the minutes of the 6th meeting of the UK Regional Haemophilia Centre Directors Committee on 16 September 1991 [HCDO0000441] and your comments at section 13 of the minutes; and the discussion at section 8 of the 25th meeting of UKHCDO Directors on 1 October 1993 [HCDO0000493]).

118.1. There was no policy in any of these centres other than the policy of often discussing the death certificate with the relatives before filling out the form. This is a legal document and one has a duty to make it as accurate as possible. This really didn't pose any difficulties with hepatitis C since this never acquired the stigma or level of awareness attached to HIV. Therefore if someone died from Liver failure or hepatocellular carcinoma, the certificate would put this as the principle cause of death, caused by HCV and Haemophilia or blood product therapy.

118.2. The problem with HIV (which was occasionally discussed even with the patients themselves ante-mortem) is that the condition was associated with such stigma in the 1980s and 1990s that some patients kept it a secret even from their children and close relatives and wished it to remain a secret. My view was that it should feature explicitly on the certificate. I did not wish to distort the statistics. This led to some difficult conversations with already distressed relatives as we sought to achieve a set of words which was true but might be less explicit for the uninitiated lay-person. For example, rather than say the patient had died of "AIDS", one could name the AIDS-defining illness from which they had died, for example as cerebral Lymphoma or Pneumocystis, Carinnii Pneumonia or cryptosporidiosis and attribute that to haemophilia or blood product therapy. Haemophilia would always appear as a contributory cause. A straightforward certificate would give the AIDS-defining illness as the principle cause of death caused by HIV secondary to Haemophilia so that the entire sequence of events was quite clear.

118.3. In Manchester, all patients dying from either HIV or complications of hepatitis C, would, if this was contracted from blood products, have an inquest. In that situation

the death certificate is completed by the Coroner. I know the local Coroner to be a very compassionate and sensitive man and he is only following a very straightforward interpretation of the law in relation to iatrogenic death. However, the Inquest takes place months or even years after death causing a good deal of distress to the families.

119.What were the retention policies of (a) Sheffield, (b) the Liverpool Centre and (c) the Manchester Centre in relation to medical records during the time you were practising there?

119.1.We were subject to the hospital medical records policy full details of which may be obtained from the Trusts in question and full details of which I have probably never known. It is my understanding that this information has already been requested from the Trusts in question. The following generalities are probably universal and certainly applied in Liverpool and Sheffield: I apologise for any inaccuracies but I am not a Medical Records Officer-

119.2.Medical records were preserved and retained for a minimum of 6 years after the patient has died and longer if the managing clinician requests it.

On taking up post in Manchester, I requested that none of our records be destroyed.

If patients are not seen for a period of ≥ 3 years, their notes may be destroyed or microfilmed.

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

120.1.Although I understand that it was not uncommon to maintain an active sub-file with core information for emergency consultations to minimise delay in getting data when patients are admitted or seen as an emergency, this is not something that we have done in any of the centres in which I worked at the time that I worked in them.

121.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?

121.1. Even though I have been conducting clinical research since before the advent of data protection legislation, I have not kept any named patient data anywhere but within the hospital for reasons of data security and confidentiality. In any case, according to GCP (Good Clinical Practice: the rules that regulate the conduct of clinical research), each individual subject file is anonymised (the patient only identified by a study number) and the storage of the data is regulated, has to be in a secure hospital facility and retained for 15 years, after which it may be destroyed.

121.2. To keep patient notes at home would be a disciplinary offence and is not something I have ever done.

122. *In November 2002 the Haemophilia Society raised with you difficulties which patients were experiencing in obtaining copies of medical records (see the letter of 26 November 2002 with enclosures [HCDO0000266_024; HCDO0000266_026 and HCDO0000266_027] to you and your reply dated 17 December 2002 [HCDO0000266_004]).*

a. *In your reply you explained that you would discuss with the UKHCDO executive whether it would be helpful to issue some guidance. Was guidance issued and if so when?*

122.1. The matter was discussed and my recollection was that this was a common problem without a ready solution and was not peculiar to the patients. I have recently encountered similar problems obtaining complete records to address individual Rule 9 "criticisms". Many patients had multiple volumes of notes (up to 7), many feet thick and going back many decades. Often the binding would be in poor condition and the older volumes falling apart. When seeing such a patient in outpatients one did not need to consult their notes relating to the 1940s and so only the more recent volumes would be presented to clinic with the rest remaining in storage. The sheer volume of notes stored in general became a major issue for

many larger hospitals who eventually resorted to off-site sub-contracted notes storage, in our case with "Iron Mountain". In this way older and newer volumes could become separated and some volumes may just get lost.

122.2. It was not thought that a guideline from UKHCDO would help and so none was formulated.

b. You refer to being the subject of malicious complaints and vilified in the local press. Please provide details.

122.3. In 1995, the widow of one of my ex-patients, GRO-B GRO-B attempted to sue me and 8 years later she referred me to the GMC with similar allegations. GRO-B GRO-B GRO-B GRO-B These complaints were dismissed and no proceedings ever issued because the allegations were completely without foundation

Appendix to Section 4: PUBLICATIONS:
(As of 1/7/2020, in reverse chronological order)

Original Articles:

1. Bukkems LH, Heijdra JM, Mathias M, Collins PW, Hay CRM, Tait RC, Mangles S, Myers B, Evans G, Bailiff B, Curry N, Payne J, Austin S, Gooedhart TMHJ, Leebeek FWG, Meijer K, Fijnvandraat K, Chowdary P, Mathot RAA, Knossen MH. For the UK –EHL outcomes registry)PTO-CLOT Collaboration. A novel enriched population pharmacokinetic model for recombinant factor VIII-Fc fusion protein concentrate in Haemophilia A patients. ***Thrombosis and Haemostasis*** 2020, 120(5): 747-757.

2. Hart DP, Hay CRM, Liesner R, Tobaruela G, Du-Mont B, Makris M. Perioperative laboratory monitoring in congenital haemophilia patients with inhibitors: a systematic literature review. ***Blood Coagulation and Fibrinolysis*** 2019, 30(7); 309-23.

3. Oldenburg J, Hay CRM, Jiminez-Yuste V, Peyvandi F, Schved JF, Szamosi J, Winding B, Lethagen S. Design and prospective observational study on the effectiveness and real world usage of a recombinant factor VIIIFc (rFVIIIFc) compared with conventional products in haemophilia A: the A-SURE study. ***BMJ Open*** 2018, 028012.

4. Volkers P, Hanschmann KM, Calvez T, Chambost H, Collins PW, Demiguel V, Hart DP, Hay CRM, Goudemand J, Ljung R, Palmer BP, Santagostino E, van Hadveld EM, van den Berg M, Keller-Stanislawski B. Recombinant factor VIII products and inhibitor development in previous untreated patients in severe haemophilia A combined analysis of three studies. ***Haemophilia*** 2019, 25(3); 398-407.

5. Scott MJ, Xiang H, Hart DP, Palmer B, Collins PW, Stephensen D, Sima CS, Hay CRM. Treatment Regimens and outcomes in severe and moderate haemophilia A in the UK: The THUNDER study. ***Haemophilia*** 2019, 25(2); 205-12.

6. Mathias MC, Collins PW, Palmer BP, Chalmers E, Alemelu J, Richards M, Will A, Hay CRM. The immunogenicity of ReFacto AF (Monoroctocog alfa AF-CC) in previously unteated patients with haemophilia A in the United Kingdom. **Haemophilia** 2018; 24(6); 896-901.

7. Scott M, Hay CRM, Elkhalifa S, Tower C, Cocker M, Thachil J, Scott M et al Management of Pregnancy in type 3 von Willebrand Disease with alloantibodies. ***Br J Haematol***, 2018, 182(3); 440-42

8. Zozulya N, Kessler CM, Klukowska A, von Depka M, Hampton K, Hay CRM, Jansen M, Bichler J, Knaub S, Ranjaran S, Zozulya N. ***Haemophilia*** 2018; 24(1); 70-76.

9. Gruppo RA, Malan D, Kaposcsi J, Nemes L, Hay CRM, Booggio L, Chowdary P, Tagariello G, Drygalski A, Hua F, Scaramozza M, Shi H, Arkin S. Safety, pharmacokinetics and pharmacodynamics of Marzeptocog alfa (recombinant

VIIa variant): Results from a single, ascending-dose, phase 1 study in subjects with haemophilia A and B. ***J Thrombosis & Haemostasis***, 2018, 10; 1984-93..

10. Collins PW, Quon DVK, Makris M, Chowdary P, Kempton CL, Apte SJ, Ramanan MV, Hay CRM, Drobic B, Hua Y, Babinchak TJ, Gomperts ED. Pharmacokinetics, safety and efficacy of a recombinant factor IX product, trenocagog alfa in previously treated haemophilia patients. ***Haemophilia*** 2018, 24(1); 104-112.

11. KJ Pasi, Ranjarajan S, Georgiev P, Mant T, Creagh MD, Lissitchkov T, Bevan D, Austin S, Hay CRM, et al. An RNAi Therapeutic Antithrombin in Hemophilia A or B. ***NEJM*** 2017, 377;819-828.

12. Hay CRM, Xiang H, Scott M, Collins PW, Liesner R, Dolan G, Hollingsworth R. The Haemtrack home therapy reporting system: design implementation strengths and weaknesses: a report from UKHCDO. ***Haemophilia*** 2017, 23(5); 728-735.

13. Hay CRM, Xiang H, Scott M, Collins PW, Liesner R, Dolan G, Hollingsworth R. The Haemtrack home therapy reporting system: Design, Implementation, strengths and weaknesses: A report from the UK Haemophilia Centre Doctors Organisation. ***Haemophilia*** 2017. DOI: 10/1111/hae.13287 Epublished in advance of print.

14. Scott M, Nummi V, Lassila R, Xiang H, Hay CRM. Weekly recombinant FIX prophylaxis for severe Haemophilia B in normal clinical practice. ***Haemophilia*** 2017 May; 23(3) e240-43. Doi:10.1111/hae.13226.

15. Pike GN, Cumming AM, Thachil J, Hay CRM, Bolton Maggs P, Burthem J. Evaluation of the use of rotational thromboelastometry in the assessment of FXI deficiency. ***Haemophilia*** 2017 May 23(3): 449-457.

16. Hay CRM, Sharpe T, Dolan G. and UKHCDO. Use of the UKHCDO Database for a post-marketing surveillance study of different doses of recombinant factor VIIa in haemophilia. ***Haemophilia*** 2017 May; 23(3),376-382.

17. Pike GN, Cumming AM, Thachil J, Hay CRM, Burthem J, Bolton Maggs P. Evaluation of the use of Global Haemostasis assays to monitor treatment in factor XI deficiency. ***Haemophilia*** **2**017 March 23(2); 273-283.

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Section 5: UKHCDO *

123.Please describe your involvement with UKHCDO (including any of its working parties, committees or groups), including your periods as Vice-Chair and as Chair.*

123.1.*Please note that UKHCDO changed its name in 1996 from the UK Haemophilia Centre Directors Organisation to the UK Haemophilia Centre Doctors Organisation. This change was associated with a broadening of the membership to include all doctors managing patients with haemophilia rather than just the centre directors.

123.1.1. Member of UKHCDO since 1987.

123.1.2. Chairman UK Haemophilia Centre Doctors Organisation **(UKHCDO)** 2005-2011.

123.1.3. Director, of the **UK National Haemophilia Database (NHD)** since 2002.

123.1.4. Vice-Chairman UKHCDO 1997-2005.

123.1.5. Treasurer of the UKHCDO 1992-97.

123.1.6. Trustee of UKHCDO (Registered Charity) 1992-2011.

123.1.7. Director **UKHCDO Ltd** since 2003.

123.1.8. Chairman: UKHCDO Inhibitor Working Party 1993-2005.

123.1.9. Member Inhibitor Working party 2005-2020

123.1.10. Chairman, UKHCDO Data Management WP 1998-2005 (member since).

123.1.11. Member of the Committee of Regional Haemophilia Centre Directors of the UK 1987- .

123.1.12. Member of the UKHCDO Advisory Committee -2020

123.1.13. Member Therapeutic Guidelines Taskforce of UKHCDO 1996.

123.1.14. Member Information Technology Working Party of UKHCDO 1996-98.

123.1.15. Member of the UKHCDO Paediatric Working Party 1993-2005.

123.1.16. Member of the UKHCDO Von Willebrand Working Party 1996-2000.

123.1.17. Clinical Lead; DH National Procurement Team, UK Coagulation Factor Procurement 2005/6 and 2009/10 (seconded part time to DOH 1/9/09-1/9/10) and member of the procurement group working with the Central Medicines Agency of DH and the NHS England since that time. .

123.1.18. Member of the Advisory Group, and reporting to, the Health Protection Agency and DH Blood Policy Unit on vCJD 2009-10

123.1.19. Northern Representative. **Haemophilia Clinical Reference Group** (CRG) advising the **National Commissioning Board and NHS England** since 2011.

123.1.20. North West Representative on the National Non-Malignant Haematology

Speciality Group of the **NIHR (CRN) [National Institute of Heath Research Clinical Research Network** since 2011.

123.1.21. Member of the Advisory Group to the Dept. of Health on support for individuals infected with hepatitis C or HIV by blood transfusion or blood products 2008/ 9

123.1.22. Secretary Haemophilia Alliance 1999-2002.

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

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

124.1.UKHCDO is a registered charity. It became a registered charity in 1993.

124.2.The aims of the organisation are published on our website WWW.UKHCDO.org and the constitution of UKHCDO is attached as an WITN3289082 (UKHCDO Constitution). Our mission statement is as follows:-

> *"The United Kingdom Haemophilia Centre Doctors' Organisation is an association of medical practitioners who work within the Haemophilia Centres of England, Scotland, Northern Ireland or Wales and have an interest in the care of people with Haemophilia or other inherited bleeding disorders.*
>
> - *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."*

124.3. UKHCDO does this by reviewing arrangements and organisation of the care of bleeding disorders and the safety and efficacy of current treatments and treatment regimens, , by publishing clinical and laboratory guidelines and making representations to the commissioners, NHS England, Scotland and Wales as patient advocates and by collaborating closely with The Central Medicines Agency (a branch of DH, recently transferred to NHS England) to achieve good value for the NHS whilst ensuring procurement of the best products for our patents.

124.4. UKHCDO also conducts observational research using data collected routinely for patient management. UKHCDO does ***not*** conduct interventional research.

124.5. UKHCDO also organises triennial (now every 5 year) audit or peer review of Haemophilia Centres to ensure that standards of clinical care are maintained or improved.

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

124.6. The membership, committee structure and procedures of the organisation have evolved since the inception of the organisation as the UK Haemophilia Centre Directors Organisation (1968-1999) to the UK Haemophilia Doctors Organisation (1999 to date)

124.7. **Advisory Committees (including Historical Committees):-**

124.7.1. 1976 - 1989 - Haemophilia Reference Centre Directors – last meeting 13/02/1989

124.7.1.1. Centre Directors from the Haemophilia Reference Centres only, - Cardiff, the Royal Free, Sheffield, Manchester, Oxford (? St Thomas').

124.7.2. 1989 – 1995 - UK Regional Haemophilia Centre Directors Committee – first meeting 11/09/1989

124.7.2.1. A *representative* from each Region plus the Executive Committee.

124.7.3. 1996 – 2000 - UK Haemophilia Centre Directors' Organisation Executive Committee – has existed under various titles since at least 1996 and consists of an elected Chairman, Vice Chairman, Treasurer and Secretary.

124.8. However, the current structure dates back to 1996 and is described below:-.

124.9. **Membership of UKHCDO**: The current membership is made up of nominated doctors of all grades permanently employed to look after patients with bleeding disorders. Prior to 1991, membership was limited to Haemophilia Centre Directors and the organisation was known as the UK Haemophilia Centre Directors Organisation. Organisations associated with UKHCDO include The Haemophilia Nurses Association, The Data Managers Forum and the Chartered Physiotherapists Association.

124.10. **The Executive Committee: (11/9/2000 to present) :** UKHCDO is chaired by a chairman elected for three years by the membership of UKHCDO. Other members of the executive, proposed and seconded by the membership and elected if more than one member is proposed, include the Vice Chair, Secretary and Treasurer, each with a three year term. The Executive meets monthly by phone and reports to the advisory committee and membership. .

124.11. **Trustees of UKHCDO (the charity)**: These are the members of the Executive Committee.

124.12. **The Advisory Committee:** This is made up of a representative from each Comprehensive Care Centre (CCC) and a single representative from a Haemophilia Centre (smaller than a CCC). Also present are all Working Party Chairs, the Director of the Database, the Executive Committee Members, a representative of the HNA and the CPA. Others may be invited, e.g. a representative of NHSE or the Haemophilia Society. Usually a number of members

may be present wearing more than one hat. The advisory meets three times a year in person and reports to the executive and membership.

124.13. **Annual General Meeting**: All members are invited to this meeting. On alternate years there is also an attached scientific meeting. There is a business meeting at which accounts have to be agreed etc. to which only members a representative of the HNA, CPA and the Haemophilia Society and invited participants observers may attend. There is also a presentation of national bleeding disorders statistics (published in our annual report and on our website which is open to anyone (non-members) to attend.

124.14. **Working Parties and Task-Forces**: Working parties have a term of three years after which they must disband or reconstitute. Historically, in the last century, some working parties continued for years without renewal. Some working parties were constituted intermittently for a specific task such as the Prophylaxis Working Party, The Emergency Admissions Task Force and Therapeutic Materials Task Force. Typically Task Forces are constituted to produce an evidence based Guideline and are disbanded after completing the designated task. Some historic Working Parties have permanently disbanded since they were no longer required e.g. HIV Working Party and Hepatitis Working Party. Others have been in more or less permanent existence under various Chairs e.g. Paediatric Working Party, The Inhibitor Working Party and (under various names) the Data Management Working Party, about which more below. Working parties are expected to meet at least three times a year. Apart from completing tasks, and conducting observational research they are expected to report back to the Advisory Committee regularly, to the AGM and to provide an annual report which is published in the Annual Report and may be viewed on our website WWW.UKHCDO.org. Each Working Party has a chairman nominated by the Chairman or Executive. The membership was made up of members selected for their interest and experience and invited non-members. Many WPs are multidisciplinary. Several of these have patient and Haemophilia Society representation, including the Data Management Working party (DMWP) and Data Analysis Group.

124.15. **The Data Management Working Party (DMWP):** This is the governing body of

the National Haemophilia Database. It is traditionally chaired by the Vice Chair of UKHCDO. The membership is made up otherwise of the Chair of UKHCDO, all the Working Party Chairs, the statisticians from the database, a representative of the HNA and CPA, a commissioner or two (currently the lead commissioner for bleeding disorders from NHSE, William Horsley), a representative of the Haemophilia Society (usually the CEO) and one or two patient representatives representing the patient group rather than the Haemophilia Society. Patient participation and Haemophilia Society Representation on this group dates back at the very least to the early 1990s and has always been much valued. This group meet face to face twice a year and consider policy and management issues, outputs from the database, the direction of travel etc. The group reports back to The Advisory Committee and the AGM and produces an Annual report.

124.16. **Data Analysis Group (DAG):** The DAG was constituted two years ago as a subgroup of the DMWP for the purpose of reviewing all requests to the database for data or analysis and to prioritise the work of the database. All outputs (reports and manuscripts) are also reviewed. The group meets once a month by Zoom call under the joint-chairmanship of me and Prof Peter Collins. The membership is largely drawn from the membership of the DMWP, and includes Working Party chairs, the statisticians from the database, two patient representatives (who are also biostatisticians) a representative of the Haemophilia Society and a commissioner. Patient participant has been both very active and useful.

124.17. **UKHCDO Ltd:** UKHCDO Ltd is the commercial arm of the registered charity (UKHCDO). It has four shares held in trust for the organisation by the trustees of the charity. Originally established to manage the annual general meeting, the profits of which are gifted to the charity, the company now also manages the National Haemophilia Database and also managed the finances of the Triennial Audit of Haemophilia Centres. The Directors of UKHCDO Ltd are currently: Dr Ri Liesner, Prof CRM Hay, Prof PW Collins, Prof CA Ludlam, Dr Kate Talks, Dr A Will, and Prof P Chowdary. The Database Manager is Mr Andrew McNally. The board meets three times a year and reports to the Advisory Committee and AGM.

c. *The relationships between UKHCDO and pharmaceutical companies.*

124.18. I would say that the relationship between UKHCDO and the manufacturers was and is fairly "arms-length". Whereas individual Haemophilia Centres used to negotiate to purchase their own products direct from the manufacturer, this has been managed through a national contract framework agreement since 20O5. This process will be described more fully elsewhere in this report but has been managed in partnership with the CMU (Central Medicines Unit a branch initially of DH and now of NHS England (NHSE)) and NHSE (Scotland and Wales), and in the early days, with DH.

124.19. Industry comes to the AGM, where they are permitted to set up a trade exhibition but not to attend the business meeting.

d. *How UKHCDO was funded.*

124.20. To start with and for probably the first 25 years of its existence, UKHCDO was unfunded. Prior to achieving charitable status, UKHCDO had no funding other than the profits from the AGM (approximately £20,000/year). Members then paid a £20/year membership fee (recently abolished) yielding about £2000per year. UKHCDO therefore has an income of £20,000-£30,000 per annum.

124.21. Funding of UKHCDO Ltd is described elsewhere in my response to Q128.

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

124.22. Minutes were sent to all members. All minutes from all committees and Working Parties are available to Haemophilia Centre staff on a secure, password protected UKHCDO SharePoint site (Collaborate).

124.23. Guidelines were published and hard copy sent to all members. All guidelines are also available from our Website (WWW.UKHCDO.org) for the past 15 years or so and from the Wiley (publishers) website and various search engines such as PUBMED. Our website is open for anyone to explore and has a hyperlink

connecting from the Haemophilia Society website.

124.24. The annual report is distributed to all members, Commissioners, DH, the Haemophilia Society and any patients wishing a copy and Industry. A summary of the annual statistics has been available on our website WWW.UKHCDO.org since its inception and over the past two years the past five years' Annual Reports have been available on our website for anyone to download. There is a hyperlink between our website and the Haemophilia Society website. The Annual report for the year 2018/19 is attached as an example (WITN3289083)

124.25. The patient information leaflets about the National Database were sent to every centre. This is described more fully in my response to Q129. However, this leaflet is also downloadable from our website and the Haemophilia Society website has a hyperlink to our website patient page accessible through the following link: -

https://urldefense.proofpoint.com/v2/url?u=https-3A__haemophilia.org.uk_2019_07_04_getting-2Dinformation-2Dfrom-2Dukhcdo-2Dan-2Dupdate_-23more-2D6655&d=DwIFAg&c=bMxC-A1upgdsx4J2OmDkk2Eep4PyO1BA6pjHrrW-ii0&r=qZtphTgJUfWa0-jANC7Ym4QAXbkGOmF9R9reCUAl8fM&m=So6eAuJbYo7KHPnj2sAWjOIqzLPiS6Wtxd2cjeenPS0&s=7_2j7-c51HM5CwYme4qTZEGVAVKLYBtDuffKfQIXOKM&e=

124.26. Age-specific information leaflets and consent forms are accessible to Haemophilia Centres through the "Consent" module of the National Haemophilia Database Centre interface. These are attached as an exhibit in relation to Q129.

124.27. We ensure that the Database is inspected every two years or so by the Hospital Caldecott Guardian to ensure that we are complying with the Data Protection Act, Caldecott principles and the principles of fair data handling. The Caldecott Report has been published on our website since the inception of the website.

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;*

124.28. In the early 1990s, I published papers on the effect of intermediate and high-purity products on the immune system and argued for the change to high-purity products, particularly for HIV positive patients. In 2000-2002 I organised a national contract swap mechanism on behalf of UKHCDO, which permitted us to maintain children under the age of 10 on recombinant factor VIII by shuffling supply around the country from centre to centre, when the supply of recombinant factor VIII was reduced by 50% overnight.

124.29. I was a member of the 1996 Therapeutics Task force that recommended "Recombinant for all" (WITN3289048). I have been centrally involved in the process of National Procurement since it started in 2005 (WITN3289043). This is more fully described elsewhere.

ii. *the manufacture of blood products;*

124.30. See above.

iii. *self-sufficiency*;

124.31. This is an issue that was active in the nineteen seventies, mostly before I qualified as a doctor and with which I have never been involved. I therefore have no special knowledge of this.

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

124.32. DDAVP was recommended in various guidelines dating from 1983, 84 and 88 (WITN3289041, WITN3289042 and WITN3289044). I was not a member of any of the advisory groups formulating those guidelines. I was a member of the 1996 Therapeutic Materials Guideline, which .promoted "recombinant for all".

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

124.33. By the time I became a Consultant and Centre Director and member of the Regional Committee of UKHCDO, all the products in use where virally attenuated. I participated in debates about further improvements in product safety such as the introduction of dual viral inactivation, high purity products and the campaign for recombinant products.

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

124.34. I was not involved in policy documents about this other than in general discussion in the Advisory Committee.

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

124.35. Neither UKHCDO nor the UK National Haemophilia Database has a sample depository and therefore neither organisation has ever needed to arrange to take consent for the storage of samples.

124.36. The Genetics Working Party of UKHCDO helped design the consent form, which is used at a local level to obtain consent for genetic testing for bleeding disorders. This is a service requirement unrelated to research, though the results are kept in both NHD and the local database, for which consent is obtained (WITN3289054 and WITN3289055)

viii. *heat treatment;*

124.37. See answer to Q124 v.

ix. *other measures to reduce risk;*

124.38. See answer to Q124.

x. *vCJD exposure; and*

124.39.This is more fully discussed in section 7,

xi. *treatments for HIV and hepatitis C.*

124.40.I was never a member of the Liver Disease or HIV Working Parties and so my involvement with policy in relation to this was limited to participating in debate in the Advisory Committee.

When addressing this question, please include a description of your involvement in the production of UKHCDO's Recommendations on Choice of Therapeutic Products for the Treatment of Non-Inhibitor Patients with Haemophilia A, Haemophilia B and Von Willebrand's Disease (third edition enclosed by way of example, [PRSE0003809]).

124.41.I was a member of the 2006 Therapeutics Products Task Force, whose recommendations published in 2007 recommended, amongst other things "recombinant for all" (WITN3289048).

125.At the 18th meeting of the UKHCDO AIDS Group on 11 September 1989 (minutes enclosed [HCDO0000536_001]), there was a discussion about carrying out a study of HIV in sexual partners of haemophiliacs (at which you were reported as saying that you suspected there were more HIV positive partners than those known); it was also noted that information was not collected on children born to HIV positive fathers. (See also the discussion at the 9th meeting of the Regional Haemophilia Centre Directors Committee on 4 September 1992 [HCDO0000444]).

125.1.This was a reference to the fact that some partners of our patients refused testing, in some cases for many years. In at least two cases, their partner's widows presented to me for testing very shortly after their husbands had died (both fortunately HIV-negative).

a. *What was the basis for your view that there were more HIV positive partners than those known?*

125.2.Only that some spouses refused testing and in some cases refused testing for a

very long time.

b. *What if any work was undertaken by UKHCDO to establish the likely numbers of HIV positive partners?*

125.3. We surveyed the population by questionnaires at intervals. These have been viewed by the Inquiry investigators.

c. *If such work was undertaken, what were its findings?*

125.4. These findings and examples of the Questionnaires are to be found in the UKHCDO response to its Rule 9 request.

d. *What if any work was undertaken by UKHCDO to collect information on, or establish the likely numbers of, children born to HIV positive fathers?*

125.5. As far as I am aware, this was not investigated but, anecdotally, I am not aware that any HIV positive children were born to HIV positive fathers or that HIV was transmitted from infected men to family members who were not in a sexual relationship. Indeed, until really quite recently HIV positive men were always recommended to use barrier contraception. Consequently, very few children were born to this group. Haemophilia Centres, including all the ones I was involved with gave out a selection of condoms and other barrier devices to patients for many years.

125.6. What is clinically relevant here is not so much the HIV status of the father but that of the mother since HIV may be vertically transmitted *in utero.* I have commented on this elsewhere.

e. *If such work was undertaken, what were its findings published/recorded?*

125.7. Please, see above.

126. At the 18th meeting of the UKHCDO Executive Committee on 11 February 2000

(minutes enclosed [HCDO0000473]) there was a discussion about issues that had been raised by the Department of Health and the Department was reported to be "anxious for information" about social services support.

a. *What kind of information was being sought by the Department of Health and for what purpose?*

126.1. I do not remember.

b. *What information was provided to the Department of Health by UKHCDO?*

126.2. I do not remember.

c. *Reference was made in the minutes to support being withdrawn from some patients. What if any steps were taken by UKHCDO to address this issue?*

126.3. This issue had to be addressed at a local level by Haemophilia Centres. UKHCDO has no direct patient responsibility and was not in a position to address this problem directly though discussion in the Advisory Committee may have been helpful for individual members in giving them some guidance to help them approach the problem. Over the years, there have been recurring generic problems arising from patients being reassessed and having their benefits reduced. This occurred because assessments for benefits became tougher in general and also because patients' level of disability may also have changed. These had to be dealt with on an individual basis by the Centre Director and social worker to support an appeal. A classic example of this is that most HIV positive patients received a higher rate allowance that was based on a medical assessment from their centre that they *might* have less than 6 months to live. Unsurprisingly, after ten years or so, this was questioned, since the life expectancy of those who survived to 1995 was transformed by triple anti-retroviral therapy. Also, joint replacement greatly reduced the level of disability suffered by many of our patients

d. *To what extent did patients under your care receive support from social services and how did that change over time?*

126.4. Most patients with severe haemophilia and all who were not working and most that had HIV were in receipt of some benefits, either in relation to their disability or life-expectancy. Supporting these applications and appeals was an important part of the work of the Haemophilia Centre. Please see also previous answer.

National Haemophilia Database (NHD)

127. Please describe the establishment and operation of the National Haemophilia Database, its purpose and objectives, your involvement in it, the range and kind of data recorded in the Database and how data is collected and organised.

127.1. The National Haemophilia Database was established in 1968 in Oxford under the leadership of Dr Rosemary Biggs. The objective of the database was initially to establish how many patients with bleeding disorders there were and what their treatment requirements were. This was necessary partly because there was an aspiration to become self-sufficient in blood product therapy at that time.

127.2. I first became directly involved with the database in 1998 in my capacity as Chairman of the Data Management Working Party. In that capacity, I helped Miss Rosemary Spooner (administrative assistant for the NHD) collate the national statistics and annual report and have presented the annual report to the AGM every year since. In the late 90s, the database was in need of technical updating and in 2000 I visited Oxford with Dr Rob Hollingsworth, my software engineer, to assess the situation and devise a strategy with Miss Spooner. We subsequently worked with Miss Spooner to upgrade the system. When Miss Spooner retired in 2002, this caused a crisis for NHD, since the database was unfunded and Oxford DHA would not fund a replacement for Miss Spooner. UKHCDO invited proposals to be presented to the Advisory Committee and after presentations from Oxford and Manchester voted to move the Database to Manchester Royal Infirmary. The Paper archive was moved to safe storage in Manchester Royal Infirmary. I have been the Director of the database since that time.

127.3. The data collected, how it is collected and how it is organised are fully described

in the final section of the UKHCDO Rule 9 response, which I wrote. I would refer you to that report.

128. *Please explain how the work of the National Haemophilia Database has been funded over the years; how it is currently funded; and what if any financial contributions have been offered or made by (a) pharmaceutical companies and (b) the Department of Health.*

128.1. From its inception in 1968/9 until the database moved to Manchester in 2002, the database was effectively wholly funded by Oxford Health Authority. It was based in The Churchill Hospital Oxford, in the Haemophilia Centre. They paid the salary of Mrs Rosemary Spooner, a part time secretary and whichever Director was in charge (Dr Rosemary Biggs, then Dr Charlie Rizza and then Dr Paul Giangrande). NHD ran on a shoestring and had very limited capacity.

128.2. In 2002 Rosemary Spooner retired and Oxford Health Authority made it clear that they felt it was inappropriate for a district health authority to be funding a national function and said they would not replace Miss Spooner. UKHCDO invited Oxford and Manchester to formulate proposals for the future funding and development of the NHD considered these and voted that it should move to Manchester Royal Infirmary.

128.3. Initially, we had no funding of any sort. The annual report was three years in arrears, as was data transcription from paper to computer. Consequently, our data was of no real interest to anyone at that time and this had to be addressed as quickly as possible, not least to attract funding support from NHS bodies. In the short term, unrestricted grants were obtained from *all* the industrial suppliers. I also approached the Department of Health to determine what sort of data would be useful for healthcare planning and whether there was any possibility of obtaining NHS funding for the database.

128.4. Over the years, and until the reorganisation of the Health Service caused us to deal far more with NHS England (Scotland and Wales), DoH funded a variety of projects, including our involvement in "Recombinant for all" in 2005 and the initial

two contracts for National Procurement 2011 (described more fully in the response to the UKHCDO Rule 9 and elsewhere) and our HCV lookback in 2011. No funding has been provided for the recent HCV survey or for ongoing vCJD surveillance from any source

128.5. NHS England (Scotland and Wales) have provided annual funding since 2006. This has never been adequate to fully fund the database and has not increased significantly for over seven years, even though our outputs, in terms of clinical outcome reports to NHS England (Scotland and Wales) have increased enormously in recent years. We are currently renegotiating this Service Level Agreement because NHS England is reviewing their funding of all disease databases and their funding has not increased commensurate with their vastly increased demands.

128.6. Industry have provided unrestricted grants to fund non-commercial epidemiological analyses, and post-marketing safety and efficacy surveys, usually at the behest of the Regulator, The European Medicines Authority (EMA), who generally require post-marketing pharmacovigilance as a condition attached to the initial product license. A lot of this data is reported through the manufacturer to the Regulator, EMA (WITN3289084, WiTN3289085 and WITN3289086) and we have even participated in meta-analysis of our data conducted independently by the EMA (WITN3289087). We have also received funding from industry for outcome analyses of new treatments, requested by NHS England. Market reports have also been produced for industry which show high level analyses of usage trends for their products and an analysis of the way in which their products are being used. .

129. *Please explain how the question of patient consent in relation to the National Haemophilia Database has been approached over the years. (Amongst the documents enclosed with this letter, you may wish to consider: section 7 of the minutes of the 18th meeting of the UKHCDO Executive Committee on 11 February 2000 [HCDO0000473]; minutes of UKHCDO Data Management Group on 8 August 2000 [HCDO0000013_286]; section 11 of the minutes of the 1st meeting of the UKHCDO Advisory Committee on 11 September 2000 [GGCL000089]; section 12 of the minutes of the 1st AGM of UKHCDO on 29 September 2000 [GGCL000085]; letter from*

Professor Ludlam and Dr Lowe dated 14 May 2002 [HCDO0000264_107]; minutes of meeting of UKHCDO Data Management Group on 21 October 2002 [HCDO0000109_026]; letter from you dated 24 November 2003 to Dr Dennis [HCDO0000108_035]; section 8 of the minutes of the 22nd meeting of the UKHCDO Advisory Committee on 17 July 2006 [HCDO0000745_001]; section 12 of the minutes of the 18th Annual General Meeting of the UKHCDO on 3 November 2017 [HCDO0000516]) Please address in your response the extent to which there have been differences of opinion and approach amongst haemophilia centre directors in relation to this issue.

129.1. The level and nature of the consent required for the database and observational research have evolved over the past 40 years. Our consent arrangements have reflected this, both in our database research and observational research conducted independently of the database. It is important to emphasise at the outset that the database only conducts observational research and whilst UKHCCDO members may participate in interventional clinical trials at a Centre level, these are not conducted on behalf of UKHCDO or the Database. Our research is limited to the analysis of data collected routinely for other purposes.

129.2. A notable exception to this general rule was the variant Jacob Kreutzfeld study where cellular samples were obtained and autopsies requested, but that was processed as an interventional study with full ethical approval etc. and is described more fully, with exhibits, in section 7.

129.3. We have been consistently advised over many years, by both The Information Commissioner (based at Data Protection House, Wilmslow) and the NHS Research Authority Confidentiality Advisory Group (NHSRA-CAG), that we do not need consent to collect the data used for NHS purposes and onward transmission to, say, NHSE. The question of consent for observational research using anonymised or pseudonimised data collected routinely during the course of normal clinical management has only emerged relatively recently as far as we are aware and has become a progressively more active issue with the passage of time. We have regularly reviewed this issue and sought advice and guidance from relevant authorities. This advice has often been contradictory or inconsistent and has also

changed with time. Our approach to this has consequently changed over the years. We have also arranged for the Caldecott Guardian to inspect the database and its procedures at regular intervals every two years or so to ensure that we are complying with Caldecott principles, the Data Protection Act and the principles of fair data handling.

129.4. Before the advent of the 1998 Data Protection Act, it was not considered that consent was required for the collection and processing of the data held by the NHD and none was sought. All research conducted by the database at that time was observational and did not require any data not routinely collected.

129.5. I first became involved in the issue of consent when I assumed the Chairmanship of the Data Management Working Party in 1998/9. One of the first things the group had to address was compliance with the Data Protection Act of 1998, which was to become mandatory in 2000. This was much discussed in The Data Management Working Party, The Advisory Committee and the AGM, as outlined in the disclosures from the IBI (HCDO0000473; HCDO0000013_286, GGCL0000264_107; GGCL0000085; HCDO0000264_107; HCDO0000109_026; HCDO0000108_035, HCDO0000745_001 and HCDO0000516). I sought advice from the caseworkers at Data Protection House in Wilmslow first by phone and then in a meeting there in August of 2000. They were very helpful, first pointing out that when new, such an act was in effect "skeleton legislation" and that the flesh would be put on the bones by case law. They advised that we should obtain consent for the research purposes of the data collection and analysis but that since this was observational research that implied, informed, consent would be adequate and that written consent would not be necessary. We discussed the practicalities of obtaining implied consent, given that some patients came for review as infrequently as every three years and therefore it could take years. They advised that it was acceptable to obtain consent on an opportunist basis (i.e. when the patient presented to the clinic or the centre) over a period of years. This view has recently been reiterated by the National Ethics Committee and by the NHSRA-CAG.

129.6. This was extensively discussed in the various UKHCDO Committees and the

consensus view was that we should write a patient information leaflet and that this should be presented to the patient and they should be given the opportunity to opt out of research should they so wish. This is the model that has been followed by most if not all Disease Databases in the UK over most of the past 20 years.

129.7. I drafted the patient information leaflet and it was subsequently edited and finalised by the Data Management Working Party, The Advisory Committee, the Haemophilia Nurses Association, The Haemophilia Society and various patients chosen by the Haemophilia Society. The leaflet has been reviewed and revised and rewritten at intervals since that time with the same multi-stakeholder editorial input except that more recent versions have also been reviewed by the Lead Commissioner for Haemophilia at NHSE. Copies of all the patient information leaflets and my letters to the Haemophilia Centre staff giving instructions on how to obtain and document implied consent are included as WITN3289088 to WITN3289097 The first leaflet was also distributed with a copy of "The Bulletin" by the Haemophilia Society and I wrote an article for "the Bulletin" describing the work of the Database. The leaflet was well received. Each time the leaflet was revised 30,000 copies of the leaflet would be printed and distributed to centres. The common elements to each were a description of the data collected and the purpose of the database, our approach to data security, what we did with the data including industry involvement and the involvement of the regulator and finally their rights under the Data Protection Act and their right to opt-out. Centres were asked to record that the patient had been given the leaflet because I know that some patients subsequently forgot and said that they had not received one. This would be recorded in the patient's notes and/or the Centres HCIS system (computerised Haemophilia Centre Information System).

129.8. This approach to consent had broad agreement from the clinicians and professions allied to medicine. Only two Haemophilia Centres (Great Ormond Street and Bristol Adults) felt it necessary to obtain written consent, something they have done for a number of years.

129.9. This model of obtaining implied consent has been followed until the last two years, since which time we have been obtaining written consent. The chain of events

leading to this change is as follows. The National Haemophilia Database had a contract with the Office for National Statistics and its successor organisations, most recently NHS Digital for the provision of death certification data which went back to the late nineties. In 2013, NHS Digital questioned whether we had adequate consent. For a period of several years whilst they were reorganised, NHS Digital was, by common consent, a very difficult organisation to deal with. They were very difficult to communicate with, issued contradictory and varying advice and we went round in circles without making any progress in our attempt to unravel the problem for three years. They stopped sending us data in 2014 and in 2016 suggested we deal with NHSRA-CAG.

129.10. This led to a very constructive meeting, requested by me, with the full NHSRA-CAG at Skipton House in October 2017.They advised me that most Disease Databases were in the same position that we were and that some were also reviewing their consent processes. They agreed that we did not need permission to collect data for the NHS but the problem was that we also used the data for research and that our system of obtaining implied consent whilst common to almost all UK Disease databases was no longer considered adequate. This was not a DPA issue but related to our common law duty of Confidentiality. They advised that to be compliant we would need to move to a system of written informed consent. They advised that it would be acceptable to obtain consent over a period of years in an opportunist way, as before. They wanted an annual progress report.

129.11. Since that time GDPR has come into force and one of the major changes from the DPA of 1998 is that an opt-out system is no longer acceptable and an opt-in system would be required.

129.12. Accordingly, and after extensive discussion within the UKHCDO, we developed a protocol for the Database, developed a series of age-specific information sheets and consent forms and applied successfully for ethical approval. The ethical approval and protocol are attached as WITN3289098 and WITN3289099. and the age-specific patient information sheets and consent forms are attached as WITN3289101 - WITN3289108 and the slide set describing to Haemophilia Centre

staff how to obtain written consent and how to securely upload the consent form into the National Haemophilia Database is attached as WITN3289100. It was necessary for NHD to have a record of who had given or withheld consent so that Centres could easily review who had consented and who not and so that NHD could avoid using data from those individuals who had withheld consent for research purposes.

129.13. We started to obtain written consent in 2019 and had obtained written consent from over 2000 individuals and appeared on course to gain consent from most patients over a three to five year period. This progress has been interrupted by the Covid-19 lockdown.

129.14. Following a deferred application for final CAG approval earlier in the year, we met with representatives of CAG by Zoom in June 2020. Whilst acknowledging the enormous effort we had made to obtain written informed consent, they told us that since 2017 NHSRA CAG had realised, through their experience with other large disease databases, that it was impractical to obtain written informed consent from all patients, especially under the current Covid-19 circumstances. They advised that this rendered such databases eligible for Section 251 support, which they very strongly recommended we apply for. This regulatory support, provided by the 2006 NHS Act, permits temporary exemption from the Common Law Duty of Confidentiality such that confidential patient information may be transferred to the applicant without them being in breach of the common law. In practice, this means that UKHCDO, being the responsible controller of this data, can should we wish as part of our observational research activity, disclose data (anonymised or pseudonimised) to third parties without being in breach of the common law of duty of confidentiality. The process of application for section 251 is comprehensive and robust and requires the applicant to provide evidence and absolute reassurance that its information governance processes and procedures are fit for purpose.

129.15. They advised us to make two Section 251 applications, one for research and one for the NHS purposes to which our data is being put, including pharmacovigilance and reports to the regulators through the manufacturers (see elsewhere in this report). They allocated a caseworker to lead us through the application process,

which has been extremely helpful. The section 251 applications were submitted to NHSRA on 17.8.2020 and NHSRA-CAG was considered by NHSRA CAG on 3.9.2020. We have been informed that CAG have recommended approval of our applications and at the time of writing we are awaiting final confirmation from the Secretary of State for Health, The Right Honourable Matt Hancock.

130. *In the enclosed minutes of the 18th meeting of the UKHCDO Executive Committee on 11 February 2000 [HCDO0000473] (at section 13 headed Annual Returns) it was recorded that information about Hepatitis C in haemophilia patients had been requested by the Department of Health. Please explain what information was sought by the Department of Health and for what purpose, and what information was provided by UKHCDO to the Department of Health.*

130.1. This question is addressed fully in my response in the final section of the UKHCDO response to its Rule 9 request in the section entitled "Hepatitis C" and is also comprehensively addressed in section 10 of this report. ..

131. *On 25 July 2003 you wrote to the Macfarlane Trust (letter enclosed [HCDO0000612_001]), stating that it had become clear to you that there were "discrepancies between the estimates of surviving haemophilia patients in your database and in the national haemophilia database". You asked the Macfarlane Trust to provide you with a list of the patients with HIV who had died, together with their date of death. Did you receive this information from the Macfarlane Trust? What attempts were made to ensure that the national haemophilia database's figures were accurate?*

131.1. I did not receive this information from the MacFarlane Trust. . NHD sent questionnaires to centres regularly and chased them for data.

132. *In the minutes of the 18th Annual General Meeting of the UKHCDO on 3 November 2017 [HCDO0000516] you presented current knowledge of Hepatitis C status and stated that "There are over 5000 individuals whose exposure or status is not known". You proposed requesting from centres "the most recent HCV test result including those who are dead for a total of about 7000 patients". Was this work undertaken and if so what did it show?*

132.1.This is described in detail in section 10 of this report.

Section 6: Pharmaceutical companies /medical research/clinical trials

133.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.

133.1.Yes, I have at various times attended international advisory committees for the following Companies: Alnylam, Baxter/Shire/Takeda (the last three are successor companies) Novo, Pfizer, Roche, Sobi. These tend to be not commercial or directly commercial in nature. The last one I attended (Sobi, by Zoom) concerned COVID-19 and how it affected the haemophilia community and I don't think anyone even mentioned a product. These meetings often concern clinical research and treatment trends and horizon scanning. They provide a valuable educational opportunity for the participants and an opportunity to interact with senior colleagues from other countries.

133.2.I have not attended UK domestic Advisory Committees for the past 20 years as a matter of policy.

133.3.I have not made a list of these and cannot therefore provide further details.

134.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.

134.1.Yes. This is highly regulated by the ABPI code (Association of British Pharmaceutical Industries) and whichever similar code applies in the country in which the meeting is to take place. Remuneration is also regulated and is calculated on a "fair market value" basis based on the amount of time taken for the

meeting including preparation in reading papers specific to the agenda or preparing slides. This is not negotiable...

134.2.I have also acted as invited speaker for commercially sponsored educational symposia at national and international scientific meetings.

135.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.

135.1.Please, see above, responses to Q133-5.

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

136.1.No.

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

137.1.No.

138.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.

138.1.No.

139.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?

139.1. I have to make declarations to UKHCDO, my Trust, the CMU (and previously PASA) and when I was more heavily involved with them The European Medicines Agency. These have to be updated every year or so.

139.2. For many years now, it has also been normal at the beginning of any presentation to any scientific meeting whether the session is a commercially sponsored symposium or any part of the program to show a declaration slide giving details of any pharmaceutical shareholdings participation in sponsored symposia, participation in advisory panels etc.

139.3. Furthermore, it is universal practice mandated by the ABPI Code and similar codes operating throughout the world that brand names are never used in any presentations. Products are either anonymised or referred to by their pharmaceutical title. This applies to commercially sponsored symposia as well as other scientific sessions.

139.4. In addition to that, to obtain CME points (continued medical education), and therefore a good audience, commercial symposia are presented under the auspices of an educational establishment (either a University or learned society) who assess the content in advance of the meeting and who may suggest amendments and award the CME points. Consequently, the content of the symposium must be educational and must not be promotional.

139.5. It is also mandatory that all authors of any scientific publication make a declaration of any potential conflict and this is printed at the end of the paper, after the acknowledgement and a brief account of the contribution of each author to the study and to the final manuscript. The publishers will not process the paper and publish it without this being completed.

139.6. One final point I would make is, that it is my practice and that of all the colleagues I know over many years to use the products of several manufacturers to maximise security of supply and to minimise the influence of any single manufacturer. Similarly, although Manufacturers may sponsor attendance to scientific meetings (also declared), I make a point of accepting invitations from as wide a selection of

sponsors as possible to avoid any accusation of bias. This is also widespread practice amongst colleagues.

140.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.

140.1.Yes, as described elsewhere in this report.

140.2.I have participated in many licensing studies and post-licensing pharmacovigilance studies, as may be seen from my publication list. Licensing studies provide anonymised data submitted to the regulatory authorities (EMA and FDA) who provide a product license that enables the product to be sold for use for the specific licensed indications. When granting a license, particularly for a rare disease such as haemophilia, where the number of subjects available for licensing studies is limited, the regulatory authorities will often mandate that a post-licensing safety and efficacy study (pharmacovigilance) be conducted. The conduct of such studies has become an increasingly important part of the work of the database and is described, with examples, in the previous section.

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

141.1.Yes, of course. Please see my list of publications and examples included amongst exhibits.

142.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?

142.1.Research funding is declared as for any other funding, even though research funding does not go to any specific individual.

142.2.It may be beneficial to explain the way in which regulatory studies are funded and

the funding pathway in the United Kingdom.

142.3. All research funding, including any payment specifically related to the role of Principal Investigator or Chief Investigator of a study would go directly to the hospital R&D Department. After a study and its protocol and patient materials gain ethical approval, the study requires R&D approval. The R&D department, working with the research coordinator and the sponsor (in this case a pharmaceutical company), will negotiate a reasonable price for any additional blood tests, the number of visits, the visit content and any procedures involved in the trial including an element for the work of the R&D department and the research team (including the principal or chief investigator, which could be me or a colleague. It is considered an ethical issue that the trial should not be run at a financial loss, effectively at the expense of the NHS. I actually play very little part in these negotiations, which are fairly rigid anyway using an NHS template and price-list. Once the trial starts, this is managed by my research coordinator and all payments go to the R&D Department to pay for facilities, labs and the salaries of the research team (everyone *except* me because the NHS is already paying my salary).

142.4. I work in a teaching hospital. I am expected to do clinical research including licensing studies. My Job Plan does include an element of time set aside for research.

Section 7: 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?

143.1. Variant CJD emerged in the mid-1990s as the human version of spongiform encephalopathy in cows. It was recognised early that it had many features that distinguished it from classical (human sporadic or hereditary) Jacob Kreutzfeld disease, not least deposits of prion protein outside the central nervous system, notably in lymphoid tissue. This raised what was then a theoretical possibility that

the condition could be transmitted by blood or blood transfusion. In 1997, the first blood donor to develop vCJD was reported and there were further cases in 1999 and 2000.

143.2. Until December 2003, when the first case of vCJD in a recipient of blood donation was reported, there was no evidence of haematogenous spread. Thus, between 1997 and 2004, haematogenous spread remained a theoretical possibility only. A second possible case of spread by blood donation was reported in July 2004.Not all recipients of an implicated blood donation or its components went on to develop vCJD. Those that did develop vCJD from blood donation had all received a unit of red cells. No recipients of blood components or fractionated plasma products had developed vCJD.

143.3. VCJD appeared only to occur in patients or blood recipients who were homozygous (two copies of the gene) for the prion protein. This remains the case. This gave rise to the theoretical possibility that recipients of an implicated product who were heterozygous (one copy of the gene) might never develop vCJD but could be a "carrier" and pass it on to others and therefore be "at public health risk" of passing it on but not developing vCJD themselves. Although the concept of being "at public health risk" was explained to patients it is a difficult concept. Very few patients understood the concept and it caused considerable confusion, which witness statements to the Inquiry would suggest persists to this day. Most of the precautions taken subsequently related to this public health risk and were aimed not to protect the patient but to protect others from the theoretical possibility of onward transmission. These precautions were reviewed by the Health Protection Agency from time to time and gradually eased as evidence accumulated that the patients were neither developing vCJD nor transmitting the condition to others.

143.4. By 2004, 9 blood donors had developed vCJD and, between them, had donated 23 donations. The recipients of those donations were traced and followed and some did, indeed, develop vCJD after periods of up to 8.5 years.

143.5. Although no cases of vCJD apparently transmitted by a plasma donation or administration of pooled fractionated plasma products have ever been reported,

this was a theoretical possibility and the actions and precautions described in the following sections and the exhibits attached were taken to mitigate this theoretical possibility and to monitor for the occurrence of vCJD..

143.6. From the outset, it seemed most likely that the risk of transmission of vCJD by plasma products would be very small and possibly zero, though the risk could not be completely discounted without years of follow up and surveillance. Only transmission through whole blood transfusion had been described. This representing a relatively large dose of the prion protein. Given that the prion was white cell associated and plasma is white cell-depleted and then diluted with 50,000 other donations before fractionation, the dose in the donor pool would be extremely small. The fractionation process was also thought to remove residual prions. Given the relatively long incubation period (up to 8.5 years has been reported) it would take years of surveillance before this risk could be completely discounted, however.

144. Please describe your involvement in decisions as to what information to provide to patients about vCJD, both in your capacity as Chair of UKHCDO and in your capacity as Director of the Manchester Centre. Please address in your answer the 2004 notification process, the 2006 notification process and the 2009 notification process. Please also answer the following questions:

a. *What discussions took place (a) within UKHCDO, (b) with other organisations (including the CJD Incidents Panel and UK Health Departments) and (c) within the Centre?*

144.1. For UKHCDO, Professor Frank Hill led our response, both as Chair of UKHCDO up to 2005 and as Chair of the Transfusion Transmitted Working Party (TTI WP) subsequently during my Chairmanship, which ran from 2005 until 2011. I worked very closely with Professor Hill throughout this time, first as vice Chair of UKHCDO and then as Chair and also as Director of the National Haemophilia Database from 2002. Hence some of the letters coming out of UKHCDO to the membership bore both our signatures. It will also be apparent from the many logos at the head of many of the communications (Exhibits) that nationally, this was a multi-agency

response which was very much led by the Health Protection Agency and CJD Incidents panel. There were several potential risk groups other than patients with bleeding disorders including recipients of immunoglobulin and recipients of blood and blood components. It was important that communications to all risk groups should be consistent and coordinated and so the wording of these communications was largely handed down to us from HPA, with some discussion about some of the drafts.

144.2. It was important, to ensure that the patients received accurate information, that they should hear it from us first and not filtered and paraphrased by the media. So those communications were embargoed until they went out and the patients were notified before anyone else. This sometimes caused problems. For example, the 2004 patient notification had to be rushed out against a very short deadline and without the opportunity to edit what we regarded as not very "patient friendly" wording because a parliamentary question had been lodged and the response would be reported by the media within a few days. We had to communicate to patients as a matter of urgency so that they heard from us before hearing from the media. It was also important that centres would be informed so that they would be in a position to address any resultant patient concerns. This resulted in us having to send out a very long and complicated, and confusing communication written by HPA, which we could not alter and which has caused enduring confusion in the patient group. UKHCDO members were very unhappy about this. Many centre directors, including myself sent out additional letters to explain in layman's terms what the first letter meant.

144.3. When significant new evidence emerged or there was a review of policy, there would be some discussion between HPA and UKHCDO in which I participated and we would add our perspective and feedback any problems or disagreements that we had. However, it was always my perception that HPA were very much directing this and since there were several other risk groups involved, that seemed entirely reasonable.

b. *What steps were Centres/Centre Directors asked to take?*

144.4. Centre Directors were asked to do different things at different times as evidence emerged and policy developed, as illustrated by the attached Exhibits. The exhibits attached are grouped into those relating to the national notification in 2004 (WITN3289109 - WITN3289119), the national notification in 2009 (WITN3289120 to WITN3289133), the false notification in 2010 (WITN3289134 and WITN3289135) explored in Q150 and the national de-notification in 2013 (WITN3289134 - WITN3289138), when the risk period for potential vCJD was reduced. There are also exhibits that relate to the notification forms (WITN3289139 - WITN3289142) and to the ethical approval and running of the vCJD study (WITN3289143 - WITN3289152)

144.5. In 1997, when the first case of a blood donor developing vCJD was reported, UKHCDO discussed this and it was decided that, as a precaution, we should avoid the use of pooled blood products manufactured from UK-sourced plasma. BPL products manufactured from UK plasma were withdrawn. BPL was able, by autumn 1999 to obtain a supply of US plasma to continue manufacture. I was able to switch products in Manchester very quickly. Other centres may have taken longer and I suspect but do not know that some directors may have felt that this was an extreme action to take for a small and theoretical risk (see also response to Q146). I also wrote to my patients to explain what was going on and to update them on the current state of knowledge in relation to vCJD (see response to Q145 and HSOC0015148).

144.6. The Variant Jacob Kreutzfeld Disease Incidents Panel was formed in 2000 to assess and advise on the risk of patient to patient transmission of vCJD.

144.7. In 2004, all Haemophilia Centres were directed to write urgently to all patients with bleeding disorders, regardless of their risk, to update them of the risk and the policy in relation to vCJD. This change in policy responded to reports of two whole blood recipients who had developed vCJD after receiving donations from a donor who had developed vCJD after donating their blood. This was the first fairly convincing evidence that vCJD could be transmitted by whole blood transfusion (WITN3289109 - WITN3289119: 2004 Notification).

144.8. Centres were also provided with a list of implicated batches of concentrate (batches which had a plasma donation in the plasma pool from a donor who had developed vCJD after donating their blood) (WITN3289116). This list was updated in 2006. Centres were asked to trace and list all recipients of these donations and to fill out a form (WITN3289116) and return this form to the National Haemophilia Database. This form detailed whether the patient was at risk at all (i.e. had received UK sourced blood products during the period of risk) and whether they had received an implicated batch (listed on the form) and if they had, how many units had been administered. The form also asked whether the patient had been seen and had elected to be told of their exposure. This was an unusual situation since there was no test and no treatment for vCJD. For that reason, UKHCDO decided that patients should be given the choice to be told or not told whether they had been exposed to an implicated batch or not. The choice was to be recorded at the time. All patients were offered general advice and information in relation to vCJD and qualified reassurance. For the avoidance of doubt, where the vCJD report form says "not told", it does not mean that the patient was not seen but only that they had chosen not to be told whether they had been exposed to an implicated batch or not. A significant proportion of patients, including many who had not been exposed to an implicated batch, chose not to be told whether they had been exposed or not. One copy of the form was to be filed in the notes and one sent to the NHD where the data was collated and anonymised data shared with HPA.

144.9. Coordinating with SNBTS and BPL, UKHCDO and the NHD, we attempted to trace the fate of all the implicated batches, all of which had expired by the time this exercise was undertaken. Unfortunately, BPL were unable to provide an accurate list of the centres supplied with these batches because some products had been supplied direct to Haemophilia Centres but others had been distributed through the Transfusion Centres. It was necessary to use the list of batches and for all centres to go through their records to see if they had received any of those batches and if so, which patients had used them. This was a very difficult and time consuming exercise and, in the end not all of each batch could be traced. In some cases about 80% of an implicated batch could be accounted for and in others as little as 52%. For some batches, not fully accounted for, we could at least be

confident that they had not been supplied to our region or centre. This left us with three levels of assessed risk: -

144.9.1. There were patients who had not been exposed to UK-sourced blood products during the period of risk. These patients could be reassured.

144.9.2. There were patients who had not been exposed to implicated batches as far as we could determine but who had been exposed to UK-sourced blood products. Given the long incubation period, there was the possibility that a blood donor could develop vCJD resulting in a new implicated batch being identified. These patients could only be given relative reassurance and told that they had probably not been exposed, with caveats as above.

144.9.3. There were patients known to have been exposed to an implicated batch or batches and, with many mathematical assumptions their risk could be calculated based on the number of units used. These assumptions were initially based on the worst case analysis and were consequently very, very pessimistic. This was subsequently reassessed and the risk estimate greatly reduced as time went by. These patients could be told that they had been exposed to an implicated batch but still offered relative reassurance because the risk was considered very small.

144.10. The detailed recommendations on managing the public health risk are described in the 19-page recommendations issued jointly by HPA and NHS Scotland and Ireland on 7/9/2004 (WITN3289112).

144.11. On 16/2/2009 Professor Hill and I wrote to all Haemophilia Centre Directors in relation to a haemophilic patient had died from cancer but that at autopsy an incidental finding of a small collection of prion protein had been found in the spleen. The clinical significance of this finding remains uncertain to this day but it was potentially evidence of possible transmission of vCJD by blood products (WITN3289120). This again required that all patients with bleeding disorders be informed using a standardised letter (WITN3289129) and using standardised

patient information leaflets generated by the Health Protection Agency and Health Protection Scotland (WITN3289121 - WITN3289133). As before, GPs were also informed.

144.12. Subsequent UKHCDO discussion caused Professor Hill and I to write again to the membership of UKHCDO on 1/4/2009 (WITN3289124) This letter was primarily to reinforce and revitalise our attempts to identify all patients who had been exposed to an implicated batch of concentrate and to attempt to account for all the implicated blood product that had been issued to centres. We noted that some centres had not sent any such data to NHD and had identified no at-risk patients even though we had been informed by BPL that implicated stock had been supplied to those centres. Furthermore some centre directors, including some appointed after 2006 (when the list of implicated batches had been updated and expanded for the last time) had realised that their patients had not been risk assessed. To facilitate this process, all centres were sent a spreadsheet prepared by the National Haemophilia Database listing all patients registered at their centre known to the database to have been treated with BPL products during the period of risk and to request that the patients be cross-checked and risk assessed. The report forms were send out again and NHD chased centres for further data.

144.13. In 2010, I wrote to all Haemophilia Centre Directors to inform them about the mistaken identification of a relatively small number of infrequently treated patients who had been identified as at risk in error (WITN3289134 and WITN3289135). This situation had arisen because, although the patients falsely notified had been treated with BPL products during what had been considered the period of risk 1980-2000, the product used had been manufactured from US-sourced plasma. This exercise is discussed in greater detail in relation to Q150 and the circumstances are described in detail in my letter (WITN3289134).

144.14. As time went by, it became apparent that had the HPA assessment of risk of transmission of vCJD, based on a series of worst-case assumptions, been correct then we would have observed several affected patients. We had, in fact, observed none. The public health risk of vCJD transmission was reassessed by Public Health England and the CHD Incidents Panel and as a consequence of this

assessment it was concluded that patients treated *only* with blood products derived from UK plasma during 1980 to 1989 were at no greater risk of developing vCJD than the general population. Consequently, it was decided to identify and de-notify patients who had only been treated with UK-sourced products manufactured in 1980-89. At the same time, it was considered that endoscopes used in at-risk patients no longer needed to be quarantined and could be release for routine use.

144.15. On 25/4/13, Dr Gerry Dolan, then Chair of UKHCDO, wrote to all Haemophilia Centre directors with instructions for the identification and de-notification of the estimated 500 patients affected in this exercise. As detailed in this letter, a patient information leaflet written by HPA was included and NHD would provide a spreadsheet to each centre giving a list of the patients we suspected would be involved in this denotification. Centres were enjoined to carefully check this spreadsheet because we suspected that there may have been some inaccuracies, the data being only as good as the data submitted to the database (WITN3289136 - WITN3289139).

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

144.16. Please see above.

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

144.17. Please see above.

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

144.18. I wrote to my patients first in 1997 (HSOC0015148), when it became apparent that a blood donor had been reported to have developed vCJD, when we decided to switch patients away from concentrates manufactured using UK plasma donations. Please see also response to Q 145. There were further official country-wide notifications in 2004 and 20019 and 2013 as described above. The problem was also frequently discussed in clinic and in out-of-clinic sessions, as required.

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

144.19. This matter was extensively discussed with the patients in clinic by me, my consultant colleagues and by the Haemophilia Specialist Nursing Staff and by our Haemophilia Nurse Counsellor. The information given to patients is illustrated in the patient correspondence attached as exhibits. but required a lot of explanation. The concept of being "at public health risk" i.e. theoretically capable of transmitting the prion to others whilst not developing the condition oneself was almost universally misunderstood. In general, my concern was to put the risk, which was always considered very small and which was probably zero, into some sort of context.

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

144.20. They were unable to donate blood, though patients with bleeding disorders and a past history of blood product therapy are not allowed to donate anyway.

144.21. Surgery on the gut or central nervous system had to be conducted using disposable instruments and endoscopies used only endoscopes that were then quarantined and only subsequently used for that patient.

144.22. The following advice was shared with patients considered at risk by the Health Protection Agency via their centre director. (See exhibits)

"Advice on how to stop CJD spreading to other people

You have been identified as being at increased risk of CJD. You can reduce the risk of spreading CJD to other people by following this advice

- Don't donate blood, No-one who is at increased risk of CJD or who has received blood donated in the United Kingdom since 1980 should donate blood
- Don't donate organs or tissues, including bone marrow, sperm, eggs or breast milk
- If you are going to have any medical or surgical procedures, tell whoever is treating you beforehand so they can make special arrangements for the instruments used to treat you

You are advised to tell your family about your increased risk. Your family can tell the people who are treating you about your risk of CJD if you need any medical or surgical procedures in the future and are unable to tell them yourself."

145.In a letter dated 26 November 1997 addressed to Mr GRO-A *[HSOC0015148], you set out measures which you had decided to take at the Manchester Haemophilia Centre in relation to vCJD.*

a. Please confirm whether this letter was sent to all patients of the Centre in Manchester and, if not, which categories of patients it was sent to.

145.1.This is an example of a standardised letter written by myself and Dr Caroline Shiach, which we sent to all patients on home therapy, as far as I remember.

b. What was the basis for your statement in the letter that "there is a small theoretical possibility that vCJD might be transmitted by blood transfusion"?

145.2.This was written at a time when a single blood donor had developed vCJD but when no recipients of blood or blood components from such a donor had developed the disease itself and so transmission of vCJD by whole blood had not been demonstrated. The risk was theoretical at that time.

145.3.Even once a small number of blood transmission cases had been proven, the risk remained *"small"*, and as far as factor VIII/IX concentrate was concerned has remained *"theoretical"* since no patients with bleeding disorders have ever

developed vCJD. The aim of this letter was to inform the patients but to put what was then considered a small risk (as opposed to the current assessment of probably no risk) into some sort of context.

c. *Please provide details of the meeting that you arranged to provide patients with further information. What evidence was presented and what information was provided to patients at the meeting?*

145.4. I arranged a meeting in a lecture theatre which had a seating capacity of 250. I have little memory of this meeting, which took place almost a quarter of a century ago. I assume that I told them what was and was not known and had questions and an open discussion.

146. In a letter to Dr Ludlam dated 21 January 1998, headed 'Implementation of our Recommendation on CJD' [HCDO0000133_188], you described the responses of various centres to UKHCD's recommendation. Please:

a. *Explain what the recommendation was and the reasons for it.*

146.1. We had recommended that patients should be switched away from their current BPL concentrates manufactured from UK plasma to either recombinant products or plasma-derived products manufactured from American plasma or BPL products manufactured from American plasma once that became available. We made this recommendation because the UK plasma source had to be considered potentially a risk for transmission of vCJD at that time.

b. *Set out what you recall about the difficulties which centres had in complying with the recommendation.*

146.2. The supply of alternative products was initially inadequate for the whole UK. Recombinant factor VIII/IX had not quite been made available for children and BPL had not yet obtained alternative supplies of plasma for manufacture from the United States.

c. *Explain why some centres were "not fully sold on the policy" and what "financial problems" or "revenue consequences" you were referring to*

146.3. There were many reasons related both to the epidemiology and to the details of manufacture for thinking that fractionated pooled plasma products were intrinsically unlikely to transmit vCJD. VCJD had only been transmitted by whole units of cellular products (red cells) and it was known that the vCJD prion was white cell-associated. Concentrate was made from acellular plasma. A single infected donation would be diluted up to 50,000 times (with 50,000 donations in the plasma pool prior to fractionation) and it was thought that any residual prion would be taken out during the fractionation process. This assessment of very low risk was probably the consensus view but the majority also felt that we should follow the precautionary principle of avoiding the theoretical risk as far as possible. In fact, it would appear that vCJD is not transmitted by fractionated pooled blood products since no patient worldwide has contracted vCJD from this source as far as we can tell.

146.4. Some centres that used a lot of 8Y, an inexpensive BPL product, would have had to find significant additional funding to make the switch away from 8Y at that time.

147. At the 18th meeting of the UKHCDO Advisory Committee on 16 May 2005 (minutes enclosed [BART0000924]) you reported "the trouble Manchester is having with endoscopies". Please explain what problems the Manchester Centre was experiencing and how, if at all, they were resolved.

147.1. The problem was that it was impossible, in theory, to sterilise an endoscope for the vCJD prion without stripping it down and reconstructing it, so once an endoscope had been used in an at risk patient, we could use it again for that patient but not for any other patient. The risk of transmission of vCJD was theoretical and I think we now know it doesn't happen but at the time we did not know. For that reason endoscopes used in patients at risk were quarantined and only used for the at-risk patient in whom it had been used. In that way, we very rapidly ended up in a position where 75% of the hospital's endoscopes were in quarantine. In Manchester, we actually ended up buying a £50,000 double-balloon endoscope

for one of our patient's sole use. There was a real danger that the endoscopy service of the whole hospital would collapse for want of endoscopes. Eventually funding was made available for the purchase of additional instruments and after a period of years the regulations were relaxed and the risk-period reassessed and shortened.

147.2. I should add that Manchester was typical of hospitals around the country with large haemophilia services.

148. On 16 and 17 January 2007 (letters enclosed [HCDO0000131_007; HCDO0000131_008; HCDO0000131_009 and HCDO0000131_006]) you sent to all UKHCDO members details of a fourth case of vCJD transmitted by transfusion of whole blood:

a. It appears that UKHCDO decided that there was no need for patients to be notified directly about this news. Is this correct, and if so, what were the reasons for that decision?

148.1. This news revealed nothing new other than there had been an additional case transmitted by whole blood and that the incubation period, at 8.5 years, was unusually long. None of this altered HPA or UKHCDO Policy. It was anticipated that there might be some press coverage and so centres were informed, in case they had missed it and would have to field calls. It was felt that there was nothing to be achieved by another mass-mailing of the patients and that it would only heighten their anxiety whilst nothing had essentially changed.

b. You anticipated that patients might contact their centres as a result of reports appearing in the press. Did that happen and if so, to what extent and what concerns were voiced by patients?

148.2. There was, as I recall, little press coverage and few, if any, calls from concerned patients.

149. What led you and Professor Hill to write to centres on 15 May 2009 (see the enclosed

letter [CVHB0000111_017])? What did you ask centres to do? Did centres comply with the requests set out in the letter of 15 May 2009?

149.1. Professor Hill had principle responsibility for the conduct of the vCJD lookback exercise starting when he was chairman in 1999-2005 and continuing after that in his capacity as Chairman of the Transfusion Transmitted Infections Working Party (TTIWP). This working party was effectively a successor working party to the Hepatitis and HIV working parties.

149.2. We wrote in 2009 as our third major notification to centres, to report progress in identifying all patients at risk and to ask centres to have another look to identify further patients and to attempt to account for the distribution of all implicated batches of clotting factor concentrate. The TTI WP kept this lookback under review and reported back to the Advisory Committee. We also reported to DH and the Health Protection Agency. This was our final attempt to identify all patients and to account for all the implicated product use. BPL was unable to tell us, because of the way in which the product was distributed, sometimes through transfusion centres, which centres had been supplied with which batches and in which amounts. Consequently, it was necessary to supply all centres with all the implicated batch numbers and ask them to check their records and see if they had used any. Some centres records were poor and they were unable to comply. In the end, we could account for the fate of 80% of some batches but as little as 52% of others.

149.3. It was generally known who had received UK manufactured concentrates during the period of risk and all of these patients were considered "at public health risk". Many/most would not have received an implicated batch, but unless they were *known* to have received an implicated batch one could not be sure.

149.4. What we asked them to do is explained in the letter. We provided them with a spreadsheet, which listed all patients reported to NHD as having had BPL products during the period of risk, showed those whose vCJD report form had been returned to the |NHD and asked centres to fill in the gaps. One difficulty was that patients move about and some may have been given an at-risk batch in their previous

centre, collating the data from successive centres proved difficult.

149.5.I think the vast majority of centres did their best but it was a challenging task.

150.In a letter dated 15 April 2010 [HCDO0000616_007], Dr Giangrande wrote to you regarding two patients who had mistakenly been informed that they were at risk of developing vCJD. You are not asked to comment upon the circumstances of those patients, but to set out the extent to which the mistaken notification of at risk status was a problem more generally; how it was addressed (whether by UKHCDO or others); and whether there were systematic steps that could have been taken which would or might have avoided the problem of patients being incorrectly told that they were at risk.

150.1.This mistaken notification primarily involved patients with factor XI deficiency treated with factor XI concentrate and some patients with von Willebrand's disease attending two centres (Oxford and the Royal Free). The circumstances which led to this are set out in detail in the letter that I wrote to the membership of UKHCDO and the HNA, in my capacity as Chairman (WITN3289134). The result of the Royal Free investigation to identify affected patients is also attached (WITN3289135). The reason that so few patients were affected is that the Royal Free has the largest cohort of factor XI patients in the country and, unlike other centres managing such patients (such as Manchester), uses factor XI concentrate rather than plasma. As the exhibits show, we wrote to all centres asking them to identify those patients who had only been treated with BPL products manufactured from US plasma. This only affected a few infrequently treated patients with mild bleeding disorders because almost all the others had also been treated with UK-plasma sourced products during the period of risk.

150.2.With hindsight, rather than defining the period of risk by the period during which at-risk products might still have been circulating, it might have been better to also have included an element for date of manufacture. However, that would have made an already complicated tracing process even more involved and my suspicion is that it would also have led to mistakes at a centre level.

Section 8: The Haemophilia Society

151. Please provide details of your involvement with the Haemophilia Society. In particular, please describe:

a. the work undertaken by you as a member of the Society's Medical Advisory Panel, insofar as relevant to the Inquiry's Terms of Reference;

b. the work undertaken by you as a member of the Society's Health Sub-Committee, insofar as relevant to the Inquiry's Terms of Reference.

151.1. During my time as a consultant Haematologist, the Haemophilia Society has intermittently run a Medical Advisory Committee of some sort. This met a couple of times a year at the Society HQ in London and several doctors would attend to informally discuss any issues of the day. I can't remember seeing minutes of these meetings. I felt that I always had a friendly and collaborative relationship with the Haemophilia Society going all the way back to my time as a senior registrar in Sheffield, when the local Haemophilia Society group paid my expenses to act as a Haemophilia Society delegate to their Annual Residential Seminar. Although the medical community and Haemophilia Society perspective obviously had some differences, there was broad general agreement throughout this time on the general desired direction of travel and general objectives and it made sense to collaborate with one another to try to progressively improve Haemophilia care in the UK and to act as the patient's advocate.

151.2. During my time as chairman of UKHCDO, if I had to be in London for a committee meeting, I would often arrange an additional short informal meeting with the Society CEO or the DH Blood Policy Unit to maintain contact and to discuss the issues of the day. I think these meetings were very useful to maintain an ongoing dialogue and a constructive and collaborative relationship.

152. On 25 November 1994 you wrote (letter enclosed) to Mr Barker of the Haemophilia Society [HSOC0005123], asking to have a "chat" about hepatitis C, expressing

concern that "the whole thing is getting out of hand" and wanting to talk about the Society's position. Please explain what the purpose of this letter was. Did you meet with, or have a discussion with, Mr Barker or anyone else from the Haemophilia Society about your concerns and if so what was discussed and decided?

152.1. This was a request for clarification of the Haemophilia Society's position on litigation in general, since there was a great deal of litigation in progress at this time. My sentiment was that for many patients to pursue unsustainable allegations of negligence would only delay the achievement of any no-fault compensation scheme whilst creating a great deal of work along the way and raising false hopes amongst the unsuccessful litigants. It did not seem fair to anyone, least of all the litigants themselves, to encourage them in the belief that they might have a valid case when they did not.

152.2. This was a slightly circular problem, however, as I allude to in the letter (HSOC0005123). So long as DH maintained that since there was no negligence there would be no compensation, the patients felt that they had no other option but to resort to the law and their doctors were caught in the middle of this impasse. However DH felt that they could not agree any scheme of compensation whilst litigation was ongoing for fear of undermining the legal process. As I said in my letter "*If the society wants patients who have contracted hepatitis C to obtain some compensation, I am not sure that encouraging them in their mistaken belief that they have a good case of negligence is the right way to go about it.*"

152.3. My letter (HSOC0005123) also makes reference to the press coverage also referred to in Q 122, which concerned a family in whom three brothers with severe haemophilia A (<1% Factor VIII) eventually tragically died, two from HIV and the third from hepatocellular carcinoma. The relatives of all three attempted to sue for negligence, alleging incorrectly that they did not have severe haemophilia at all and could have been treated with DDAVP or, in the final case claiming incorrectly that his diagnosis of HCC was delayed because I had not involved hepatology. None of these cases progressed but the dreadful plight of the family was extensively reported in the Liverpool Echo with interviews from relatives.

Section 9: The financial support schemes

153. What if any involvement did you have (and in the case of EIBSS continue to 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? Please provide as much detail as you can.

153.1. I was involved in explaining the Macfarlane Trust and the Skipton fund to my patients and supporting their applications for support or for ex-gratia payments from those bodies. I have had no involvement with the Eileen Trust or the Caxton Foundation.

153.2. I have been involved in offering advice to DH about the Skipton Fund and the revision to the Skipton Fund, as explored below.

154. In relation to the Skipton Fund, your CV (provided by you to the Inquiry with your first statement as WITN3289002) records that you gave advice to the Department of Health on the setup of the Skipton Fund. Please explain what advice you provided and detail any other involvement you had in the establishment of the Skipton Fund.

154.1. Professor Hill and I met informally a few times with DH officials at Skipton House (I think it was Charles Lister and then David Gutowski) to discuss possible schemes. I recollect that DH had not wished to agree anything until the HCV class action and other litigation were settled, since a scheme of compensation might undermine their legal position in such an action. Eventually a scheme emerged from DH and we were asked to comment on it and to advise on how it could be made to work. A major issue over which we (Prof Hill and I) and the Haemophilia Medical Community as a whole disagreed with DH was eligibility for the scheme. DH took the view that only the relatives of those patients who had died from liver disease *after* the date of inception of the scheme would be eligible for payment. We considered that this was unjust and warned that it would cause considerable bad feeling (as indeed, it did). This advice was rejected at the time but changed in 2010 (see below).

154.2. The criteria used to determine who would and would not receive a payment were devised by Hepatologists and the amount to be paid and cut-off dates for eligibility were decided somewhere in DH.

155. Your CV also records your involvement on the advisory panel on revision of awards from the Skipton Fund in 2010/2012.

a. Please describe that involvement.

155.1. I assume that the Inquiry is referring to the Expert Working Group chaired by Professor Brian Gazzard, which produced the report listed as DHNI0000371? There were, in fact, two groups with overlapping membership. Dr Gazzard's group, of which I was a member, reviewed the natural history of HCV to better advise DH on the structure eligibility and operation of a payment scheme. Membership of the group is listed on page 15 of DHNI0000371. Dr Mike Makris, Dr Gerry Dolan and I represented UKHCDO on that group.

b. What advice was provided by the panel/expert working group? You may wish to consider the enclosed draft report entitled "Reviewing the natural history of Hepatitis C infection" [DHNI0000371]. What further advice/report(s) were provided by the expert working group?

155.2. The recommendations of the group are summarised on paged 13-15 of DHNI0000371. In outline, the group recommended that patients with chronic HCV (defined as abnormal LFTs for >6 months) and serious liver disease should receive a payment identical to that given to patients with HIV and if co-infected should receive two payments. Those with serious liver disease or serious problems secondary to HCV such as B-cell lymphoma would receive this higher level regular payment.

155.3. I remember that there was a great deal of discussion in this group around chronic fatigue and other alleged extrahepatic symptoms possibly referable to chronic HCV. A small minority of patients were thought to be very severely affected by this

but since it could not be quantified, was subjective and its relationship to HCV was uncertain, the group decided *not* to include this as a serious extrahepatic manifestation of HCV. The group felt that most patients with non-severe chronic HCV were asymptomatic and only 5-10% of those without severe liver disease complained of significant fatigue or "brain fog". This would be a major bone of contention subsequently between activists and the advisory group.

155.4. The report was largely written by DH, Professor Gazzard and others.

c. *What, if any, role did you/the group have in the production of the enclosed report dated 25 November 2010 entitled "Review of support to patients affected by contaminated blood: Assumptions used in modelling" [SKIP0000031_059]?*

155.5. SKIP0000031_059 was produced by a different group of which I was also a member. Membership of this group of advisors is listed in Annex A on page 12 of the report. Membership of the two groups overlapped.

155.6. This group met on 15/11/2010 to review modelling assumptions around the future funding and organisation of the enhanced payment system envisaged for patients infected with HCV. DH produced the report (SKIP0000031_059).

d. *What, if any, role did you/the group have in the production of the enclosed report entitled "Review of the support available to individuals infected with Hepatitis C and/or HIV by NHS-supplied blood transfusions or blood products and their dependants" [PRSE0003033]?*

155.7. Whilst I am listed as one of the advisors for this report, as detailed in previous answers. I had no hand in writing the final report or reaching the major policy decisions.

e. *On 28 January 2011 you wrote to the Department of Health, Social Services and Public Safety in Northern Ireland regarding the review of the Skipton Fund payment scheme. Please provide a copy of that letter and explain what prompted it. You received a response dated 10 February 2011 (enclosed, [DHNI0000315])*

which stated that the Minister was currently considering the expert review team's report and recommendations. What, if any, further discussions or communications did you have regarding the position in Northern Ireland?

155.8. My recollection is that all the devolved administrations agreed to implement the scheme as in England.

f. In November 2012 you attended a meeting with Anna Soubry, other members of the expert group and campaigners (please see the enclosed minutes [STHB0000690]). What was the purpose of that meeting and the reason for your involvement in it? What, if any, further involvement did you have following the meeting?

155.9. Prof Gazzard, one of the DH modellers and I were invited to meet with Anna Soubry, then Junior Minister for Health, and a group of campaigners to explain the award to them and to give them an opportunity to discuss this.

155.10. We were invited as members of the Advisory Group, essentially to defend our advice and to explain the award. The campaigners took this as an opportunity to re-iterate the demands that emerged from the Independent Archer Inquiry.

155.11. The campaigners were, as the minutes of the meeting show, very unhappy with the award, our assumptions and the way in which the whole thing had been approached. They considered this award inadequate because they wanted all HCV infected patients, including those who had cleared the virus spontaneously, to receive a regular monthly payment, regardless of the severity of their liver disease and without any other entry criteria. They wanted a financial award largely modelled on the Southern Irish Settlement. They also challenged all the scientific advice. The award did not address in any way many of their demands, as outlined in appendix 5 of PRSE0003033, pages 65 and 66, which I have reproduced below for ease of access. Their demands, envisaged lump sum payments of up to a £500,000- £1000,000 for each patient, appeared unrealistic to DH and were not really addressed in the meeting.

The following list reflects the representations that have been received from the campaigners since July 2010. It has been collated from the written submissions of the campaigners, comments made in their meetings with the Parliamentary Under Secretary of State for Public Health, Anne Milton MP, and correspondence received by the Department of Health. Any that go beyond the terms of reference of the review have not been considered in the report.

Compensation

- Evidence gathered during the course of the review shows a fairly wide range of views on the level of payments that this patient group should receive, in respect of both HIV and hepatitis C infection:
  - the minimum wage, - c£11k pa gross (£5.75 per hour, 40hr week);
  - lump sum of £100k-£150k, followed by recurrent annual payments of £3,600-£6,000 for Skipton Fund Stage 1 patient, followed by lump sum of £300k for Stage 2 payment;
  - HIV and hepatitis C stage 2 patients to receive £18k pa; hepatitis C stage 1 patients to receive £5-7k pa; widows and orphans eligible for unspecified discretionary payments.
  - a lump sum of £200k-£300k;
  - individual assessment of need – one campaigner estimated this at a lump sum of c£400,000 plus (unspecified) regular payments for each type of infection.
  - individual assessments of loss – two of those affected cited figures of c£500k - c£800k.
  - payments equivalent to those in Ireland – estimated average lump sum of c£750k for an infected individual.

- Compensation on a par with Ireland. Lump sum payment followed by regular payments. Other submissions suggest applicants should have choice on how they receive payments
- Regular payments for those infected with hepatitis C, on a par with those received by HIV patients
- Skipton Fund stage 2 payments are only made when patients are close to death –the trigger for stage 2 payments needs to be improved

- DH should pay interim lump sum payments while the scheme is being set up
- On-going payments should rise in line with the RPI
- Payments should not be means tested
- Payments should be based on individual assessments
- Payments should be made to the widows/dependents of those who died before August 2003
- On-going payments to widows of those who either have died since August 2003, or will die. (NB: they make no distinction about what the patient dies of, i.e the implication is that they do not need to die of hep C to qualify)
- Compensation for carers. Backdated. Some suggest this should be a lump sum
- Payment should be made through DWP
- Payments should not be means tested, or taxable, or taken into account in calculating benefits
- The Macfarlane and Eileen Trusts and Skipton Fund should remain in existence to provide on-going support
- Payments should be made to those who clear the virus. Implicit that this should include those who clear in the acute phase

reatment/Care

- Free prescriptions
- Free NHS care for all health needs
- Extend patient representation in all health care decision making
- Make home nursing free of charge (is currently charged for, and DLA/Carers allowance does not pay for 24/7 care)
- Priority access to counselling (within 1 week). Or make provision in the financial settlement to cover this cost privately
- Give GPs the ability to apply for additional funding to enable them to meet their patients needs
- Commissioners for Trusts should be able to access additional funds for haemophilia patients
- Put haemophilia treatment and ethics on the curriculum of medical schools

ther

- Government to establish a comprehensive insurance scheme

155.12. There was no follow up to this meeting.

156. *On 23 January 2004 you wrote to Zubeda Seedat at the Department of Health [HCDO0000254_712] regarding the Hepatitis C ex gratia payment scheme, stating that "It seems fair that those who cleared the viruses spontaneously get nothing (particularly since this includes one of our most gratuitously unpleasant activists who claims [sic] his life has been ruined by this virus he does not have)". Please explain why you considered it fair that those who cleared the virus spontaneously get nothing; who you were referring to when you described "one of our most gratuitously unpleasant activists"; and why you considered the exclusion of one individual relevant to the fairness of the proposed scheme.*

156.1. Zubeda Seedat had sent me a draft press release regarding the inception of the Original Skipton settlement and its details and had requested my comments. The draft press release seemed fine.

156.2. There had been some debate about eligibility for the scheme and the consensus was that patients who had never had any evidence of chronic liver disease (i.e. those with no evidence of abnormal liver function tests for >6 mths.) should not be eligible for the scheme. These would include the 30% who had been exposed to HCV but who had cleared the virus spontaneously. This decision was widely considered to be fair, since those patients may have been exposed to HCV but had never had and never would have any clinical problems resulting from that exposure. This decision would much later be endorsed by the expert group chaired by Prof Gazzard in 2010 (above).

156.3. Whilst the aside about my patient was clearly an inappropriate non-sequitur, which I regret, it was written in anger. Whilst I have always had a great deal of sympathy for the patient campaign for recompense and have done a great deal over the years to argue for compensation and to facilitate payments, I found the tactics used by a small hard core of activists to be antagonistic and often counterproductive. Their demands, heavily influenced by the Irish Settlement (PRSE0003033) were also, arguably unrealistic. At the time of writing this e-mail, the activists' tactic was to put their doctors under pressure to support them by rather paradoxically reporting them to the General Medical Counsel for

professional misconduct. A number of Centre Directors had been reported to the GMC at that time with a variety of baseless and untruthful accusations.

157. *In an email from you dated 13 August 2004 to Peter Stevens [HCDO0000254_719] you stated that it was "worrying but not surprising that many eligible patients are unaware of the Skipton Fund". Please set out the steps that you (or the Manchester Centre) took to inform patients of this fund; what if any steps were taken (to your knowledge) by other centres; and what if any steps were taken by the Department of Health, UKHCDO and/or the Skipton Fund to address this problem.*

157.1. I wrote to all my patients in Manchester who had been infected with HCV to inform them of the scheme. If new patients came under our care from other centres, we established their HCV status and made sure they knew about the scheme. If it became apparent that a patient had progressed to "serious liver disease", we made sure they knew about the stage 2 payment.

157.2. I don't know what other centres did.

158. *At the AGM of the UKHCDO on 13 October 2005 (attended by you as incoming Chairman) [BART0000904] one of the attendees "pointed out the problem that arose if patient's notes had been lost, and therefore could not provide evidence of chronic hepatitis". The suggestion at the meeting was that such patients should appeal "saying that there is no information available due to destroyed notes". Was this a widespread problem? As far as you are aware, to what extent, if at all, did the suggested route of appeal, with the patient pointing out that notes had been destroyed, succeed? Were there patients under the care of the Manchester Centre who experienced this difficulty and, if so, what happened to their applications to the Skipton Fund?*

158.1. This was not a widespread problem but neither was it an isolated issue. Increasingly, the Skipton fund based their decisions on an objective analysis of the available evidence but that evidence was quite varied and even if the notes had been lost or destroyed a computer record of results plus a death certificate was often adequate. Infrequently, in the absence of any evidence at all, applications

failed. A more frequent occurrence was that a patient, wife or relative would claim that patient had had cirrhosis in an attempt to obtain a higher level or regular payment when there had never been any evidence to suggest cirrhosis. Such applications failed because the available evidence showed that they did not have cirrhosis. A blank application form is included for information (WITN3289153)

159. *Please consider the enclosed letter dated 18 January 2011 from you to Rowena Jecock at the Department of Health concerning the deadline for the registration of dependents of patients who died before the inception of the Skipton Fund [ABMU0000015]. Please set out what you can recall about this issue and your/UKHCDO's involvement in it.*

159.1. As detailed before, it was widely considered throughout the Haemophilia Community that it was unjust to exclude widows of patients who had hepatitis C but died before the inception of the Skipton Fund from the provisions of that fund. As one of the widows pointed out to me, the widows of her two brothers in law who died from AIDS were compensated but she was not when her husband died of hepatocellular carcinoma secondary to HCV. I agreed with her that this was an obvious injustice. In late 2010, as a part of the revision of the Skipton Fund payments, it was agreed that this should change but DH set a deadline of the 31st of March 2011 for new applications, which was considered unrealistic by UKHCDO members and likely to cause further resentment amongst patients and their relatives. This was extensively discussed in the UKHCDO Advisory Committee, which I chaired (WITN3289154 1n WITN3289155: Minutes Advisory Committee 17.1.2011 and 1/7/2011).

159.2. The deadline was not changed but some leeway was provided in that, the form had merely to be requested by the deadline so that the application could be registered by that time but could be completed at a later date. This was an enormous amount of work for Haemophilia Centres to complete over a very short period of time. The minutes of the Advisory Committee of 1/7/11 (WITN3289156: Minutes of Advisory 1.7.11) detail progress made in this regard in the previous 7 months: - 499 applications for forms for patients who had died prior to 29/8/03 had been made before the deadline of which 347 had already been filled out and

returned. At that time, 138 had been approved and a further 98 were likely to be approved after checking. 28 had been declined and 47 were under further consideration (I do not know about the other 36!).

160.Please consider the enclosed letter dated 28 November 2008 from the Skipton Fund to you [ABMU0000013], concerning the Skipton Fund's new requirement for supporting documentation to be supplied for all applications to the scheme. Please set out what you can recall about this issue and your/UKHCDO's involvement in it.

160.1.As Chairman of UKHCDO, I made the membership aware of this development and it was also discussed in the Advisory Committee. As Mr Fish, The Skipton Fund Administrator, said, by 2008 most of those who were going to apply to the scheme had done so and so this did not present a practical problem for most applicants. Where the centre did not have the older treatment records, in most cases the National Haemophilia Database would have some helpful information and data from the database was, indeed used on occasion to support applications.

161.In the enclosed minutes of the Combined 41st Advisory Committee and 12th Annual General Meeting of the UKHCDO on 3 October 2011 [HCDO0000510] you are recorded as reporting (in relation to the Skipton Fund) that "where information was missing there was a tentative agreement that cases would be decided on the balance of probabilities". Please set out your knowledge of this "tentative agreement" and whether it was implemented.

161.1.I have no further evidence in relation to this. This would require specific case knowledge of borderline cases. By the way, this part of the AGM (HCDO0000510) was presented and chaired by the incoming chairman, Dr G Dolan.

162.Your CV states that you are a member of the advisory group on support for individuals affected with HCV or HIV by blood transfusion or blood products and that the group "still meets occasionally". Please:

162.1.This appears to be the same group explored in Q155 and Q156. This is an error

in my CV, which should have been updated. The group met once or twice and did some business by e-mail but completed its business in a year.

163. To what extent, during your time at (a) the Liverpool Centre and (b) the Manchester Centre, did staff (including you) inform patients about the different trusts or funds?

163.1. When the Macfarlane Trust was set up, I wrote to my HIV positive patients in Liverpool and invited them to a meeting to discuss the fund. My social worker and counsellor were present. I remember the meeting partly because I was unprepared for the enormous anger that the scheme would engender amongst the patients. They objected to its complexity and the need to "go cap in hand" to apply for support. The fact that the Macfarlane Trust was set up as a discretionary charity to provide means-tested income top ups, one-off grants, means tested winter payments and benefits advice and was therefore entirely based around poverty caused enduring resentment amongst the patients right across the country and was not peculiar to Liverpool . Our team would discuss the scheme and support applications to it.

163.2. When the Skipton fund came into existence I wrote to all patients infected with HCV in Manchester and I seem to remember we also had a big meeting in the main lecture theatre.

163.3. These schemes were often discussed in clinic.

164. Did (a) the Liverpool Centre and/or (b) the Manchester 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.

164.1. We did not have a written policy but we did check that eligible patients had applied. The schemes were discussed at practically every weekly multidisciplinary meeting at that time. I asked that copies of application forms be filed in the notes. I made patients aware in clinic as did our social worker and nursing staff during their patient interactions.

165.What kind of information did (a) the Liverpool Centre and (b) the Manchester Centre provide to the trusts and funds about, or on behalf of, patients who were seeking assistance from the trusts and funds?

165.1.We provided whatever evidence was appropriate, given the nature of the application. In the case of the Macfarlane Trust, this would often be evidence of hardship or clinical need. For example, in the early days of HIV, when drenching night sweats were a common problem, Macfarlane would pay for additional sheets. They also paid for respite holidays and made grants for various other things.

165.2.For Skipton applications, we would review the notes with the form and frequently arrange additional investigations so that we were in a position to provide the strongest case possible. For example, one of the criteria for serious liver disease is the SGOT/ALT ratio. Most labs do not do SGOT routinely anymore and so we would have to get the patient in specially to do this and would repeat all the other tests so that we had the most up to date information. We would also organise ultrasound or a Fibroscan. I have attached a blank Skipton application form for information (WITN3289153).

166.What kind of support or assistance was provided by you and/or (a) the Liverpool and/or (b) the Manchester Centres to patients making applications for financial assistance?

166.1.This was a significant element of the work of running a haemophilia centre during the 90s 2000s. The applications were commonly generated on the advice of the social worker and supported by letters from the social worker, the patient and the medical staff.

167.Did (a) the Liverpool Centre and/or (b) the Manchester 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.

167.1.This is very similar to Q168 so I will take both together.. We did not act as a gateway. This was a point of principle and also necessary so that the Centre staff

could distance themselves from the sometimes contentious adjudication process, which always lay with the Macfarlane Trust or the Skipton fund and not with the Haemophilia Centre.

167.2. We would advise on what had succeeded and failed in the past and what could be tried. We would do our best to support all applications, however likely or unlikely they were to succeed. Macfarlane were particularly inconsistent in their decisions, which made it difficult to offer patients useful advice.

167.3. Many applications to Skipton were clearly unlikely to succeed, especially when patients with non-serious or even no liver disease wished to apply for a stage 2 award. Nevertheless, we filled out the forms and gave whatever evidence we had.

168. Was either 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.

168.1. No. We (medical, nursing and social work staff) helped patients and their relatives to make applications and we told them what requests usually did or did not succeed but we did not block or discourage claims we suspected might be unlikely to succeed See above, Q167.

169. 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?

169.1. There were constant complaints about the Macfarlane Trust. I think this was, to some degree, inevitable because people with Haemophilia felt that it was demeaning to have to make relatively petty applications. This was compounded by the varying policies Macfarlane appeared to be operating, as judged by the success and failure of similar applications. These complaints were assuaged to a degree by the granting of regular payments to patients with HIV.

169.2.I think that, with the exception of the major internal fraud referred to in Mr Fish's letter (ABMU0000013); the Skipton Fund was quite well run. We may not have been happy with the exclusion of patients who had died prior to the inception of the scheme but the criteria set were reasonably objective and predictable and consistently applied so that we could offer patients reasonably reliable advice on the likely decision of the Skipton panel.

170. *What if any dealings have you had with EIBSS? Have there been difficulties or shortcomings in the way in which it operates or takes decisions or in its dealings with applicants for assistance?*

170.1.I have had no dealings with the EIBSS.

Section 10: HCV Lookback

171. *Your CV records that you led and directed the National HCV Lookback Exercise on behalf of the Department of Health between 2010 and 2013, using the National Haemophilia Database. Please provide full details of this exercise, its purpose and objectives, how it was undertaken, whether and if so to what extent it achieved its objectives, and your involvement in it. (You may wish to consider the enclosed documents: Summary Note of Third Meeting between the Haemophilia Alliance and UK Health Departments held on 19 November 2010 [HCDO0000272_004]; your letter to UKHCDO members dated 7 July 2011 [ABMU0000019]; an undated letter headed "Dear Colleagues … RE: Hepatitis C Look-back Exercise" [ABMU0000020]; section 9 of the minutes of Combined 37th Advisory Committee and 11th Annual General Meeting of UKHCDO on 12 November 2010 [HCDO0000509]; section 8 of the minutes of the Combined 41st Advisory Committee and 12th Annual General Meeting of the UKHCDO on 3 October 2011 [HCDO0000510]).*

171.1.The Recommendations of the Non-Statutory Archer Inquiry were discussed in the meetings of the Haemophilia Alliance (HCDO0000272_004) and considered by DH. Whilst many of the requests were not accepted or pursued by DH, they did

favour some form of hepatitis C lookback exercise.

171.2. UKHCDO had very little data on HCV at that time. We could estimate a *minimum* number of patients who had been exposed based on the number reported to the database as having been treated with fractionated plasma-derived clotting factor concentrates manufactured during the period of risk (before 1987). We acknowledged that this was probably a moderate underestimate because we did not feel that we had reliable treatment data on occasionally-treated patients with mild bleeding disorders since many of these patients were treated outside haemophilia centres and their treatment would not be reported in to the centre. This group of patients included a significant proportion of patients who were lost to follow up and who consequently may or may not have been tested.

171.3. The Blood Policy Unit of DH, having agreed the major objectives of such an exercise, invited UKHCDO to submit a proposal for an HCV lookback in 2010. That proposal is attached as WITN3289157, WITN3289158, WITN3289159 and WITN3289160. It should be noted, however, that since UKHCDO have no direct patient involvement or responsibility many of the objectives of this exercise would have to be fulfilled by Haemophilia Centre teams at centre level and UKHCDO/NHD could only facilitate those aspects of the exercise by providing data and chasing the centres up (WITN3289161). The principal objectives of this exercise were as follows:

- **Principal Objectives:**

1. To document those patients with bleeding disorders already tested.
    a) To establish what proportion have hepatitis C.
    b) To establish whether they have been offered treatment and if they have what was the outcome.
    c) To establish the number of patients who have died from complications of hepatitis C.

2. To identify patients exposed to blood components or blood products during the period of risk, who have not been tested for hepatitis C.
    a) To offer them advice and hepatitis C testing.
    b) If they are viraemic with hepatitis C, to assess the severity of their liver disease.
    c) If they are viraemic with hepatitis C, to offer referral to a hepatologist and/or treatment as appropriate.
    d) If infected and fulfilling basic eligibility criteria, to arrange registration with the Skipton Fund.

171.4. To this relatively limited list, DH added that they wanted an estimate of the proportion of patients with severe liver disease and a breakdown of the proportion with different HCV genotypes and an estimate of those treated so far and the outcome of that treatment. DH wanted this data for healthcare planning and also to estimate likely Skipton fund and treatment cost. Unfortunately, to plan for the expenditure likely to be incurred through the Skipton fund, it was also necessary to document the number of patients infected but now deceased. I say "unfortunately" because it proved very labour-intensive for centre staff to determine the HCV status of patients who had, in many cases died many years before. Whilst it would have been desirable to know these additional data items it proved impossibly burdensome for centres to collect and report so much data on so many patients without additional cente resources at a centre level.

171.5. DH agreed a budget of £150,000, which was not based on a work estimate and proved inadequate. There was no funding for centres to collect the data. They agreed a 12-month timescale for the lookback.

171.6. We started by assuming that all patients who had been registered with a bleeding disorder prior to the advent of HCV testing of all blood donations in October 1991 were potentially at risk. There were about 27,000 of these, a third of whom were already deceased. The vast majority of these were seldom-treated or never-treated patients with mild bleeding disorders.

171.7. To start with, we adopted a similar strategy to that which we had adopted for the

vCJD lookback exercise in that we sent pre-populated spreadsheets to all centres, listing all the patients that had been registered with that centre at any time prior to October 1991. The spreadsheet asked about HCV status and treatment history, HCV genotype (if known) and for evidence of serious liver disease and treatment for HCV and its outcome. We created an electronic report form or portal for reporting of results.

171.8. The additional items requested by DH proved too burdensome for the centres to provide and consequently we negotiated with DH to collect these items from a randomly selected 10% of the patient group, so that we could extrapolate from this cohort.

171.9. Early responses (WITN3289160 and WITN3289161) showed that where a patient had moved around the country and been managed by more than one centre, the first centre would often report that the patient had been treated with blood products, whereas the second would often report that they had not used such products. This indicated that many centres were ignorant of some of their patient's early treatment history probably administered in another centre. Furthermore, 10% of eligible patients with an unknown treatment history had evidence of previous exposure compared with 1% of those known never to have been treated and 15% of those known to have been treated with blood components.

171.10. Unfortunately, the majority of the reports that came back, over 8000 of them, indicated that the HCV status was "unknown". By this they meant that it was unknown to the person filling out the form and not that the patient had never been tested. However, that gave us very little idea of the extent to which potentially at-risk patients had or had not been tested. About 90% of the reports were for patients still alive and therefore being actively followed up, because of the greater difficulty involved in obtaining data on deceased patients. We did not seek data on patients who had died prior to 1992 and the advent of HCV testing since the test was not available during life.

171.11. In the end, the study was considered too ambitious and after three years, with less and less data coming in, the exercise was wound down. Many centres had sent

no data at all and only a minority had sent all the data requested (WITN3289162.) We did obtain limited data, which has been included in the subsequent, less ambitious lookback exercise of 2018-20. The data is summarized in the report that follows (

Hepatitis C Look-back Report

This report is comprised partly of data imputed from the treatment records of NHD, collected over many years, and partly from data collected specifically in a HCV look-back exercise conducted from 2010. Centres found the look-back exercise burdensome and difficult and the data is consequently incomplete. Many patients were probably lost to follow-up. Some extrapolations are possible, however.

Table 1 Estimate of number of patients exposed to hepatitis C, based on historical clotting factor concentrate exposure during the period of risk

Coagulation Defect	Alive	Dead	Total
Haemophilia A	2,632	1,828	4,460
Haemophilia A Carrier	114	30	144
Haemophilia A with Liver Transplant	7	13	20
Haemophilia B	698	240	938
Haemophilia B Carrier	61	6	67
Haemophilia B with Liver Transplant	2	3	5
von Willebrand disease	568	163	731
von Willebrand with Liver Transplant	0	1	1
F.V deficiency	2	0	2
F.VII deficiency	20	1	21
F.X deficiency	23	1	24
Factor X deficiency with Liver Transplant	0	1	1
F.XI Deficiency	46	14	60
F.XII (Hageman) defect	5	0	5
F.XIII Deficiency	17	2	19
Fibrinogen Deficiency	5	1	6
Prothrombin Deficiency	1	0	1
Combined V+VIII Deficiency	2	2	4
Other combined diagnoses	4	3	7
Acquired Haemophilia A	17	94	111
Acquired Haemophilia B	1	1	2
Acquired von Willebrands	2	11	13
Platelet defects	15	1	16
Miscellaneous	1	1	2
Unclassified bleeding disorder	16	2	18
Temporary coagulation defect, now normal	15	0	15
Total	**4,274**	**2,419**	**6,693**

Table 1 shows 6,693 patients considered at risk of HCV by virtue of concentrate use during the period of risk for HCV, broken down by diagnosis and whether they are alive/dead. This is based on concentrate use reported at the time to NHD. We think that this segment of the data is fairly complete and that 100% of these patients will have been exposed to HCV and that 25-30% of these will have cleared the virus spontaneously. Four thousand, two hundred and seventy four of these patients are still alive.

Table 2 Estimate of number of patients *potentially* exposed to hepatitis C, based on historical exposure to blood components

Coagulation Defect	Alive	Dead	Total
Haemophilia A	347	148	495
Haemophilia A Carrier	53	14	67
Haemophilia B	7	12	19
Haemophilia B Carrier	8	1	9
von Willebrand disease	469	126	595
F.V deficiency	3	3	6
F.VII deficiency	5	1	6
F.X deficiency	2	1	3
F.XI Deficiency	12	7	19
F.XII (Hageman) defect	5	3	8
F.XIII Deficiency	1	0	1
Fletcher factor	1	0	1
Fibrinogen Deficiency	7	2	9
Prothrombin Deficiency	1	0	1
Combined II+VII+IX+X Deficiency	1	0	1
Combined V+VIII Deficiency	5	0	5
Other combined diagnoses	2	0	2
Acquired Haemophilia A	0	3	3
Acquired von Willebrands	0	2	2
Platelet defects	5	2	7
Miscellaneous	0	1	1
Unclassified bleeding disorder	8	1	9
Temporary coagulation defect, now normal	4	1	5
Total	**946**	**328**	**1,274**

Table 2 shows a further 1,274 patients, considered *potentially* at risk of exposure to HCV by virtue of reported exposure to blood components during the period of risk for HCV (prior to the advent of HCV testing of donors in September 1992). This is also broken down by diagnosis and whether they are still alive or dead. This is based on treatment reports to NHD at the time. None of these patients is known to the database to have been treated with a clotting factor concentrate. The extent of their blood component exposure and hence the size of their risk will vary, but extrapolation of testing reports below implies that about 15% of these patients will have been exposed to HCV. Two thirds of these patients are reported to NHD as "*HCV status unknown*", either because they have not been tested or because documentation of their HCV status cannot easily be found. A significant proportion of these patients are probably lost to follow up at the reporting centre, have moved or are not reviewed regularly.

We strongly suspect that there was under-reporting of occasional treatment of mild bleeding disorders and so suspect that far more patients were treated than had been reported to NHD over the years. For that reason, we felt obliged to also consider all patients not included above but registered with a bleeding disorder during the period of risk (approx. 18,000 pts) to be potentially at risk of HCV exposure unless the centre could confirm that they had never been treated with blood products or concentrates.

Of the 9,090 patients whose previous treatment history was reported as "unknown", HCV status was reported as also "unknown" in 7,567. Of the 1,523 patients whose treatment history was reported to us as "unknown" but who had been HCV tested, 398 had evidence of active HCV and 21 of past but cleared HCV. Thus 27.5% of those members of this group who were tested and had a test result reported to us had evidence of previous exposure to HCV.

Were this to be found in the whole of the 18,000 patients for whom we have no treatment reports, we would expect about 5,000 additional patients to have been exposed to HCV whose exposure to HCV is not documented or who have not been tested. It is likely that there is both testing and reporting bias, however, and that those treated are less likely to be lost to follow up and more likely to have been tested than those never treated. The true number of patients exposed is therefore likely to be significantly lower than this estimate. However, unless this group are tested and reported we cannot make an accurate estimate.

We would strongly recommend that all patients diagnosed with a bleeding disorder before September 1992 should be tested for HCV because centres (and the patients themselves) will frequently have no idea what their treatment history is

Table 3 Hepatitis C potentially eligible patients

Hepatitis C Potentially Eligible Patients	n	%
Number of eligible patients *	29,484	
Number of patients Alive ǂ	24,643	84%
Number of patients Deceased ǂ	4,841	16%

** Patients born before 01/01/1991*

ǂ Alive or dead after 31/03/2013

Table 3 shows the number of patients *potentially* exposed to HCV. That includes all patients known to have been treated at some time with clotting factor concentrates or blood components during the period of risk for hepatitis C and those patients who were registered during the period of risk whose treatment is uncertain but which *may* include blood or blood products. All patients exposed to clotting factor concentrates during the period of risk will have been exposed to HCV, whereas those exposed to blood components only will have a lower risk of exposure averaging 5-10%.

Our incomplete data shows that those whose treatment is uncertain to the database because no treatment has been reported to the database are mostly untested (approx. 7000 of 9000) but a significant proportion of those who have been tested (27.5%) have evidence of exposure to HCV.

Six of 2185 patients reported never to have had treatment were found to have evidence of exposure to HCV. This prevalence is in keeping with the background prevalence of HCV in the general population and probably does not represent infection from the use of blood products.

Table 4 Hepatitis C Look-back reports

Of those patients for whom a report has been submitted	n	% of submitted	% of eligible
Number of Reports Submitted	14,252		
Number of patients Alive	12,983	91%	44%
Number of patients Deceased	1,269	9%	4%

Table 4 shows that reports were received for 14,252 patients, 12,983 still alive, slightly less than 50% of the patients alive and eligible for the study.

Table 5 HCV Look-back: Exposure to Blood Components or Clotting Factor Concentrate and HCV status (live patients only)

Treament	Ab Neg	Ab Pos, Ag Neg	Ab Pos Ag Pos	Not known	Ab pos Ag N/K	Total
None	42	3	4	2,565	1	2,615
Blood Components	245	11	28	82	2	368
Clotting Factor Concentrate or both	291	239	444	140	26	1,140
Not known	1,035	332	382	4,784	22	6,555
Total	**1,613**	**585**	**858**	**7,571**	**51**	**10,678**

Table 5 shows the breakdown of reported blood component or concentrate use for the 12,983 patients reported to the HCV look-back. HCV status is reported as unknown for 79% of these patients and treatment history is reported as unknown for 70%.

For patients treated with concentrates during the period of risk 291/1,140 had no serological evidence of HCV exposure. Twenty five to thirty percent of patients clear the virus but clearance of antibody is thought to be less common and so this is a higher number of antibody negative patients than one might expect in a group of patients, all of whom are thought to have been exposed to concentrate at one time, albeit many years ago.

A further 849/1140 (74.5%) had evidence of exposure to HCV (Ab positive), of whom 444 (38.9%) are documented to have ongoing infection.

Three hundred and sixty-eight patients were reported to have been exposed to blood components (plasma, cryoprecipitate and platelets) of whom 41 (11.1%) had documented evidence of HCV exposure. This is a much lower prevalence than found in those patients whose treatment history is reported as unknown. However, HCV status was reported as unknown in 80 (22%) of this group.

Given that 27.5% of those with an unknown treatment history who had been tested have evidence of HCV exposure, all patients registered with a bleeding disorder whose

treatment history is uncertain should be tested for HCV. Many of these patients may have been treated with concentrates at some time.

Table 6 Diagnostic breakdown for patients reported to be HCV antibody positive

Coagulation Defect	Severe	Moderate	Mild	Unknown	Total
Haemophilia A	421	120	327	1	869
Haemophilia B	111	50	66	0	227
Females with VIII deficiency	0	0	22	1	23
Females with IX deficiency	0	2	13	0	15
von Willebrand disease					128
F.VII deficiency					4
F.X deficiency					3
F.XI Deficiency					3
Fibrinogen Deficiency					5
Combined von Willebrands + IX deficiency					1
Combined V+VIII Deficiency					1
Acquired Haemophilia A	2	0	1	1	4
Glanzmanns Thrombasthenia					1
Other platelet defects					3
Haemophilia A with Liver Transplant	1	0	3	1	5
Haemophilia B with Liver Transplant	0	0	0	2	2
Unclassified					3
Temporary coagulation defect, now normal					1
Total	553	183	547	15	1,298

Additional data was requested on a randomly selected cohort making up 20% of the live and eligible patients. It was intended to extrapolate from this randomly selected sub-set. The response to this was disappointing in general but the data is presented below.

Table 7 Number of patients alive with severe liver disease

Disease	Number of patients
Cirrhosis	67
Hepatocellular Carcinoma	7
Liver Failure	9
Liver Transplant	12

Figure 1 Genotypes

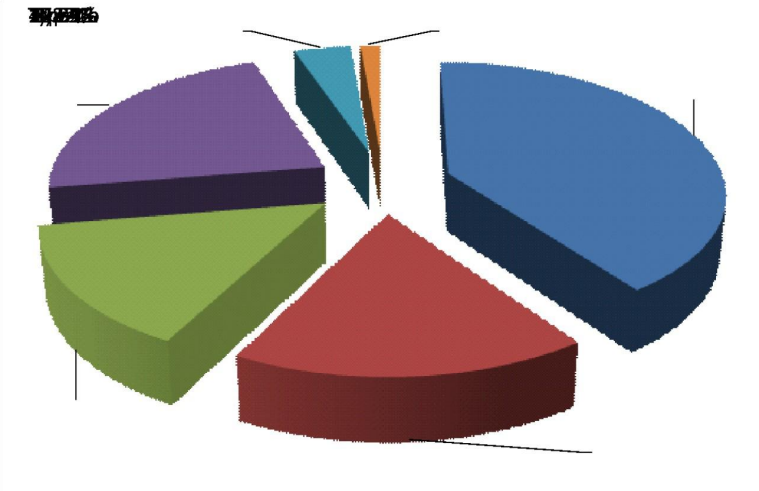

Figure 1 shows the known distribution of HCV genotypes at the time of reporting. Soime patients were treated successfully before genotyping became available and so it is now not known with which HCV genotype they were infected.

The distribution of genotypes differes from that found in the UK population in having a relative excess of type 1a and in having genotypes 4 and 5, not normally found outside sub-saharan Africa. Both these differences reflect the US and African sources of much of the plasma used to manufacture clotting factor concentrates in the late nineteen seventies and early eighties.

Figure 2 Treatment outcomes

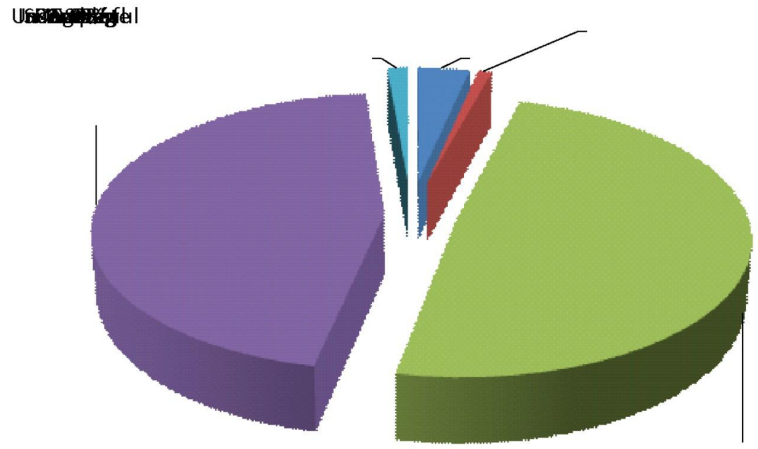

Figure 2 illustrates the proportion of patients with HCV treated successfully or unsuccessfully or awaiting or undergoing antiviral treatment for HCV. This shows a response rate (almost exclusively to interferon-based regimens somewhat less than 50%, reflecting the high prevalence of type 1 genotypes.

Figure 3 Genotypes of patients whose treatment was successful

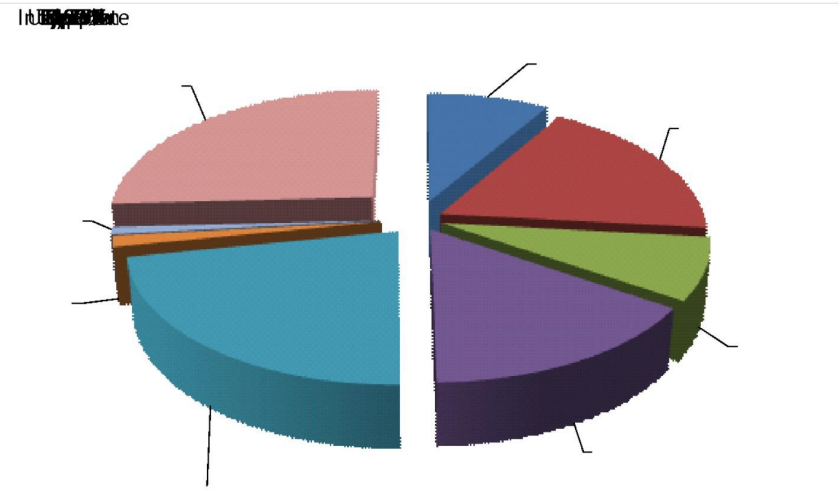

Figure 3 shows the genotypic breakdown of patients in whom antiviral therapy has successfully eradicated HCV. In 25.8% of cases, the genotype is unknown since treatment antedated genotyping. Type 2 and 3 predominate, because of the much

lower response-rate associated with Type 1 using more traditional interferon and Ribivarin regimens.

Figure 4 Genotypes of patients whose treatment was unsuccessful

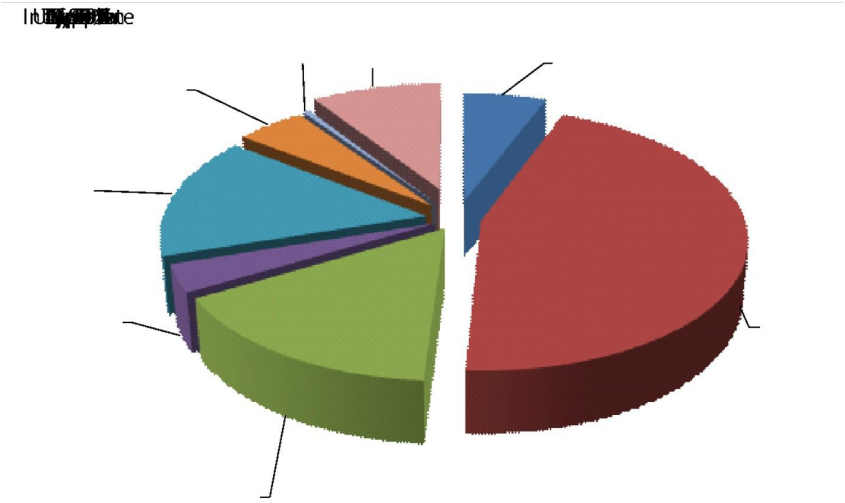

Figure 4 shows that genotype 1 predominated amongst patients in whom HCV eradication was unsuccessful. This is in keeping with the known poorer response rate of type 1 HCV to treatments current during that period.

Section 11: Current haemophilia care

172.Please describe:

a. *how the provision of care and treatment for bleeding disorders is currently organised at the Manchester Centre; and*

172.1.The Manchester Haemophilia Comprehensive Care Centre (adults) cares for about 1700 patients with bleeding disorders and is, in terms of patient numbers, the largest in the UK. Our patients are drawn from the area between Carlisle and Stafford, parts of North Wales and into the hills of Derbyshire. The service is based at Manchester Royal Infirmary and the Haemophilia Service is in the Haemophilia Centre on the second floor. We have a close working relationship with our Paediatric colleagues who are based just down the corridor in the same building in Manchester Children's Hospital.

172.2.The centre is staffed by 4 consultants specialising in Thrombosis and Haemostasis, two SpRs (Specialist Registrars), one a research registrar, 4 Haemophilia Nurse Specialists, a social worker and 3 physiotherapists, a coagulation lab and a DNA lab.

172.3.Apart from standard clinics, we have a weekly multidisciplinary Haemophilia Clinic attended by a social worker and a physiotherapist and all the nurses. There are also bimonthly joint HIV clinics, bimonthly Joint Orthopaedic Clinics and weekly joint Obstetric Clinics and adolescent Clinics held jointly with our Paediatric colleagues.

172.4.Apart from clinics, we have a weekly multidisciplinary meeting of all staff, including lab staff and conduct ward rounds daily. On Monday, and Friday, the ward round is led by the Consultant on duty for the day and on a Wednesday all four consultants go around together.

b. your current roles and responsibilities *at the Manchester Centre.*

172.5.I am a Consultant Haematologist and Director of the Adult Centre. Policy decisions

are reached by consensus amongst the four consultants in this sub-department and the professions allied to medicine. Difficult clinical situations are discussed in the multidisciplinary meeting and/or on joint ward rounds.

173.Please outline the treatments currently provided to patients with bleeding disorders at the Manchester Centre.

173.1.The centre provides haemostatic therapy for all bleeding disorders, either hospital or home-based, as is appropriate. We provide multidisciplinary care for HIV, hepatitis C, Obstetrics, including carrier testing and antenatal diagnosis, and Orthopaedics. We can also provide on-site all forms of surgery with the exception of Neurosurgery, Plastic Surgery, breast surgery and Liver Transplant surgery. We provide a support service to other hospitals to facilitate surgery in those areas that we cannot provide ourselves.

174.Please describe how you typically obtain your patients' consent to treatment.
In particular:

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

174.1.The risks and benefits of treatment are described to the patient in detail, often over several sessions if the patient has some anxiety about treatment. For changes of factor VIII concentrate we would usually write to patients outlining the proposed change and the differences with their previous product and offer to discuss it with them. For changes of type of product e.g. to extended half-life VIII/IX or Emicizumab we would always discuss the relative merits of the new treatment with patients because many patients have preferred not to change to the new products or to wait to see how others get on with it. Similarly, we do not change to Emicizumab without one or more conversations with the patient and their verbal consent. We copy the patients into the correspondence with the GP and if we are considering changing products would give them product leaflets. (Exhibit)

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

174.2. This will vary depending on the nature of the treatment. It will be described partly in relation to their existing treatment which may have a similar or dissimilar side–effect profile. They will usually be given a leaflet describing their new product and the change will be discussed with them face to face unless the change is minor between two very similar brands.

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

174.3. Again, this will depend on the nature of the treatment and the natural history of the condition for which the treatment is being offered and their current clinical state. This would be discussed in clinic.

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

174.4. That depends on the condition being treated and the natural history of the condition for which treatment is being offered either with current treatment or no treatment, depending on circumstances.

175. Please describe how you typically record your patients' consent to treatment.

175.1. Written informed consent is only recorded for invasive investigative procedures, such as liver biopsy or endoscopy, surgery, or comparatively dangerous therapy such as chemotherapy and bone marrow transplantation.

175.2. For other treatments a record is made either in a clinic letter or in the notes or both of the conversation(s) with the patients and sometimes also relatives leading up to the start of treatment. Patients are copied into their correspondence. It is also worth pointing out that most of our treatments are routinely self-administered by the patient. If they don't like it or consent to it, they will not take it. Consent is thus implied, and the discussions recorded in the notes and GP correspondence copied to the patient.

176. Do you routinely take blood samples from patients attending the Manchester Centre? If so, what information do you provide to patients about the purposes for which the

samples are being taken? Do you obtain patients' consent to the storage and use of the samples and if so how and is that recorded?

176.1. The patients usually have blood samples taken at each visit. These will be described in very general terms or not at all if the samples are routine and taken each time. If it is a new patient, the tests will be described in a little more detail but again, usually very briefly and in very general terms. The results will be discussed with the patient if they influence management as a part of the treatment discussion.

176.2. Genetic testing is described in more detail and has a written consent.

177. Please describe how you typically (a) obtain and (b) record your patients' consent to testing (of any kind).

177.1. Formal consent for blood testing, with notable exceptions, is not obtained in any healthcare setting that I know. Exceptions include genetic testing, where there is a detailed formal consent process. It should be noted that although it was general practice to counsel patients for HIV testing in the 1980s and 1990s, it has been normal for some years now to conduct HIV tests without consent for all pregnant women. I am unaware of any clinicians, least of all Hepatologists, who would take consent to test for HCV.

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

178.1. About 40 patients still have HIV. The cohort with HCV is described in Q66 and only about 5 still have active HCV infection, it having been eliminated from the others.

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

179.1. I have responsibility for all the centre's HIV positive patients because I have the longest experience and because they are all followed in the one joint HIV clinic. These are and for many years have been jointly managed with an HIV physician. I have a Joint HIV Clinic with Dr Ashish Sukthanker every two months.

179.2. Although we do not have a formal joint Hepatology clinic, we have a longstanding close working relationship with Hepatology, which clinic runs adjacent to our multidisciplinary Wednesday clinic so that joint consultations do take place. Working closely with Hepatology, we have eradicated HCV from almost all of our patients. All antiviral treatment for hepatitis B and C is managed by them and they joint manage our patients with severe liver disease.

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

180.1. We have access to clinical psychology like any other speciality but without any special access or dedicated sessions. This is probably inadequate, difficult to access and seldom used. I would also say that the need for this had waned over the years since most patients had come to terms with their HIV and HCV but since the advent of the Infected Blood Inquiry.

180.2. Lack of adequate psychological support from clinical psychologists has been identified both locally in Manchester and nationally, through the Haemophilia Centre Peer Review system to be a widespread deficiency to be rectified. We have raised this issue with our management. It is one of the more intractable problems to deal with because the funding for Clinical Psychology goes through local authorities (over which we have no influence). In many parts of the country the same problem applies to social work but fortunately, in the North West of England, we have a good establishment of hospital-based social workers. No similar arrangement exists for Clinical Psychology.

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

181.1. We have a hospital social worker, a team of Haemophilia Nurse Specialists, Nurse Specialists from STD specialising in HIV, a team of physiotherapists and consultant Haematology staff, and a wider multidisciplinary team including consultants in HIV, Hepatology, Orthopaedics, Dentistry, Obstetrics and general and specialist Surgery. We have support from a specialist coagulation lab and a DNA laboratory.

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

a. *upon patients at the Manchester Centre (without identifying any individual patient);*

182.1. Infection with HIV was obviously a life-changing event for patients with haemophilia and for their families. This was compounded in Liverpool and Manchester because the patients were, rather insensitively, informed of their test result by post rather than in person and in the very early days not provided with the level of psychological support that they required.

182.2. To some extent this deficiency also reflected the very inadequate level of staffing found in most Haemophilia Centres outside London at that time (1985) and which was recognised by the provision of "AIDS Money" to build up the local infrastructure in 1988/89. Both my immediate predecessors in Manchester (Drs Richard Wensley and Dr Guy Lucas) directed the Haemophiia Centre part-time. Dr Wensley was employed 50% by the Blood Transfusion Service and Dr Lucas also managed 50% of the malignant Haematology in the Department. I was the first full-time Director of the Manchester Haemophilia Centre despite this being the second largest Haemophilia Centre in the country by patient numbers at the time. Centres in London of similar size had a full staffing infrastructure and two or three consultants at that time

182.3. For the patients and their families, the early years after HIV diagnosis were characterised by immense anxiety and uncertainty because the natural history of

HIV was unknown and there was no effective treatment. Bear in mind also that this is a small patient community and that many patients are networked with one another and so the impact of the death of one of their number is widely felt. Treatment was introduced in the late eighties but was relatively ineffective and was poorly tolerated with many treatment side-effects. Uncertainty is psychologically very difficult to deal with and many patients dealt with this by denial, - putting the condition to the back of their minds as much as they could. This in turn made outpatient visits very stressful for them because they would worry for days on end in advance of the visit about what the doctor might say. For the same reason, a few patients defaulted from follow-up for years and many patients constantly deferred the start of therapy, sometimes for years and often to the detriment of their health. It is impossible to put one's condition to the back of one's mind when constantly swallowing pills. Accepting treatment for either HIV or HCV was, therefore, a very big psychological step for many patients, and often taken with great reluctance.

182.4. The stigma around HIV, characterised by some in the media at the time as a "gay plague" and given a very high profile by public health campaigns ("Don't die of ignorance!") made things much worse for infected patients. Many patients felt that they needed to keep their HIV a secret, sometimes even from family members. Initial ignorance of the mode of transmission sometimes caused patients to be treated unnecessarily as highly infectious by non-haematology members of nursing staff in the early years. They would barrier nurse them and wear gowns and masks and gloves, all of which was unnecessary. An important part of the Haemophilia Nursing role at that time was to educate the rest of the hospital not to over-react and only to take precautions that were absolutely necessary when dealing with this patient group. Patients found this sort of over-reaction insensitive and upsetting. Even my Dentist became nervous of treating me because she knew that I managed patients with HIV. Many of my patients couldn't get a dentist willing to manage them at all. This sort of thing added to the sense of isolation that many patients and their families felt.

182.5. By the early 1990s more patients were dying from AIDS. Most of the patients who died from HIV died in the period 1990-1995. In 1994-95 15% of the entire cohort

died in a single year. It was awful. We became very skilled at keeping people alive despite full-blown AIDS and so by the time they died most had suffered four or five AIDS-defining illnesses and had a pretty miserable last year or so of life, enduring repeated hospital admissions and a slow decline. This was, by and large, born with bravery and stoicism. By 1995, we had an average of about 4 inpatients with bleeding disorders at any one time being managed for complications of AIDS.

182.6. When patients died from HIV, relatives were distressed that their relative was placed in a body bag. Months later, there would be an inquest. This fulfils a legal requirement since these were effectively iatrogenic deaths but also opened up old wounds and was often very distressing for the family and widely reported in the press.

182.7. When the first financial award was made to patients with HIV, many patients gave up their jobs. They did not expect to live long. One or two invested the money and refused to touch it, considering it tainted. Some others went on a world tour, expecting soon to die. Most eked the award out as long as they could. Those who gave up their jobs expecting not to live long found, after the advent of triple therapy in 1995, that their life expectancy had been relatively normalised but that they were now out of work. In this way, poverty was also added to the other problems that HIV positive patients had to endure. The operation of the Macfarlane Trust often made things worse since its awards were means-tested and patients found the whole process of applying for support utterly demeaning.

182.8. Triple therapy was introduced very quickly in Manchester in 1995 and had a miraculous clinical effect. Patients stopped dying more or less overnight. We no longer had in-patients with AIDS complications. Patients who had who were very, very ill recovered and a number of these patients remain well to this day.

182.9. When one speaks to patients who survived this period, one discovers that they all expected to die soon. They had come to terms with death to some extent. The sudden transformation of their life expectancy that resulted from the introduction of triple therapy brought unexpected psychological problems of its own. Many patients expressed survivor guilt, since so many of their friends and relatives had

died. Most had considerable difficulty readjusting to a normalised life expectancy, having come to terms with what they perceived to be the inevitability of death. This was a difficult adjustment partly because it appeared superficially paradoxical and relatives and friends didn't and probably couldn't empathise. The patients welcomed better treatment, of course, but still struggled with it psychologically. A high proportion of these patients and their families were deeply traumatised by the events of the previous decade. Most knew, were friends with or were related to patients who had died, often after a protracted struggle.

182.10. A number of female carriers from families devastated by HIV chose to abort affected male foetuses rather than have a child with Haemophilia even after the advent of recombinant factor VIII. Reassurance that the treatment was now safe did not influence this decision because the emotional association between haemophilia and AIDS was so strong that those families just didn't want to have anything to do with haemophilia ever again.

182.11. A number of young men with HIV chose to avoid emotional entanglements with girls altogether because it was all just too complicated. A very few just kept their HIV a secret and did not practice safe-sex despite all their counselling. There have been a small handful of celebrated cases of "rogue haemophiliacs" across the country that infected one or more girls in this way. Many partners of patients with haemophilia and HIV chose to avoid the risk of HIV transmission through sexual abstinence even though haemophilia centres provided barrier contraception. As one wife said to me in the early 1990s "Every time I do it I think this could be killing me." Some marriages broke up and most were strained.

182.12. Couples with an HIV positive husband were advised not to have children because of the risk of HIV transmission to their partner and possibly to the child if the partner became infected. Those determined to have children were offered HIV transmission minimisation strategies and provided with predictor kits so they only had unprotected intercourse at the time of ovulation. One way or the other, few children were born to this group, which must have been a great source of sadness for them.

182.13. As time passed, treatment of HIV improved and most HCV was eradicated. Patients adjusted to their normalised life-expectancy, my perception is that most affected patients and their families slowly came to terms with their HIV and HCV, as far as it is ever possible to do so. I would compare this to a close bereavement such as the loss of a parent or child or to the loss of a limb. You never come completely to terms with the situation and the pain never goes away but as time goes by, it doesn't hurt quite so much. It isn't quite so bad. This is what most people need to be able to do to get on with their lives as best they can.

182.14. As a very broad generalisation, HCV had much less impact. In the absence of a big public health campaign there was far less awareness of the condition amongst the general public. The condition was not readily sexually transmitted and though the risk groups for HCV were exactly the same as for HIV that was not the general public perception. Furthermore, when a test became available, most (but not all) patients knew they had chronic liver disease and the natural history of the condition was generally already known and it was possible to offer most patients who did not have serious liver disease some form of qualified reassurance. We knew that in the absence of cofactors for HCV progression (HIV and alcohol and immunodeficiency) that the condition progressed slowly if at all. By the time we got a test in the early 1990s patients had been infected for up to a quarter of a century. It would be wrong to say that patients didn't worry about HCV because they undoubtedly did but not as much as they worried about HIV. Furthermore, from the mid-1990s we were curing people of HCV and we were optimistic that we would, as treatment improved, eventually cure most of them. We have never been in that position with HIV.

182.15. Clearly, the above generalisations do not apply to the unfortunate minority with severe liver disease. Many of these were co-infected with HIV. During the early 1990s 75% of those dying from complications of HCV also had full blown AIDS. Their liver disease progressed very rapidly as a direct consequence of their immunodeficiency. For patients with severe liver disease, their liver disease was a very major concern and if they were co-infected this also complicated their treatment for HIV since most of the drugs are metabolised by the liver. These patients were jointly managed by HIV Physicians and Hepatology. There is a jointly

managed HIV/Hepatology Clinic.

182.16. These are also the patients at risk of developing hepatocellular carcinoma, which may complicate cirrhosis from any cause, but particularly viral cirrhosis. All patients with chronic HCV in our practice are regularly monitored by ultrasound every couple of years and alpha fetoprotein at every visit. The weakness of this regimen, which is standard and acknowledged to be a reasonable compromise, is that hepatocellular carcinoma (HCC, Hepatoma) can arise quickly between ultrasound examinations and alpha fetoprotein is often a late marker of HCC, increasing only when the carcinoma is well developed. Furthermore, it can be difficult radiologically to tell the difference between an early hepatoma and a cirrhotic regenerative nodule. Patients with macronodular cirrhosis have a liver full of regenerative nodules. These and hepatomas both look like spheres in the substance of the liver and can be difficult to tell apart. For that reason, once HCC is suspected it can sometimes take weeks for hepatology to confirm the diagnosis.

182.17. Understandably, contracting HIV and HCV and the way that this was communicated affected some patients' trust in the medical profession. Most patients accepted that they were infected before these viruses were recognised and that whilst this was unquestionably a tragedy that it was largely not preventable. Many patients had their trust in the medical profession badly shaken but slowly learned that they could trust their doctors. This trust had to be earned by taking time to talk to patients and their relatives and by being completely open.

182.18. At the other extreme, a few patients and/or their relatives never trusted any member of the medical profession ever again. Consequently, many were unduly sceptical about medical advice and therefore selective in the medical advice that they chose to believe or accept which complicated their management and sometimes led to undesirable delays in starting antiviral treatment.

182.19. Trust between doctor and patient is a two-way thing and is an absolute pre-requisite for optimal patient management, especially when treatment escalation is to be considered and when things are going badly from the clinical perspective. Patients and their relatives who are angry and confrontational towards the team

managing them make it more difficult for the team to provide emotional support when the patient and their family need that support the most. Fortunately, there are very few patients and relatives who react in this way.

b. *The ways in which decisions about treatment and care are taken, and treatment and care are provided, at the Manchester Centre?*

182.20. The difficult patient journey this group has taken through the last 40 years should be born in mind. Most are, understandably, more questioning than average patients given that they may feel that they have been "let down" in the past. They are also a very educated and well-informed group and are used to managing their own condition. For that reason, it is important to give them the time to discuss things thoroughly, to understand what one is trying to achieve with treatment and to ensure that they fully understand the pros and cons of new treatment or treatment regimens and enable them to make informed decisions and not to rush them into treatment decisions. I encourage them to sleep on things and agree to revisit the question at the next visit. They have to understand and buy into what you recommend that they do. Treatment cannot be initiated unless the patient agrees to it. Unfortunately, in some cases, patients defer desirable treatments for far too long and sometimes default from follow up to avoid decisions they might have wished to avoid, such as the start of anti-retroviral treatment. This can result in treatment starting later than one would wish despite a great deal of effort and discussion.

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

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

183.1. Given that I have been managing patients with HIV and HCV for 37 years i.e. almost my entire medical career, this isn't an easy question. I would like to think that I have always been a sympathetic and empathic doctor and that I have always sought to obtain the best treatment for my patients and improve their quality of life wherever I can. This would have been the case even had HIV and HCV not been there, I suspect. In the absence of blood born viruses there would have been much

less impetus to develop recombinant clotting factors gene therapies and other alternative treatments. Furthermore, without HIV and HCV we would have struggled to fund an adequate staffing infrastructure for haemophilia care.

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

183.2. I am unable to answer on their behalf since this is a personal matter.

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

183.3. HIV and HCV were at the time unprecedented medical tragedies and it was recognised in the mid-1980s that the existing Haemophilia Centre infrastructure was inadequate in most centres to deal with this. Money was therefore made available to employ more people and properly establish multidisciplinary comprehensive care. This led to enormous improvements in the staffing of Haemophilia Centres and the treatment-intensity and type of therapeutic products used to treat the patients. Haemophilia is one of the most expensive conditions to treat, costing an average in excess of £100,000 per patient per year. Life expectancy of patients with haemophilia has improved and now approaches normal. Without the political influence which arose as a direct consequence of these tragedies, it would have been far more difficult, if not impossible, to persuade DH and local commissioners to fund this.

183.4. Campaigners often complain that insufficient consideration has been taken of the iatrogenic nature of their HIV and HCV. My perception is that successive administrations, whilst not exactly acceding to every request, have nevertheless regarded the arguments proffered by the wider haemophilia community with a good deal more sympathy than would otherwise have been the case. However, as a result of their plight, there is no doubt that the haemophilia community had far more influence over the years than one might expect for a group of fewer than 3000 patients.

Section 12: Other Issues

184.In a letter dated 17 November 2005 from you to William Connon at the Department of Health [HSOC0020017], you stated that "Many centre directors are already fighting a low grade guerrilla war with patient activists who want a hepatitis C public enquiry and who are reporting their centre directors to the GMC and manipulating both newspapers and television". Why did you write in these terms? What did you mean by "a low grade guerrilla war"? What did you mean by "manipulating both newspapers and television"?

184.1.The letter needs to be read as a whole in order to properly understand the context in which these comments were made. I have reproduced it below for ease of reference. This was a deliberately strongly worded letter, which I wrote in my capacity as Chairman of UKHCDO to report the sentiment of the UKHCDO membership. This letter was reviewed and edited by the UKHCDO Executive Committee before being finalised and sent out.

184.2.We had reached the end of the recombinant rollout and it emerged that the funding provided for the rollout was not necessarily going to continue. It was discussed that it might be "bundled" with other items. "Bundling" invariably involves inviting commissioners to pay for a bundle of items for less than the total cost of those items i.e. it is a budget cut by any other name. This raised the very real prospect that the recombinant rollout would be rolled back and we would have to change patients back to plasma-derived products. William Connon at DH was having to bid for more money and was not unsympathetic and the purpose of this letter was to strengthen his negotiating hand within DH.

184.3.I took the opportunity to remind DH that the beginning of the rollout had been delayed by a judicial review sought by HIV positive patients.

184.4.My comments about "low grade guerrilla warfare" relate to the strategy then being pursued by a small group of campaigners to gain greater recompense. The comparatively generous Southern Irish Settlement (WITN3289163,

WITN3289164, WITN3289165, WITN3289166 and WITN3289167) breathed new life into their campaign. They have campaigned ever since for recompense on a similar scale.

184.5. At the time in question, they were pressurising their doctors in various ways in the belief that this would apply pressure indirectly on DH. They were doing this by going to the press and media (WITN3289168: Newsnight transcript), by attempting ongoing litigation and by reporting their Centre Directors to the General Medical Council for alleged misdemeanours that had, as far as I could see, no basis in fact. Two complaints of this nature were lodged against me and are discussed in a later section. This strategy served only to alienate otherwise sympathetic doctors around the country. Apart from causing a great deal of work and distress for the doctors concerned, this strategy achieved nothing because both the employing Trust and DH distanced themselves from all doctors being investigated by the GMC.

185. In April 2007 you sent two emails to the Archer Inquiry (enclosed [ARCH0000867]), stating *"I think it is inevitable that some of your witnesses will give evidence which is both defamatory and untruthful"* and *"If you print a transcript which is libellous, which seems likely to happen given the past history of your early witnesses, then are you not publishing a libel …?"*

a. Why did you write to the Archer Inquiry in these terms?

185.1. I have reflected at length on these e-mails, the tone and wording of which I now accept was intemperate and which I regret. I was concerned that the Archer Inquiry would lack balance. Evidence was not taken under oath and the witnesses were not cross-examined. The witnesses were self-selected and there was little representation from other stakeholders such as the medical profession.

185.2. It seemed likely that campaigners would use this opportunity to repeat inaccurate allegations which they had made before in litigation and in complaints to the GMC and which would not be fact-checked and that those accused would have no

opportunity to respond. This process appeared contrary to natural justice.

b. What *did* you mean by the *"past history of your early witnesses"*? To whom were you referring?

185.3.I was referring to a small group of long-term campaigners who had repeatedly made allegations which were incorrect – see below.

c. *Why did you think it was "inevitable" that some witnesses to the Archer Inquiry would give "defamatory and untruthful" evidence? What evidence given to the Archer Inquiry do you claim was defamatory and/or untruthful?*

185.4.A minority of campaigners for recompense had sought to strengthen their case by repeating allegations against the haemophilia community in general or their doctors in particular which were incorrect. It seemed inevitable that some (but not all) campaigners would repeat the allegations they had been making over many years. Some examples of these are:-

185.4.1. "*Over 2000 patients have died from HCV".* This is a misrepresentation of UKHCDO statistics often repeated even though I, as the author of this statistic, have repeatedly pointed out their error. During the 50 year period that is referred to in this statistic, over 2000 patients with Haemophilia have died *from all causes* and not from HCV. Whilst one death from HCV is too many, far fewer have died than is commonly reported by campaigners to the media.

185.4.2. "*My doctor kept my HIV a secret for three years.*" Witnesses who report this will usually agree that they were informed of their HIV result in 1985 when the test became available. The less informed patients may not understand that we can sometimes tell them that they were infected in 1982 by retrospectively testing stored samples.

185.4.3. *"My doctor kept my HCV a secret for 12 years".* This was a common complaint made to the GMC in 2004/5. There was invariably abundant

documentary evidence that such an allegation was incorrect.

185.4.4. *"My doctor gave me HIV deliberately to see what would happen*". This allegation has, as far as I know, only been levelled at Prof CA Ludlam and is incorrect. The circumstances surrounding the Edinburgh HIV outbreak are well documented and have been widely reported. Prior to the advent of HIV testing, a single rogue donor, who ignored the donor selection process designed to exclude high risk donors, donated a unit of blood which was used to manufacture a batch of factor VIII concentrate. This was very sadly administered to 27 patients with Haemophilia most, but not all, of whom contracted HIV. The only positive effect that resulted from this tragedy was that it provided an opportunity to study a group of men whose date of first exposure could be determined retrospectively and whose dose of factor VIII could be worked out. A great deal was learned from this dreadful episode about the infectivity and natural history of HIV.

186.In the enclosed letter from Dr Joanne Kennedy (of 'Novo Nordisk') to you dated 3 July 2001 [HCDO0000013_023], reference is made to your "long-standing relationship with Charles Lister at the Department of Health" and that "he regularly seeks your advice on matters relating to Haemophilia". Please provide details of any advice sought by, or provided to, the Department of Health by you on matters relevant to the Inquiry's Terms of Reference.

186.1.I was only Vice Chair of UKHCDO at that time that this letter was written. I had attended odd meetings with DH with Prof Hill. Prior to Dr Hill's chairmanship (1999-2005) UKHCDO had no real relationship and very little dialogue with DH. It was one of Prof Hills' achievements that I sought to build on during my own chairmanship (2005-11) that we established a regular dialogue with DH. One cannot act as patient's advocate without an active dialogue.

186.2.In the late 1990s and early 2000s, dialogue was, as I recall, mainly about "Recombinant for all" and recompense for patients infected with HIV and HCV.

187. *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. (Please note that the Inquiry is aware that complaints were made to the General Medical Council by* GRO-A *and by* GRO-A *).*

187.1. There have been no complaints about me to the health service ombudsman and the only complaints I can think of that have any relevance for this inquiry are the two complaints to the GMC identified below. I will summarise these here but they are described in more detail in the contemporary reports I wrote, which are attached as WITN3289169, WITN3289170 GRO-B . Both complaints were ultimately determined to be without foundation, but any referral to one's professional regulator is inevitably both worrying and upsetting.

187.1.1. Mr GRO-A has severe haemophilia A. He originally complained to the Trust that there had been a breach of confidentiality in that our Haemophilia Centre Social Worker had asked me for clinical details to help her write a letter of support for Mr GRO-A 's claim for a higher rate allowance. He had claimed a far higher level of disability than he actually had. As is the case with hospital complaints, we had a meeting involving him, me, the Chief Executive and Head Nurse. During this meeting we told him it was normal for the team to discuss cases such as this and this was not a breach of confidentiality. He accused me of being unsupportive and I said that I was happy to support valid claims but could not support his claim because he was claiming disabilities that he did not have. He was extremely abusive and we agreed that I would no longer be able to look after him and I transferred his care to Liverpool. He lived halfway between the two centres.

187.1.2. A week after that meeting, he complained to the GMC that I had kept his HCV a secret for 12 years. I provided extensive documentary evidence that: -

187.1.2.1. He had been informed by my predecessor of his HCV antibody positivity 2 years before I took up post.

187.1.2.2. I had discussed HCV with him the first three times we met.

187.1.2.3. I had also informed him when an antigen test came along, that he had cleared HCV spontaneously.

187.1.3. Nevertheless, and in the absence of any evidence from Mr GRO-A other than the statement "*I know what I remember.*" the GMC investigation persisted for roughly two years before the complaint was closed without action. I continued to practice without restriction during the protracted investigation. This was the period when a number of Haemophilia patients across the country were reporting their doctors to the GMC.

187.1.4. Mrs GRO-A was the widow of one of my patients who had severe haemophilia A, GRO-B

GRO-B

GRO-B

187.1.5. GRO-B

187.1.6. Eight years later, when Haemophilia Centre Directors were being referred to the GMC, she repeated these allegations to the GMC. The GMC concluded the complaint without a hearing and with no further action.

187.1.7. Despite the complaints I remained in unrestricted practice throughout the GMCs investigations.

188.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.

188.1.One of the witnesses to the Inquiry, and not the relative of any of my past patients, has raised the issue of Palliative Care with me. This is not listed as one of the issues to be considered by the Inquiry.

188.2.Her father died from hepatocellular carcinoma secondary to the HCV he contracted through treatment for haemophilia. He died in distressing circumstances and was largely cared for by his daughters without much assistance from palliative care. Having been cared for over most of his life by the local Haemophilia Centre, his care will have largely devolved to Hepatology for the specialist care of the hepatocellular carcinoma from which he died. This raises several issues.

188.3. Firstly, patients and their relatives, used to dealing with Haematology may express feelings of abandonment when Hepatology take over and manage the HCC.

188.4. Secondly, when the time comes, Hepatology should in my opinion liaise with the GP and end-of life services since they are the ones actively managing the condition. This needs to involve the GP and to be coordinated. This is not always well done. In some cases, a hospice will be the most appropriate provision. In other cases, the patient may prefer to die at home and a package of care should then be provided, again this is usually coordinated by the GP working with the hospital. Relatives need help to navigate all this and they also need emotional support. This is a very difficult time for all concerned.

188.5. End-of-life care is a specialised area of medicine and nursing. The provision of Palliative Care is unfortunately patchy across the country. It can be excellent but in other cases is not provided at all.

1.3.

Statement of Truth

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

Signed GRO-C

Dated 7/10/2020

Table of exhibits:

Description	WITN number
Products used, Manchester, Liverpool and Sheffield V2	WITN3289040
UKHCDO Therapeutic Guidance 24.6.83	WITN3289041
UKHCDO Therapeutic Guidance December 1984	WITN3289042
Hay CRM procurement paper 2013	WITN3289043
1988 Therapeutic Guidance	WITN3289044
Figure 1 UKHCDO Annual Report 1986	WITN3289045
Craske Pavier Trowell bmjcred00584-0020	WITN3289046
Rizza life-expectancy bmjcred00545-0017	WITN3289047
1997 therapeutic guidelines	WITN3289048
Aledort 1985	WITN3289049
Hay 1987 blood	WITN3289050
Lancet correspondence 1985	WITN3289051
Life expectancy of Haemophilia Mejia-Carvajal et al J Thrombosis Haemostasis	WITN3289052
Farrugia Blood Transfus 2018	WITN3289053
GeneticLeaflet	WITN3289054
GeneticConsent	WITN3289055
Hay et al Didanosine for HIV	WITN3289056
Hay et al IL2 suppression by concentrate	WITN3289057
Hay et al High Purity VIII and HIV j.1365-2141.1998.00753.x (1)	WITN3289058
Initial letter describing rollout April 2003	WITN3289059
first DOH WP minutes	WITN3289060
Minutes DOH subgroup (procurement)	WITN3289061
tender letter to Haem Centres from Prof Hill Re Rollout 2003	WITN3289062
Letter Hill to Gutowski 31.7.03	WITN3289063
Final recombinant tender letter	WITN3289064
summary of awards	WITN3289065

Summary of Offers recombinant rollout 2003	WITN3289066
Recombinant rollout 2003-4 audit report	WITN3289067
Recombinant rollout audit report 2004-5	WITN3289068
National Procurement initial DH meeting Aug 2005	WITN3289069
Transfusion Leaflet 1990s	WITN3289070
GRO-B	GRO-B
GRO-B	GRO-B
Alprolix-Informationbooklet-1	WITN3289073
Elocta-infobookletpt	WITN3289074
Elocta-instructions	WITN3289075
Idelvion-Resource	WITN3289076
Idelvion-Instructions	WITN3289077
Refacto-infobookletpt	WITN3289078
Novoeight-Instructions	WITN3289079
voncento-infobookletpt	WITN3289080
Hemlibra-InfoPt-1	WITN3289081
UKHCDO Constitution 1991_09	WITN3289082
UKHCDO Annual Report 2019_forEmail	WITN3289083
Collins_Blood_2014 (2) PUP Study	WITN3289084
Novoseven postmarketing 2017	WITN3289085
Refacto PUP study 2018	WITN3289086
EMA Recombinant meta-analysis 2019	WITN3289087
Your questions answered 2001	WITN3289088
Cover Letter for 2002 Patient Information Leaflet	WITN3289089
Your questions answered 2007	WITN3289090
Cover Letter for 2013 Patient Information Leaflet	WITN3289091
2015 Your Questions Answered - Patient Information Leaflet from the NHD	WITN3289092
Your Questions Answered - 2013	WITN3289093
2015 Cover letter for NHD&Haemtrack leaflets packs	WITN3289094
Haemtrack Leaflet 2015	WITN3289095
Your questions answered 2019	WITN3289096

Covering letter 2018 NHD General Information Leaflet	WITN3289097
Ethics approval for NHD	WITN3289098
NHD_Research database_protocol v7.1 (19.2.19)	WITN3289099
Consent slide deck 7.11.19	WITN3289100
information Child 6-10 yrs	WITN3289101
Child_consent aged 5--10yrs	WITN3289102
consent form aged 11-16yrs	WITN3289103
Information sheet aged 11-16yrs	WITN3289104
Assent form UK_NHD_Young Person_(11-15yrs) Assent form final	WITN3289105
consent form _Gillick competent YoungPerson_(11-15) Patient information sheet (2	WITN3289106
. Adult Pt information sheet.	WITN3289107
Adult consent form	WITN3289108
BMJ Article 2002	WITN3289109
2004 vCJD and Plasma Products - Recommendations of the CJD Incidents panel	WITN3289110
9.9.04 UKHCDO - Letter to accompany Toolkit etc	WITN3289111
vCJD and Plasma Products - Recommendations of the CJD Incidents panel	WITN3289112
vCJD and Plasma Products - Text insert & Tables of vCJD implicated batch numbers	WITN3289113
2004 CJD Incidd=cient panel vCJD and Plasma Products - Clinical Information	WITN3289114
vCJD and Plasma Products - Information for Patients	WITN3289115
. vCJD and Plasma Products - Patient vCJD Exposure Assessment Form (H1.0)	WITN3289116
vCJD and Plasma Products - Summary of Patient Notification exercise	WITN3289117
. vCJD and Plasma Products - Enquirer Handling Protocol	WITN3289118
vCJD and Plasma Products - Media Handling	WITN3289119

Protocol	
2009 From FGHH follow on post mortem finding 2009-04-01	WITN3289120
Actions for healthcare staff-Februry 2009	WITN3289121
Actions for healthcare staff-Februry 2009	WITN3289122
Centre letter vCJD 8.6.09	WITN3289123
From FGHH follow on post mortem finding 2009-04-01	WITN3289124
Risk Calculation DH 2009.	WITN3289125
Information for Patients-generic-February2009	WITN3289126
Information for Patients-specific-February 2009	WITN3289127
letter to UKHCDO doctors-090609-FINAL	WITN3289128
Patient letter-090609-FINAL	WITN3289129
vCJD and Plasma Products - Haemophilia Doctors letter-February 2009	WITN3289130
vCJD and Plasma Products - Patient Groups letter-February 2009	WITN3289131
vCJD and Plasma Products - Patients letter-February 2009	WITN3289132
vCJD Cover letter 2009-02-16	WITN3289133
2010 vCJD notification letter	WITN3289134
Royal Free false notiofication vCJD lookback report - haemophilia - march 2010	WITN3289135
2013 01 24 LETTER_HPA to UKHCDO	WITN3289136
2013 02 04 Reassessment of vCJD	WITN3289137
2013 Dear colleague UKHCDO letter v6 Final	WITN3289138
2013 Dear colleague UKHCDO letter v6 Final	WITN3289139
II. Notification Form	WITN3289140
. III General Information Sheet	WITN3289141
V. Negative Investigations	WITN3289142
2001 0910 London MREC Approval	WITN3289143

2001 Ethics application vCJD 0103 London MREC	WITN3289144
2002 vCJD surveillance Study Frank Hill letter	WITN3289145
2003 0225 London MREC updated	WITN3289146
2006 0510 London MREC updated approval	WITN3289147
20070622 London MREC updated approval	WITN3289148
frank hill letter	WITN3289149
next-of-kin_consent_for_post_mortem_ON_HEADED[1]	WITN3289150
letter re study	WITN3289151
vCJD Notif - Updated MREC 07 06 22	WITN3289152
Stage2appform	WITN3289153
Advisory Comm Mtg Mins 17 Jan 2011-1	WITN3289154
Advisory Comm Mtg Mins 1 Jul 2011	WITN3289155
Advisory Comm Mtg Mins 3 Oct 2011 (12th AGM)	WITN3289156
Proposal to DH for Hep C lookback	WITN3289157
Appendix to Proposal to DH for Hep C lookback	WITN3289158
Minutes of Haemophilia Alliance	WITN3289159
Letter to members July 2011.	WITN3289160
Letter to members Autumn 2011.	WITN3289161
Hepatitis C Look-back report 2013-14	WITN3289162
2002 Irish Settlement	WITN3289163
Haemophiliac compensation deal agreed	WITN3289164
Irish Award 2,6 M	WITN3289165
Southern Irish Tribunal report	WITN3289166
Belfast Telegraph Disparity in awards	WITN3289167
Newsnight_17.04.07	WITN3289168
Mr GRO-A response to hospital complaint	WITN3289169
GMC GRO-A	WITN3289170