Witness Name: Professor Gordon Lowe
Statement No.: WITN3496013
Exhibits: WITN3496014-16
Dated: 29 October 2020

INFECTED BLOOD INQUIRY

SECOND WRITTEN STATEMENT OF PROFESSOR GORDON LOWE

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 14 April 2020.

I, Professor Gordon Lowe, will say as follows: -

Section 1: Introduction

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

1.1. My name is Professor Gordon Douglas Ogilvie Lowe.

1.2. My address is c/o Central Legal Office, Edinburgh.

1.3. My date of birth is GRO-C 1949.

1.4. I hold the following professional qualifications: -

1.4.1. MB,ChB (with Honours and gold medal) 1972, University of Saint Andrews

1.4.2. MRCP UK 1974

1.4.3. JCHMT Completion of Training in General (Internal) Medicine 1980

1.4.4. MD by Thesis (with Commendation) 1984, University of Dundee

1.4.5. FRCP (Edinburgh) 1986

1.4.6. FRCP (Glasgow) 1986

1.4.7. FRCP (London) 1989

1.4.8. FFPHM (Honorary) 2001

1.4.9. DSc by Thesis (Medicine) 2006, University of Glasgow

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

2.1. 1 August 1972 – 31 January 1973. Junior House Officer in Surgery, University Department of Surgery, Dundee Royal Infirmary (Professor Sir Donald Douglas). General and vascular surgery.

2.2. 1 February 1973 – 31 July 1973. Junior House Officer in Medicine, University Department of Therapeutics, Maryfield Hospital, Dundee (Professor James Crooks). General medicine.

2.3. 1 August 1973 – 31 October 1974. Senior House Officer in Medicine Rotation, City Hospital, Nottingham. General medicine, including cardiology and coronary care, gastroenterology, nephrology, diabetes and infectious diseases.

2.4. 1 November 1974 – 31 December 1977. Registrar in General Medicine, University Department of Medicine, Royal Infirmary, Glasgow (Professor

Edward McGirr). Clinical general medicine (50%), including haemophilia (1% of clinical practice) and thrombosis, endocrinology and coronary care. Teaching and research (50%).

2.5. 1 January 1978 – 30 September 1985. Lecturer in Medicine, University of Glasgow Department of Medicine, Royal Infirmary, Glasgow (Professor Arthur Kennedy); and Honorary Senior Registrar in Medicine. Teaching and research (50%). Clinical general medicine (50%), with interests in thrombosis and haemostasis (haemophilia 1%) and vascular medicine.

2.6. 1 October 1985 – 30 September 2009. Senior Lecturer in Medicine, University of Glasgow, Department of Medicine, Royal Infirmary, Glasgow (Professors Arthur Kennedy, then from 1990 James McKillop). Promoted Reader in Medicine (1992-1993), then Personal Professor of Vascular Medicine (1993-September 2009).

2.7. Honorary Consultant Physician, Glasgow Royal Infirmary (December 1985-September 2009). Teaching and research (50%). Clinical general medicine, thrombosis and haemostasis (including haemophilia, 10%), and vascular medicine (including stroke and peripheral vascular diseases).

2.8. 1983-2009. Honorary Lecturer, then Honorary Professor from 1995, Bioengineering Unit, Faculty of Engineering, University of Strathclyde.

2.9. October 2009 – present. Emeritus Professor and Honorary Senior Research Fellow, Institute of Cardiovascular and Medical Sciences, University of Glasgow.

2.10. West of Scotland Haemophilia and Thrombosis Centre, Glasgow Royal Infirmary (GRI)

2.10.1. Assisting (as Senior Lecturer and Honorary Consultant Physician), Dr Charles Forbes, Reader and Honorary Consultant

Physician, who was Co-Director with Dr George McDonald, Consultant Haematologist (December 1985-1987).

2.10.2. Co-Director with Dr McDonald (1988-1990), liaising with Dr John Davidson, Consultant Haematologist with interest in haemostasis and thrombosis and who was in charge of Blood Bank, including ordering of blood products; and with Dr Isobel Walker, Consultant Haematologist with interest in haemostasis and thrombosis (including women and children at Glasgow Royal Maternity Hospital).

2.10.3. Co-Director with Dr Walker (1991-September 2009); and also with Dr Campbell Tait, Consultant Haematologist with an interest in haemostasis and thrombosis (2000-September 2009). After Dr Davidson retired in 1996, Drs Walker and Tait were in charge of Blood Bank, including ordering of blood products and recombinant clotting factor concentrates.

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

3.1. I have been a member of the following committees, associations, societies or groups:

3.1.1. Scottish Society of Physicians, member 1979-.

3.1.2. Scottish Society of Experimental Medicine, member 1979-2009.

3.1.3. Association of Physicians, member 1979-.

3.1.4. Medical Research Society, member 1979-2000.

3.1.5. Royal Society of Medicine. Member and committee member of Forum on Clinical Haemorheology 1982-1987, chair 1985-1987. Member and committee member of Forum on Angiology 1986-1995, chair 1991-1995.

3.1.6. British Society for Haematology, member 1980-; Scientific Advisor 1994-97; member, Working Party on Fibrinogen 1995-2001.

3.1.7. British Society for Haemostasis and Thrombosis, member 1982-; committee member 1988-92; President 1990-1991.

3.1.8. International Society for Thrombosis and Haemostasis, member 1982-; Co-Chair, Subcommittee on Haemostatic Variables in Prediction of Thrombosis 1990-93 and 2004-07; Vice-President 2001-2003; Senior Advisory Member (2003-); Investigator Recognition Award 2009.

3.1.9. Scientific Services Advisory Group, Scottish Home and Health Department, member 1987-88.

3.1.10. UK Haemophilia Centre Directors (then Doctors) Organisation (UKHCDO), member of Steering Group/Executive committee 1988-2009; organiser of Comprehensive Care Centre national audit 1992-2000.

3.1.11. Scotland and Northern Ireland Haemophilia Centre Directors (SNIHCD) Group, member then co-chair 1988-2009. Including attending annual meetings with Scottish Home and Health Department (SHHD) and Scottish National Blood Transfusion Service (SNBTS); and meetings of their Factor VIII Working Party (renamed Coagulation Factor Working Party) 1988-2009.

3.1.12. Member, Scottish National Blood Transfusion Association (mid-1990s, dates uncertain).

3.1.13. Glasgow Royal Infirmary Stroke Service Development Group, chair 1993-97.

3.1.14. RCPE – Deputy Assessor 1993-99, organising UK Consensus Conferences including: fibrinogen and cardiovascular disease, platelet transfusion, rhesus haemolytic disease, autologous bone marrow transplantation, stroke, atrial fibrillation, misconduct in medical research, and lipids and cardiovascular disease. Assessor and member of Council 1999-2003, chairing Audit and Research Committee (for clinical audit, research, and development of clinical standards). Co-Chair, RCPE/RCPSG Bicollegiate Committee on Clinical Standards, 2000-2003.

3.1.15. Health Sciences and Public Health Research Committee, Chief Scientist Office, Scottish Home and Health Department, member 1995-99.

3.1.16. British Heart Foundation, Research Committee, member 1995-99.

3.1.17. Clinical Audit and Resources Group (CRAG), Scottish Office Home and Health Department, member (and member of its Clinical Outcomes Subcommittee) 1996-2002.

3.1.18. NHS Scotland Recombinant Factor VIII / Coagulation Factor Consortium, member, 1997-2009.

3.1.19. Scottish Intercollegiate Guidelines Network (SIGN). Chair of first clinical guideline on prophylaxis of venous thromboembolism 1993-1995; Chair of clinical guideline on antithrombotic therapy 1996-1999; RCPE member of Council 1998-2003; Chair of Council 2002-2007.

3.1.20. Clinical Outcomes Group, NHS Quality Improvement Scotland, member 2003-2008.

3.1.21. Chest Heart and Stroke Scotland (Charity), member of Board and member of Research Committee, 2010-2019.

3.1.22. Scottish Society for the History of Medicine, member 2014-, member of committee 2015-, Vice-president 2020-.

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 the 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 that you provided, other than those that are provided with this letter.**

4.1. Together with other Haemophilia Centre Directors in Scotland, I participated in a few meetings with the Scottish Executive Health Department as part of their inquiry, "Hepatitis C and heat treatment of blood products for haemophiliacs in the mid- 1980s", published in October 2000.

4.2. Together with other Haemophilia Centre Directors in Scotland and England, I participated in the Penrose Inquiry – as a member of the Scottish Health Boards' Haemophilia Directors Working Group (HDWG) 2010-2015, working with the Central Legal Office (CLO) for NHS Scotland; and provided written and oral evidence to the Inquiry. The Penrose Inquiry reports were published in 2010 and 2015 and are available on its website. I understand that any statements or reports that I provided for the Penrose Inquiry have been, or can be, provided to you by Central Legal Office.

5. **Please consider the evidence that you gave to the Penrose Inquiry, which is attached to this letter. Please confirm whether the contents of the above statements and oral evidence are true and accurate. If there are any matters contained in the above statements or in the oral evidence you provided to the Penrose Inquiry that you do not consider to be true and accurate, please explain what they are.**

5.1. I have read the attached evidence, and I confirm that, to the best of my knowledge and belief, in general their contents are true and accurate. Any specific matters which I do not consider true and accurate I have discussed in the relevant sections of this document. If I have in the past decade become aware of new evidence, I update my evidence given to the Penrose Inquiry in this document.

5.2. The Penrose Inquiry Preliminary Report (2010), publicly available on the Penrose Inquiry website, examined a large volume of documentary material, published and unpublished, and had the advice and assistance of independent experts in the relevant fields of medical science and technology as well as the assistance of many patients and relatives of patients who agreed to be interviewed by the inquiry staff (page 2, 1.4). For many of the questions you ask, I have referred you to relevant sections of both this Preliminary Report, and the Penrose Inquiry Final Report (2015). I have reviewed the written and oral evidence given to the Penrose Inquiry, and found it of considerable assistance in the preparation of this statement.

5.3. At this point, I wish to state that, during the Penrose Inquiry (2010-2015) I and my fellow Haemophilia Centre Directors had access to many relevant documents to which we could refer when preparing our evidence. Unfortunately, since you sent me this request on 14 April 2020, the UK-wide COVID-19 lockdown has prevented me accessing many of these documents from their relevant archives. The Central Legal Office advises me to state as a caveat that there are many of these documents that I still wish to see to allow this response to be complete and accurate, but which the CLO has been unable to provide to me at present. Accordingly, I may wish to modify this draft

statement if I obtain access to relevant documents which provide additional information to those which I have access to at the present time.

Section 2: Decisions and actions of those treating patients with bleeding disorders at the Glasgow Royal Infirmary

6. Please describe the facilities, organisation, roles, functions and responsibilities of the haemophilia centre ("the Centre") at the Glasgow Royal Infirmary ("the GRI") during the time that you worked there, and how they changed over time. In respect of this question, and those that follow, the Inquiry is aware of the evidence that you gave to the Penrose Inquiry on this matter, to which you should feel free to make reference.

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

8. Please describe your role and responsibilities at (i) the GRI, and (ii) the Centre and how those changed over the years.

a. In your evidence to the Penrose Inquiry, you explained that you had clinical and professional responsibilities beyond the treatment of patients with haemophilia, and that these varied over the years in which you worked at the GRI. In respect of each stage of your career, please set out how much of your time (approximately) would be spent treating patients with haemophilia.

8.1. There is much overlap in these three questions, so for clarity I will answer them together, in chronological sequences from 1975 to 2009.

8.2. The IBI has recently asked me, through the Central Legal Office, to prepare a list of all previous GRI Centre Co-Directors, which I have provided. For the further assistance of the Inquiry, it may be helpful to the Inquiry for me to describe also the earlier development of the Centre from 1950 to 1975.

8.3. Since 2014, I have become interested in Scottish medical history, as a member of the Scottish Society for History of Medicine, of which I am currently Vice-President. I recently co-edited a history of the development of 40 clinical specialties in Glasgow and the West of Scotland since NHS Scotland was founded in 1948. Through the collaborations of the University of Glasgow's Medical Faculty, NHS Scotland (Western Regional Health Board and from 1974 its subsequent component Health Boards), and the Royal College of Physicians and Surgeons of Glasgow, each of these 40 specialties achieved national and international recognition (1). In this history, I co-authored with colleagues the sections on the University Department of Medicine and the Department of Haematology at GRI, including their collaborative Haemophilia and Thrombosis Centre.

8.4. **GRI Haemophilia and Thrombosis Centre Development, 1950-1975**

8.4.1. Unlike some other UK Haemophilia Centres, the GRI Centre was firstly a Haemophilia and Thrombosis Centre, with roles in minimising both excessive bleeding (haemophilias) and excessive clotting (thrombosis, including thrombophilias).

8.4.2. Secondly, it has been a productive collaboration between the University of Glasgow's Department of Medicine, and the GRI NHS Department of Haematology and Blood Transfusion. Similarly, in the other three original territorial NHS Scotland Health Board Areas, their local University Medical Faculties provided input into development of Haemophilia Centres in Edinburgh (Professor of Therapeutics, Ronald Girdwood), Dundee (Senior Lecturer in Therapeutics Dr William Walker), and Aberdeen (Professor of Medicine Stuart Douglas, Dr Bruce Bennett).

8.4.3. Leslie Davis was appointed Professor of Medicine at GRI in 1945, at the time when University of Glasgow Principal Sir Hector Hetherington aimed to promote clinical research, to develop

evidence based and effective clinical specialisation and to improve health care (1). Davis had a laboratory background and a main interest in haematology. In 1951, his registrar Stuart Douglas obtained a Medical Research Council (MRC) Research Fellowship to work at its pioneering Blood Coagulation Research Unit in Oxford, with Professor Glyn Macfarlane and Dr Rosemary Biggs (2). Using a new blood test - the thromboplastin generation test - they differentiated the two main types of haemophilia: factor VIII deficiency and Factor IX deficiency. This major advance was crucial to treatment of haemophilia, as it progressed during the 1970s from crude plasma to progressively purified concentrates of these specific factors, which to this day are the mainstay of treatment and prevention of death and disability from haemophilia worldwide.

8.4.4. Development and organisation of the Centre. Returning to GRI in 1953, Douglas with Davis developed the Centre to become the West of Scotland Regional Reference clinical and diagnostic Centre. It served one of the largest geographical areas of the UK regional haemophilia centres, with a population over 2.5 million. Following their diagnosis, registration and education at the Centre, patients and families could attend their local hospital and be managed by the local physician with an interest in haematology, and by the local blood transfusion service who could order treatments with blood or plasma from the West of Scotland branch of the Scottish National Blood Transfusion Service (SNBTS); with advice as required from the Reference Centre (WITN3496014). Alternatively, and for most patients in the Glasgow area, they could self-refer and attend the Centre, where advice and treatment were available at all times. The UK Haemophilia Society started in 1954 and played a vital role in education and support of patients and families. The Centre encouraged its patients and families to join, and to attend meetings of the local Scottish branch.

8.4.5. Facilities. Patients were seen at the University Department of Medicine's Wards 2 and 3 on the first floor of the Royal Infirmary, conveniently close to the hospital entrance, casualty department, and city centre. The Haemophilia Centre room adjacent to male Ward 3 was used for reception and assessment of patients. Douglas initially diagnosed the type and severity of haemophilia in his coagulation laboratory in the Department of Medicine. Treatments with infusions of SNBTS plasma, or later cryoprecipitate, were requested from the GRI Blood Bank and given to patients in ward beds, or in ward treatment areas.

8.4.6. Thrombosis. Arterial and venous thrombosis became during the 1950's the major cause of death and disability in developing countries; and Glasgow and the West of Scotland had one of the world's highest risks of heart attacks and strokes. The Department of Medicine's wards contained not only patients with haemophilia (crippled with painful haemarthroses or muscle bleeds; or having surgery); but also patients with venous thromboembolism, or recovering from heart attacks or strokes (which were frequently fatal, either early, or when venous thromboembolism developed during prolonged hospital bedrest and immobility).

8.4.6.1. Douglas became interested in thrombosis and its treatment, authoring a textbook on anticoagulant therapy in 1962 (3), by which time heparin injections and oral anticoagulants such as warfarin were established treatments for venous thromboembolism; but their efficacy in arterial thrombosis was uncertain. As secretary of the MRC's randomised multicentre trial of oral anticoagulation in acute myocardial infarction (coronary artery thrombosis), Douglas and his GRI colleagues participated in recruitment of patients (4). This was the first of several multicentre clinical trials of antithrombotic drugs in

prevention of heart attacks and strokes, in which the Centre participated from the 1960s to 2009. Such trials were important in assessing both the antithrombotic benefit and the risk of bleeding. For every patient with congenital haemophilia and a lifelong increased risk of bleeding (I in 10,000 of the population), there are many more who are at risk of a heart attack, stroke, or venous thromboembolic event (50% of the population). Patients with thrombosis were increasingly treated with antithrombotic drugs which conferred an "acquired haemophilia" with increased risk of bleeding, and need for reversal of bleeding - often with plasma or later coagulation factor concentrates to restore clotting factor levels to normal. Douglas was therefore a pioneer of haemostasis and thrombosis becoming a scientific and medical specialty.

8.4.6.2. Douglas was joined in the Department of Medicine in 1962 by George McNicol, senior lecturer with an interest in haemostasis and thrombosis. During the 1960s, they performed laboratory and clinical studies of thrombosis and antithrombotic drugs, and co-authored authoritative reviews (5). The Haemophilia and Thrombosis Centre liaised with GRI cardiologists, stroke doctors - a specialty pioneered in the UK by geriatricians in Glasgow (1), and surgeons – general, cardiac, vascular, orthopaedic, and obstetric. Douglas and McNicol had a particular interest in fibrinolysis – the physiological process by which fibrin blood clots formed for haemostasis are dissolved. In 1963, they reported the first successful thrombolysis (clot-busting) by streptokinase in patients with acute arterial thrombosis of the limb (6). They also studied other thrombolytic agents, and antiplatelet agents which became antithrombotic drugs.

8.4.7. Development of Haematology Department. During the 1960s, Haematology across the UK was developing as a clinical and

laboratory specialty, led in GRI by George McDonald, appointed as Consultant Haematologist and Head of Department in 1962. Thereafter the Haematology and Thrombosis Centre had two Co-Directors – Douglas (in charge of the University Department's Wards 2 and 3, where most patients were seen for diagnosis, treatment and review; and of its haemostasis and thrombosis research laboratory); and McDonald (in charge of the hospital's NHS routine haematology laboratory which took over blood coagulation testing for diagnosis and monitoring; and in charge of its blood bank and blood products laboratory for provision and monitoring of blood, plasma and other blood products).

8.4.8. Succession planning. During the 1960s, Douglas, McDonald and McNicol trained their successors - Colin Prentice, Charles Forbes, John Davidson and Isobel Walker. Douglas arranged for Prentice and Forbes to train in coagulation laboratory research with Oscar Ratnoff in Cleveland, Ohio, who together with Macfarlane had discovered the coagulation cascade of interaction of clotting factors to form fibrin.

8.4.9. Tranexamic acid to reduce blood product use and hepatitis risk in haemophilia. Since the start of blood transfusion in the 1940s, blood and plasma were known to transmit viral hepatitis to transfusion recipients, and patients requiring repeated transfusions (including those with haemophilias) were known to be at increased risk. At the GRI Centre, blood liver function tests were performed routinely to identify subclinical hepatitis (7). To reduce this risk, McNicol, McDonald and Douglas sought to reduce the amount of blood products required to prevent or treat bleeding episodes in patients with haemophilia. They pioneered randomised clinical trials of synthetic fibrinolytic inhibitor drugs (epsilon-aminocaproic acid, then tranexamic acid) in prevention of bleeding episodes in patients with haemophilia (8,9). While these drugs were ineffective for treatment of musculoskeletal bleeding

(8), tranexamic acid was shown to be effective in minimising blood loss and hence minimising blood and blood product use (and thus hepatitis risk) after dental extraction and other types of minor surgery in patients with mild or moderate haemophilia (9). To this day, its use is recommended in UK and international guidelines.

8.4.10. Cryoprecipitate. In 1965, Pool and Shannon in the USA reported that freezing and thawing of fresh plasma produced cryoprecipitate – the first crude factor VIII concentrate, which was a more effective treatment of Haemophilia A and von Willebrand's Disease than plasma. At the GRI Centre, Davidson developed a pooling set to expedite cryoprecipitate preparation (10); and in 1969 the Centre reported its experience with cryoprecipitate in 25 patients, and its advantages and complications - one of which was that viral hepatitis could occur following cryoprecipitate treatment (7).

8.4.11. Bleeding and thrombosis in women, John Bonnar, a trainee in the University Department of Obstetrics and Gynaecology at GRI and the adjacent Glasgow Royal Maternity Hospital, researched with Douglas and McNicol the changes in haemostasis during pregnancy and childbirth (11), and their relationships to its bleeding and thrombotic complications, which were major causes of maternal and perinatal mortality. The Centre continued their collaborations with this Department through the appointment of Isobel Walker as consultant haematologist to both hospitals in 1978 (see below).

8.4.12. Designated nursing and junior medical staff. From 1970, a specialist Staff Nurse in Haemophilia, and a medical Senior House Officer in Haemophilia, were appointed to be based in the Centre during normal hours, deal with enquiries, and arrange treatment for outpatients and inpatients. They were trained and supervised by Consultants and Co-Directors of the Centre.

8.4.13. Changes in consultant staff. In the Department of Medicine, Douglas moved to be Professor of Medicine in Aberdeen in 1970; and McNicol moved to be Professor of Medicine in Leeds in 1971. They were succeeded as Co-Director (with George McDonald) and Head of the Department of Medicine's Haemostasis and Thrombosis Research Laboratory by Colin Prentice, Senior Lecturer and Consultant Physician. Charles Forbes was promoted Senior Lecturer and Consultant Physician in 1973.

8.4.13.1. In the Haematology Department, John Davidson was appointed Consultant Haematologist in 1970, in charge of the GRI Blood Transfusion and Blood Products laboratory, ordering treatments from the SNBTS, or on occasion from commercial manufacturers of factor concentrates, as required. He developed a national UK role in this field (12), and chaired the British Society for Haematology's Task Force on Haemostasis and Thrombosis from 1986. Isobel Walker was appointed Consultant Haematologist with an interest in perinatal haematology in 1978 at GRI and the adjacent Glasgow Royal Maternity Hospital, and developed an interest in the bleeding and thrombotic complications of women, including pregnancy complications, haemophilia carriers, women with von Willebrand's disease, and women with the genetic thrombophilias which emerged during the 1980s as common causes of premature thrombosis in women, especially during oral hormone use and pregnancy.

8.4.13.2. Comprehensive Care. Like other UK Haemophilia Centres, the Centre was developing in the 1970s as a Comprehensive Care Centre, with a multidisciplinary team which became the standard of haemophilia care (13), and which was eventually formalised in 1993 by the UK National Health Management Executive in association with the UK Haemophilia Centre

Directors Organisation (14). Staff included physicians in the University Department of Medicine (Drs Prentice and Forbes, and consultant rheumatologists advising on haemophilic arthritis Professor Walson Buchanan and Dr Carson Dick), haematologists (Drs McDonald, Davidson and Walker, with laboratory technical support), specialist nurse, hospital dentist, physiotherapists and orthopaedic surgeons for musculoskeletal problems; general surgeons, gastroenterologists, obstetricians, urologists, nephrologists and geneticists; and a social worker on Wards 2 and 3 – all knowledgeable about the multiple problems of haemophilia. The Centre trained junior doctors in the Departments of Haematology and Medicine in haemophilia, haemostasis and thrombosis; and encouraged and supervised their researches; and also taught undergraduate medical, dental and nursing students and postgraduate students about haemophilia and thrombosis in lectures and in clinical teaching on the wards, in which patients willingly participated.

8.5. **November 1974-1977, registrar in general medicine, University Department of Medicine, GRI**

8.5.1. My role and responsibilities at GRI.

8.5.1.1. In this position, 50% of my time was in the University responsibilities of teaching (10%) and research (40%, which was mainly in the field of thrombosis and vascular disease). 50% of my responsibilities were clinical, mainly in general medicine (49%) including acute general medical receiving; ward rounds and out-of-hours ward cover overnight and at weekends; and out-patient clinics in general medicine.

8.5.1.2. In 1975 the University Department of Medicine was one of the largest and most diverse in the UK (1). It had 4 university

consultants specialising in endocrinology and nuclear medicine, 2 in rheumatology, 2 in nephrology, and 2 in haemophilia and thrombosis (Drs Prentice and Forbes), plus an NHS consultant in general medicine. It had a male ward (to which the Haemophilia and Thrombosis Centre was attached), a female ward, a separate nephrology and renal dialysis unit, a separate Centre for Rheumatic Diseases in the adjacent Baird Street Hospital, and a convalescent and endocrine investigation ward in Belvidere Hospital two miles distant. Each of these specialties provided advice, treatment, research and undergraduate and postgraduate teaching and training across the West of Scotland and internationally. I was one of about 15 junior doctors in NHS and research fellowship posts, all training in general medicine and in a specialty. Wards 2 and 3 were one of GRI's four acute medical units, serving one of the UK's most deprived populations with high multi-morbidity and premature mortality, and admitting medical emergencies every fourth day.

8.5.1.3. Professor McGirr advised me as registrar in general medicine to look around the unit and choose a specialty to research in. Drs Prentice and Forbes had just lost their registrar researching in thrombosis who had moved to another unit, and in January 1975 they suggested I join them in this field. As a student and in my previous house officer posts, I had developed an interest in vascular diseases and thrombosis, so I accepted their invitation and researched a new anticoagulant drug, ancrod, which lowered plasma fibrinogen levels, and its effects on blood viscosity, blood flow and thrombosis. Collaborating with the Bioengineering Unit at the adjacent University of Strathclyde, I set up a laboratory on Ward 2 measuring blood viscosity, and participated in clinical trials of ancrod in preventing post-operative venous thrombosis in patients with hip fractures.

8.5.2. Haemophilia and Thrombosis Centre (1% of my time)

8.5.2.1. I recall that in 1975 many adult patients with haemophilia, registered at the West of Scotland Haemophilia Reference Centre at GRI, were still being treated and reviewed by haematologists on other medical wards in GRI, and in other hospitals in Glasgow and across the West of Scotland, and referred to the Centre for advice or treatment as required. I attach a flow diagram of how Haemophilia Care was provided across the West of Scotland; and Scotland in general (WITN3496014).

8.5.2.2. The patients who regularly attended the Centre on Wards 2 and 3 were mostly those living in the Glasgow area with severe or moderate haemophilia, resulting in frequent bleeding into joints and muscles requiring treatment at this time usually with plasma or cryoprecipitate, physiotherapy and rheumatological management, and rehabilitation.

8.5.2.3. Drs Davidson and Walker reviewed other patients at the Department of Haematology's out-patient Blood Clinic, and were attached to another general medical unit on Wards 4 and 5, where they could admit patients including those with acquired haemophilia who had developed inhibitors to Factor VIII, which required special treatments including plasma exchange, porcine Factor VIII or activated prothrombin complex concentrates (15,16). From 1980, they also investigated the potential use of freeze-dried SNBTS cryoprecipitate with the Centre (17).

8.5.2.4. Like the other junior doctors, I was attached to the male ward 3 for about 4 months a year, where there would be on average 4-6 in-patients with haemophilia, usually admitted with painful

and disabling musculo-skeletal bleeds. Drs Forbes and Prentice alternated spells of consultant duties on the male ward rounds (which they shared with another consultant) and in the adjacent two-room Haemophilia and Thrombosis Centre, where after the ward round they saw a few out-patients attending most days for treatment of bleeds, or for review, with the haemophilia senior house officer, haemophilia specialist staff nurse, and on occasion - for their education - other junior doctors rotating from the Departments of Medicine and Haematology, and undergraduate and postgraduate students.

8.5.2.5. Like the other junior doctors, I learned about haemophilia from Drs Forbes and Prentice on their teaching ward rounds, and over this period we each got to know the 20 or so frequent attenders, who were patients with severe haemophilia, recurrent musculoskeletal bleeds and premature arthritis, which in turn caused more joint bleeds. Their treatment was bedrest, pain relief by opiate drugs, repeated cryoprecipitate or plasma infusions, and physiotherapy. Other patients with haemophilia were admitted for internal bleeding, or surgery including dental extractions. Patients with musculoskeletal bleeds were assessed by a specialist physiotherapist, who recorded range of joint movements of knees, elbows and ankles. Such patients were referred as required to the Department of Medicine's Rheumatologists, or the Orthopaedic Surgery department.

8.5.2.6. For their convenience, especially for those living distant from Glasgow, patients were often reviewed on the same day by the hospital dentist; and often referred to the Wards 2 and 3 social worker for support.

8.5.2.7. As I stated to the Penrose Inquiry on 28 June 2011 (transcript pages 153-156), in 1976, like other junior doctors in general medicine or haematology, I participated in the out-of-hours junior doctor cover rota of the Centre from my home for this time, on occasion coming in to assess patients as emergencies. I recall that I did this for 6 months. Drs Prentice, Forbes, McDonald and Davidson had written protocols for assessment and management, updated regularly, including the type of product and usual calculated dose for each patient (duplicated in the Blood Bank, from which the product had to be requested by telephone, then prepared and delivered to the Centre by the blood porter). The junior doctors on the cover rota could ring a consultant for management advice if required.

8.5.2.8. I recall that during this time, Drs Forbes and Prentice's clinical research included pioneering work on the continuing high premature mortality from bleeding in UK patients with haemophilia (18); and on the psycho-social problems of patients with haemophilia and their families, with Ivana Markova, Professor of Psychology, University of Stirling (19). Realising that treatment with plasma or cryoprecipitate over the years had not adequately reduced this morbidity and mortality, they studied the potential role of coagulation factor concentrates which were being produced for Scotland by SNBTS. Working with the operational research unit at the University of Strathclyde, they reviewed their advantages over cryoprecipitate and plasma, and their costs and potential benefits (20).

8.6. **1978-1982, Lecturer and Honorary Senior Registrar**

8.6.1. My role and responsibilities at GRI.

8.6.1.1. In January 1978 I was appointed Lecturer in Medicine on the University Medical Unit, and honorary senior registrar in medicine by the Health Board. As in my previous registrar post, 50% of my time was in the University responsibilities of teaching (10%) and research (40%) in general medicine, thrombosis and vascular disease. For the other 50% of my time in clinical duties, 49% was in general medicine, thrombosis and vascular disease, and 1% in haemophilia.

8.6.1.2. Teaching (10%). Professor Arthur Kennedy, the new head of Department, asked me as lecturer to organise the teaching of medicine (lectures and clinical demonstrations) to Glasgow undergraduate dental students as part of their course in Human Disease. I did this until 2002, together with teaching of medical and nursing undergraduates and postgraduates.

8.6.1.3. Research (40%). Professor Kennedy agreed with my plan to continue research in general medicine with a focus on thrombosis and vascular disease. During this period I authored or co-authored many publications in this area; was awarded junior doctor lecture prizes by the Scottish Society of Physicians and the Royal College of Physicians and Surgeons of Glasgow; and joined the Royal Society of Medicine's Forum on Clinical Haemorheology, British Society for Haematology, British Society for Haemostasis and Thrombosis, and International Society for Thrombosis and Haemostasis, giving presentations at their meetings. The latter two societies were expanding to cater for training in my chosen field of thrombosis and haemostasis, which was becoming recognised subspecialty within Medicine and within Haematology. My collaborations on haemorheology continued with the Bioengineering Unit, University of Strathclyde.

8.6.1.4. Clinical duties – general medicine, thrombosis and vascular disease (49%). Professor Kennedy agreed with my plan to complete my training in general medicine (I obtained JCHMT accreditation in October 1980), then focus on training in vascular diseases and thrombosis, collaborating with the GRI University Departments of Cardiology and Surgery, and the NHS departments of vascular and orthopaedic surgery, clinical pharmacology and diabetes.

8.6.1.5. Haemophilia and Thrombosis Centre (1%).

8.6.1.5.1. Professor Kennedy and Drs Prentice and Forbes agreed that my training in haemophilia had been sufficient as part of my training in thrombosis and haemostasis, and that there were sufficient junior doctors rotating through the Centre from the Departments of Medicine and Haematology to cover the haemophilia junior doctor rota. Accordingly, together with two other senior registrars on the unit at this time, I worked with Drs Prentice and Forbes on thrombosis and vascular diseases, but not with clinical care of patients with haemophilia.

8.6.1.5.2. My only involvement with haemophilia was occasional assistance. When asked at the Penrose Inquiry on 28 June 2011 (transcript pages 153-156), I stated that I saw patients on-and-off during this time period, and was on the on-call out-of-hours rota most years until 1985. Since giving that evidence, when writing the history of the Centre, I located my diaries from 1978 to assist me with dates, and found no record of being on this rota from 1978 onwards.

8.6.1.5.3. I recall that in 1979, a Haemophilia Sister post was created to replace the Staff Nurse post, one of her roles

being to train patients and families in home treatment. I recall that at the Yorkhill Centre Dr Willoughby and the Haematology Staff Nurse also initiated home treatment about that time. The two Centres, with Professor Markova, reported their joint experience in 1982 (21), which was very positive. Dr Willoughby was succeeded by Dr Ian Hann from 1983.

8.6.1.5.4. In 1982, the GRI University Departments and laboratories moved to the new GRI University Building, vacating rooms on Ward 2, which allowed the expansion of the Haemophilia and Thrombosis Centre with a waiting area, treatment area, and three rooms for patient reviews and assessments. I set up in one room my weekly Thrombosis Clinic, reviewing patients with thrombotic and vascular diseases.

8.6.1.5.5. In the Department of Haematology, Dr Alan Burnett was appointed consultant in 1978, specialising in Haemato-oncology (1); especially leukaemia, with Dr McDonald. He performed the first bone marrow transplant in Scotland in 1980; established a bone marrow transplant unit in Ward 1 GRI in 1984; and chaired the MRC Adult Leukaemia working party, coordinating many MRC leukaemia trials. Dr Martin Rowan, consultant haematologist, specialised in myeloma; and Dr Alec Brown (a consultant physician who trained in the University Department of Medicine with Professor Douglas) specialised in lymphoma.

8.7. **1983-1985, Lecturer and Honorary Senior Registrar, seconded to NHS medical unit**

8.7.1. My role and responsibilities at GRI.

8.7.1.1. By 1983 I had been in my lecturer and honorary senior registrar post for 5 years, and at my annual review the senior registrar review committee started to question Professor Kennedy and myself about my applications for consultant physician posts. Afterwards, Professor Kennedy informed me that at this time of austerity and competition there was little prospect of the University promoting me to Senior Lecturer, as I had not yet submitted my MD thesis; and that the Health Board considered Haemophilia and Thrombosis was well-provided by 5 consultants (4 after Dr Prentice left that year to become Professor of Medicine in Leeds) and did not need another Senior Lecturer with Honorary Consultant status in this specialty. He gave me a few months off clinical duties to finish and submit my MD thesis; then transferred my clinical duties to Professor Lawson's GRI medical unit on Wards 4 and 5, which was short of clinical staff, to broaden my experience and portfolio for future application for consultant jobs in general medicine with an interest in thrombosis and vascular disease. Around this time, my two colleague senior registrars were likewise seconded to Professor Lawson's unit, or to the rheumatology unit, to broaden their clinical experience, while continuing their researches in thrombosis with Dr Forbes.

8.7.1.2. Teaching (10%). This continued as before.

8.7.1.3. Research (40%). During this period, I submitted my MD thesis on blood viscosity and vascular diseases to the University of Dundee, which awarded me this degree with Commendation in 1984. I was awarded the Croom Prize Lecture by the Royal College of Physicians of Edinburgh in 1985. I authored or co-authored many more publications, and expanded my collaborations, including with the GRI MRC Hearing Unit, University Institute for Neurological Sciences at the Southern

General Hospital, and the University Department of Medicine and University Department of Ophthalmology at the Western Infirmary,

8.7.1.4. Clinical duties – general medicine, thrombosis and vascular disease (49%). These continued as before, but my general medical duties were performed on Professor Lawson's unit instead of Wards 2 and 3. Drs Davidson and Walker were the haematologists on Professor Lawson's unit and joined the other medical staff after morning ward rounds for coffee and general discussions, which allowed us to update each other on our researches in haemostasis and thrombosis. They had, since Professors Douglas and McNicol left GRI, continued their research interests in the contributions of fibrinolysis to thrombosis (on which Dr Walker based her MD thesis), and were founder members of the International Society on Fibrinolysis and co-editors of its Journal. From 1983 I too had started research in fibrinolysis (in relation to post-operative venous thrombosis) and we all attended annual European Fibrinolysis Research Workshops in Leiden.

8.7.1.5. Haemophilia and Thrombosis Centre (1%).

8.7.1.5.1. I continued to have little involvement with in-patients with haemophilia, not being on wards 2 and 3. When asked at the Penrose Inquiry on 28 June 2011 (transcript pages 156-159), I stated that I spent about 2 hours a week at the Centre over this period. Since giving that evidence, when writing the history of the Centre, I located my diaries from 1978 to assist me with dates, and found that this was for my weekly thrombosis clinic at the Centre. I recall that I was only occasionally asked to see patients with haemophilia if no other doctor was available.

8.7.1.5.2. In April 1985 the University informed me that I would be promoted from Lecturer to Senior Lecturer from October, and that the Health Board would then interview me for an honorary (funded by the University, not by the NHS Health Board) NHS consultant position. Professor Kennedy and Dr Forbes agreed that, if I were awarded honorary consultant status, I could return from Professor Lawson's unit for clinical duties on wards 2 and 3 in general medicine and haemophilia.

8.7.1.5.3. By this time, Dr Forbes was Chair of the UKHCDO AIDS group and had appointed Dr Patricia Wilkie for part-time HIV counselling of patients, and they were applying for a research grant for her to continue this for 2 years. By June, they had obtained this grant; and had counselled the HIV positive patients. In view of my forthcoming promotion and possible honorary consultant appointment, Dr Forbes included the Haemophilia Sister and myself in the Greater Glasgow Health Board AIDS Information and Advisory Group, which he was chairing. At this group's first meeting on 31 May (PRSE0001606), we met with consultants in Infectious Diseases, Virology, Microbiology, Sexually Transmitted Diseases, Haematology, SNBTS, Dentistry and Public Health. The group reviewed AIDS information, and progressed Health Board policies and care plans, which included joint reviews of patients with haemophilia who were HIV positive with consultants in Infectious diseases, and also hospital admission policies for these patients.

8.7.1.5.4. The Health Board granted me an appointment as Honorary Consultant from October 1985, but I did not receive confirmation until December. I returned to Wards 2 and 3 and joined Dr Forbes in consultant review of

patients at the Haemophilia Centre. Drs Forbes and McDonald as Centre Co-Directors attended UKHCDO meetings (Dr Forbes became Chair of UKHCDO from 1986); and meetings of the Scotland and Northern Ireland Directors (SNIHD) Group, SNBTS, and Scottish Home and Health Department (SHHD); and they made all the Haemophilia Centre policy decisions.

8.8. **1986-1987, Senior Lecturer and Honorary Consultant**

8.8.1. My role and responsibilities at GRI.

8.8.1.1. Teaching (10%). This continued as above.

8.8.1.2. Research (40%). Dr Forbes and I agreed that he would focus on research in haemophilia, while I would continue my productive thrombosis research programme. I initiated a programme of collaboration with UK epidemiological studies in researching the associations of haemostatic and rheological variables, measured in our University research laboratory, with cardiovascular disease, which continued until my retirement. In the Royal Society of Medicine, I became a member of the Forum on Angiology (vascular medicine) and promoted the development of this specialty.

8.8.1.3. Clinical duties – general medicine, thrombosis and vascular disease (40%). These continued as before, in Wards 2 and 3.

8.8.1.4. Haemophilia and Thrombosis Centre (10%).

8.8.1.4.1. I shared with Dr Forbes consultant duties for in-patient and out-patient reviews. We worked closely with the new Haemophilia Sister, Ishbel McDougall.

8.8.1.4.2. The focus was at this time was on continued HIV counselling and monitoring of HIV positive patients, their families and partners; together with Dr Wilkie and Infectious Diseases consultants (initially Drs Dermot Kennedy and Campbell Love). For wives and female partners of HIV positive patients, Consultant in Sexually Transmitted Diseases Jennifer Somerville, and Consultant Obstetrician and Gynaecologist Mary Hepburn, who were also much involved with HIV positive drug users, were very helpful.

8.8.1.4.3. A few additional patients with haemophilia who were HIV positive transferred to the Centre from other hospitals in the West of Scotland, or from Centres outside Scotland. There were no further HIV seroconversions, because all factor concentrates were virally inactivated. However, after a patient in Edinburgh developed non-A non-B hepatitis in 1986, SNBTS increased its degree of heat treatment of Factor VIII concentrates (from 68 degrees C for 24 hours, to 80 degrees C for 72 hours) and this was available from 1987, resulting in no further cases of non-A non-B hepatitis. The Penrose Inquiry investigated this in detail: "The Inquiry notes that the PFC's success in being able to provide all Haemophilia A patients with a product that did not transmit HCV was a considerable achievement." (Penrose Inquiry Final Report, Executive Summary, page 24).

8.8.1.4.4. Dr Forbes moved to be Professor of Medicine in Dundee from September 1987; and Professor Kennedy and Dr McDonald agreed that I should replace him as Centre Co-Director, which was approved by UKHCDO at the end of the year.

8.9. **1988-1990, Senior Lecturer, Honorary Consultant, Co-Director of Centre**

8.9.1. My role and responsibilities at GRI

8.9.1.1. Teaching (10%). This continued as above.

8.9.1.2. Research (40%). Having succeeded Dr Forbes as director of the University Department of Medicine's Haemostasis and Thrombosis research laboratory, and as Dr Forbes transferred some of its funding and staff to Dundee, I spent much time and effort with Professor Kennedy and my research collaborators in GRI, other Glasgow hospitals, and the Universities of Dundee and Edinburgh in replacing and maintaining laboratory staff and obtaining new funding. I continued my thrombosis and vascular disease research programme.

8.9.1.3. Clinical duties – general medicine, thrombosis and vascular disease (40%). These continued as before, in Wards 2 and 3.

8.9.1.4. Haemophilia and Thrombosis Centre (10%)

8.9.1.4.1. As Co-Director with Dr McDonald, I met frequently with him and Dr Davidson to review the GRI Centre's policies, including treatments for patients with haemophilia and von Willebrand's disease. Dr McDonald and I shared representation of the Centre at meetings of UKHCDO; and meetings of SNIHD Group (with and without SNBTS and SHHD). At these meetings, I had the advantage of the expertise of Dr McDonald (Centre Co-Director since 1962), who had attended these meetings since 1969.

8.9.1.4.2. For information on blood products and their risks of hepatitis transmission, Dr McDonald and I appreciated Dr Davidson's expertise as Head of the Department of Haematology's Blood Bank and Blood Products Laboratory. Likewise we benefitted from the expertise in Scotland of colleagues at the Edinburgh Royal Infirmary Centre: Dr Christopher Ludlam, who had studied these since 1980 with SNBTS, who were also based at Edinburgh Royal Infirmary, and his trainee Dr Henry Watson, who became consultant and Director at the Aberdeen Royal Infirmary Centre (22). Dr Ludlam chaired the Factor VIII Working Party (renamed Coagulation Factor Working Party, CFWP) from May 1988, which coordinated development and supply of SNBTS blood products. At UKHCDO committee meetings, such expertise was also provided by colleagues including Drs Peter Kernoff and Christine Lee at the Royal Free Hospital Centre, London (23,24). Dr Kernoff drafted the first UKHCDO guidance on choice of therapeutic products for the treatment of non-inhibitor patients with haemophilia A, haemophilia B or von Willebrand's disease in May 1988 (25).

8.9.1.4.3. At Yorkhill, Dr Brenda Gibson, who had trained in Haematology at GRI, replaced Dr Ian Hann (who had moved to Great Ormond Street Hospital, London) as Director of its Centre; and also attended these meetings. Dr Gibson and I organised monthly meetings for staff at the GRI and Yorkhill Centres to discuss developments in haemophilia care, and collaborations including transfer of patients from Yorkhill to GRI.

8.9.1.4.4. To manage the increasing workload of the Haemophilia Centre, including frequent review and support for patients

who were HIV positive and their families and partners, Dr McDonald and I worked with GRI managers to appoint a Staff Grade specialist Haemophilia Nurse (Elizabeth Little) to assist the Haemophilia Sister. For support and counselling to replace Dr Wilkie, whose grant had finished at the end of 1987, we worked with the Glasgow Social Work Department who allocated a senior, experienced social worker (Miriam Guthrie) to the unit. Together with colleagues in infectious diseases, rheumatology, physiotherapy, dentistry and other surgery, our consultant team of haematologists and physicians (Drs McDonald, Davidson, Walker and myself) maintained and expanded the Haemophilia service.

8.9.1.4.5. Like Dr Forbes before me, I (and Dr Gibson) met regularly with Philip Dolan, Chairman of the local branch of the Haemophilia Society, to discuss developments at our Centres. We continued to organise regular local Haemophilia Society meetings at our Centres. At its first meeting in GRI with myself as Centre Co-Director in January 1988, I updated attenders on all developments in the Centre. We all agreed to work with GRI and NHS Greater Glasgow Health Board to develop a new, larger Centre. However, despite our joint efforts, limitations of space and the competing demands of other developing specialties within GRI delayed the opening of the New Centre until 1999.

8.9.1.4.6. At this difficult time of coping with HIV infection, to boost morale for Haemophilia Centre staff, patients and their families, the Centre organised with the local branch of the Haemophilia Society two summer boat cruises, in 1988 (on Loch Katrine) and 1989 (on the River Clyde).

8.9.1.4.7. In September 1988, I attended the first joint meeting of the British Society for Haematology (BSH) and the British Society for Haemostasis and Thrombosis (BSHT) in Cardiff, which was a great success. The societies' committees agreed to hold such joint meetings every 3 years; and proposed that the next should be held in Glasgow in 1991, with Dr Davidson as BSH President, and myself as BSHT President. We agreed, appointed Dr Walker as meeting secretary, and the three of us met regularly to organise this meeting until 1991.

8.10. **1991-1996, Reader then Professor, Honorary Consultant, Co-Director of Centre**

8.10.1. My role and responsibilities at GRI

8.10.1.1. Teaching (10%). This continued as above.

8.10.1.2. Research (40%). Professor Kennedy retired as head of the Department of Medicine in 1990 and was succeeded by Professor James McKillop. He fully supported my continuing thrombosis and vascular disease research programme. I was promoted by the University to Reader in 1992; then to Personal Professor of Vascular Medicine in 1993.

8.10.1.3. Clinical duties – general medicine, thrombosis and vascular disease including Stroke Medicine (40%). These continued as before, in Wards 2 and 3. I was appointed chair of the GRI Stroke Service Development Group in 1993, and worked with 4 consultants in geriatric medicine to develop a Multidisciplinary Stroke Service, including specialist nursing sister, physiotherapist, occupational therapist and speech and language therapist. Professor McKillop agreed that I become

clinical lead for a new weekly Stroke Clinic with this team, and I ended my participation in the Unit's general medical clinic.

8.10.1.4. Haemophilia and Thrombosis Centre (10%)

8.10.1.4.1. After Dr McDonald's retiral in 1990, Dr Davidson was appointed Head of the Department of Haematology. He and Professor McKillop agreed that Dr Walker should replace Dr McDonald as Co-Director of the Centre; and Dr Davidson continued as Head of the Blood Bank and Blood Products laboratory. The three of us shared consultant cover of the Centre.

8.10.1.4.2. As the fourth consultant at the Centre, Dr Rajan Madhok was appointed consultant rheumatologist at GRI. At the Centre's weekly review clinic, he and our specialist physiotherapist would review all patients with musculoskeletal problems and discuss management of these with the rest of the Centre team. This included reviews of home treatment; if indicated, a period of prophylaxis; and referring patients to GRI consultant orthopaedic surgeon Ian Kelly for consideration of joint replacement surgery.

8.10.1.4.3. Dr Walker established a Thrombophilia Clinic in the GRI Out-patient Clinic block. With Ian Greer, Professor of Obstetrics and Gynaecology, she developed a combined clinic for management of gynaecological issues and pregnancy in haemophilia carriers, patients with von Willebrand's disease, and patients with thrombophilias (26). She continued her research studies in thrombosis and thrombophilias, co-founding and co-directing the European Concerted Action on Thrombosis (ECAT) External Quality Assurance Scheme (ECAT NEQAS).

With Dr Campbell Tait, who later succeeded Dr Davidson as consultant in the Centre, she researched the prevalence and genetics in the West of Scotland population of congenital thrombophilias, such as deficiencies of antithrombin, protein C and protein S.

8.10.1.4.4. The CFWP and SNBTS developed their programme for manufacture and supply of high purity Factor VIII concentrate. Dr Walker and I participated with colleagues in the CFWP in clinical trials of this concentrate, and the product was licensed. SNBTS provided funding for a clinical assistant and a secretary at the Centre to assist with these trials; posts which in due course were continued and funded by the Health Board.

8.10.1.4.5. Following the discovery of the hepatitis C virus (HCV) as the major cause of non-A non-B hepatitis, routine screening of blood donations and of Haemophilia Centre patients who had received blood products was introduced throughout the UK in September 1991. The GRI Centre added HCV testing to its routine surveillance for hepatitis, in accordance with UKHCDO discussions and guidance (27). Patients with positive HCV tests were given information on the virus and its possible effects; and advice on precautions to minimise transmission, testing of sexual partners, minimising alcohol intake and the need for regular follow-up. This was supplemented with leaflets from the British Liver Trust and/or the UK Haemophilia Society.

8.10.1.4.6. Patients who were HCV carriers were referred to consultants at the GRI Gastroenterology Clinic for further investigation and treatment, including consideration of treatments with interferon or liver transplantation. From

1996, all GRI patients were seen at a weekly Haemophilia / Hepatitis C clinic held at the Haemophilia Centre by newly appointed Consultant Hepatologist John Morris, his Viral Hepatitis Nurse Specialist Sister Margaret Neilson, and the haemophilia nurses. Patients co-infected with HIV were treated by Infectious Diseases consultant Andrew Seaton.

8.10.1.4.7. The SNIHCD study of viral safety of SNBTS Factor VIII/IX concentrates was completed and published in 1993 (28). No patient developed abnormal liver function tests, or antibody to HCV or HIV. Following reports of hepatitis A virus (HAV) transmission by some factor concentrates in other countries, UKHCDO recommended in 1992 that patients receiving blood products be screened for immunity from previous exposure (positive antibody) and if negative, advised vaccination. The GRI centre reported that the prevalence of HAV was no higher in patients than the general population, and that no patient developed antibody in the study of viral safety of SNBTS Factor VIII/IX concentrates (29).

8.10.1.4.8. In 1990, I had proposed to UKHCDO that National UK Clinical Audit of Haemophilia Centres be developed. After a pilot study with Dr Ludlam, Edinburgh, and Dr Mayne, Belfast, this was initiated across the UK in 1992, with a triennial inspection and report by a haemophilia director from another UK Centre (30). The audit was later expanded to include a haemophilia nurse specialist, and a patient representative, from other haemophilia centres (31). It continues to this day.

8.10.1.4.9. The Glasgow Centres (GRI and RHSC) were designated Haemophilia Comprehensive Care Haemophilia Centres by UKHCDO in 1993.

8.10.1.4.10. In 1994, the GRI Centre was the first to report an association of severe haemophilia A with osteoporosis (32), which was later confirmed in a meta-analysis of studies (33).

8.10.1.4.11. In a collaboration with the University Department of Surgery, the Centre reported an association of activated fibrinolysis with adverse outcomes of acute upper gastro-intestinal bleeding; and suggested future randomised trials of tranexamic acid (34). Subsequent trials reported that tranexamic acid reduced bleeding and mortality in such patients (35); as did later trials in patients with trauma - CRASH-2 Study (36), in women with post-partum haemorrhage - WOMAN Study (37), and in patients with traumatic brain injury (CRASH-3 Study) (38).

8.10.1.4.12. From 1994, the UK Government promoted the development of hospital trusts, competition for service provision, business managers and business plans. Dr Walker and I were asked to prepare a business plan for adult haemophilia care in the West of Scotland, and we emphasised that only GRI could provide the services of a Comprehensive Care Centre (13,14). In NHS Scotland, these UK "competitive business model health reforms" fortunately did not compromise the organisation of haemophilia care.

8.11. **1996-2009, Professor, Honorary Consultant, Co-Director of Centre**

8.11.1. My role and responsibilities in GRI.

8.11.1.1. Teaching (10%). This continued as above until 2002, when I was appointed Chair of the Scottish Intercollegiate Guidelines Network (SIGN), involving secondment for one day a week to their office in Edinburgh. Professor McKillop agreed that I discontinue my notional half day weekly session for organising teaching of medicine to the dental students, which I had done since 1979.

8.11.1.2. Research (40%). I continued my thrombosis and vascular disease research programme. These were increasingly in the field of haemostatic variables in prediction of cardiovascular disease, for which I was awarded: the Royal College of Pathologists Kettle Lecture in 2005, given at the annual meeting of the British Society for Haemostasis and Thrombosis (39); my DSc thesis by the University of Glasgow in 2006; and an Investigator Recognition Award by the International Society of Thrombosis and Haemostasis in 2009.

8.11.1.3. Clinical duties – general medicine, thrombosis and vascular disease (40%). I retired as Chair of the GRI Stroke Development group in 1997 when the Acute Stroke Unit opened; then with Professor McKillop's agreement I ended my participation in the weekly stroke clinic in 2002 when I became Chair of SIGN.

8.11.1.4. Haemophilia and Thrombosis Centre (10%)

8.11.1.4.1. In 1996 Dr Walker became Head of the Haematology Department and of the Blood Bank and Blood Products Laboratory. Dr Davidson retired GRO-A. Campbell Tait succeeded Dr Davidson as Consultant Haematologist with an interest in Haemostasis and

Thrombosis at the Centre; and became Centre Co-Director in 2001. He developed genetic mutation identification of haemophilia carriers, and genetic counselling, with the University Department of Medical Genetics, then with Professor Ludlam's national genetic haemophilia service in Edinburgh. He also developed transfer of adolescent patients from Yorkhill in joint clinics with Elizabeth Chalmers, who succeeded Brenda Gibson who specialised in Haemato-Oncology. A new Haematology/Oncology Unit opened in 1996 at Yorkhill, with dedicated haemophilia facilities.

8.11.1.4.2. In 1996, UKHCDO recommended that recombinant Factor VIII concentrate was the treatment of choice for those with Factor VIII deficiency, being free from human pathogens. The emergence in 1996 of a new variant of Creutzfeld-Jakob disease (vCJD), identified by the CJD Surveillance Unit in Edinburgh, added to the case for their use. Professor Ludlam (Chair of UKHDCDO) and I met with the Chief Medical Officer and senior NHS Scotland management, to request that NHS Scotland and SNBTS develop a procedure to progressively replace SNBTS factor concentrates with recombinant concentrates. This was agreed, and a national Recombinant Consortium established for this purpose. The purchase of these products was managed by National Services Scotland, and distributed to blood product laboratories including GRI. Operational managers were appointed at Haemophilia Centres, including GRI, from 1997 to coordinate product purchase and usage. The great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK. Home delivery of concentrates for home treatment started in 2007.

8.11.1.4.3. In 1999 the GRI Haemophilia and Thrombosis Centre moved one floor downstairs to a large, modern Centre in Ward 1 at the hospital entrance. This was vacated by the Regional Bone Marrow Transplant Unit, which moved elsewhere in GRI; and eventually to Gartnavel General Hospital (1). The expanded facilities in Ward 1 allowed development by Dr Tait of an out-patient venous thrombosis diagnosis and treatment service at the Centre, administered by Thrombosis Nurses.

8.11.1.4.4. Dr Walker was President of the British Society of Haematology in 1999; and was awarded Personal Professor in Perinatal Haematology by the University in 2003.

8.11.1.4.5. Following the finding of VCJD prion in blood donors, information letters on VCJD risk were prepared and sent by UK Centres to all patients registered with haemophilia from 2001-2009; and surveillance for vCJD in recipients of blood and plasma products was initiated: to date no clinical cases have been reported in UK patients with haemophilias.

8.11.1.4.6. In 2004, the Centre nursing staff received the annual Health Board nursing award, nominated by Centre patients. The Clinical Assistant was appointed Associate Specialist in 2005.

8.11.1.4.7. Dr Tait's researches in thrombosis included studies of the use of warfarin in local community patients with atrial fibrillation; and the prediction of recurrent venous thromboembolism. Professors Walker, Greer and I were much involved in production of clinical guidelines on

thrombosis prevention and treatment; and we performed systematic reviews and cost-effectiveness analysis of thrombophilia screening for prediction and prevention of thrombosis in high risk situations (pregnancy, hormone use and surgery) (40).

8.11.1.4.8. Professor Walker and I both retired in 2009, and were succeeded as GRI Co-Director (with Campbell Tait) by Catherine Bagot. The University reorganised its structures in 2010, replacing Faculties and Departments with Schools and Institutes. Our research area of thrombosis and vascular diseases continues in the Institute of Cardiovascular and Medical Sciences, which awarded Dr Tait a personal Professorship in 2017; in which Dr Bagot is a member; and I continue as Emeritus Professor and Honorary Senior Research Fellow. Professor Walker continues as Director of the UK NEQAS in Blood Coagulation.

9. Approximately how many patients with bleeding disorders were under the care of the Centre when you first started working there and over the years that followed?

9.1. I refer you to the Penrose Inquiry Preliminary Report (2010), Appendix 1: UKHCDO Data. The numbers given for patients registered at the GRI Centre are: 118 1975, 268 1980, 312 1985, 344 1990, 487 1995, 580 2000, 596 2005, 613 2010. The largest increase was in patients with von Willebrand's Disease. The numbers treated were reported annually to UKHCDO, and should be available to the Inquiry from UKHCDO.

a. The Inquiry understands that adult patients were treated at GRI and children at Yorkhill. Please confirm whether or not this is correct. If it is, please explain how care was transferred once a child reached adulthood (and when

that was assessed to be). Were any children with haemophilia treated at GRI during your time working there?

9.2. This is correct.

9.3. In Scotland children legally reach adulthood at 16 years, but I recall that it was the Centre Director at Yorkhill who would decide when would be an appropriate time to discuss transfer of the individual patient to GRI. I recall that this would depend on several factors, including maturity, presence of an affected sibling of similar age, education (at school, or in Yorkhill during hospital admissions), and the views of the family.

9.4. When I became Co-Director in 1988, Dr Gibson at Yorkhill and I arranged regular meetings of our Centres' staff, at which potential transfers would be discussed routinely. When Dr Tait joined Dr Walker and I as Centre consultant, one of his remits was to work with Dr Chalmers at Yorkhill to organise more phased transfers, involving a series of meetings and visits to GRI before transfer. You could ask Drs Chalmers and Tait for further information on this.

10. What decisions and actions were taken, and what policies were formulated, by you and by your colleagues at the Centre regarding the importation, manufacture and use of blood products (in particular factor concentrates) during the time that you worked there?

10.1. In NHS Scotland, I recall the "self-sufficiency" policy was that SNBTS routinely supplied to Haemophilia Centres blood and most blood products, including plasma, cryoprecipitate and plasma concentrates, as requested by the Blood Bank and Blood Products Laboratory at each Centre. For GRI and its related hospitals, this was organised by the Consultant Haematologists, Dr Davidson then Dr Walker, who were in charge of the GRI Blood Bank and Blood Products Laboratory, which served the whole of GRI, including providing products not only for patients with haemophilias; but also for

treatment of acute major bleeding, surgery, reversal of anticoagulation, thrombophilias, etc.

10.2. For treatment of haemophiliacs, in the event that SNBTS products were either not available in sufficient quantity, or were not suitable (for example, providing insufficient levels of von Willebrand factor for patients with severe von Willebrand's disease; or for patients with Factor VIII inhibitors, for which SNBTS products were usually ineffective) my recollection is that my predecessor Co-Directors Drs Prentice or Forbes would discuss with Drs McDonald and Davidson what blood products from other manufacturers might be suitable, agree a choice, and then Dr Davidson would negotiate purchase.

10.3. When I succeeded Dr Forbes as Co-Director, I would likewise discuss with Drs McDonald and Davidson, and we would agree a choice - which, from their first issue in May 1988 (25) would be informed by the current UKHCDO recommendations. When Dr Walker succeeded Dr McDonald as Co-Director in 1990, the same procedure occurred. From 1996 Dr Walker was in charge of the Blood Bank and Blood Products laboratory and she would order them.

11. Who was responsible for the selection and purchase of blood products (in particular factor concentrates) for use at the Centre? What particular products were used for treating patients at the Centre, over what period of time and for which categories of patients?

In addressing this issue, please answer the following questions:

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

11.1. Centre Co-Directors would discuss this as required with Dr Davidson, who would then order and purchase the products from the Blood Bank and Blood Products laboratory. From 1996 Dr Walker would order and purchase them.

11.2. For a list of products used at the Centre 1969-1991, this information was collated by the Penrose Inquiry and presented in Appendix 1, page 568-571 of its Preliminary Report (2010). If you wish information for other years, I suggest you contact the current Centre Directors. From 1996, I recall that NHS Scotland progressed the transition from blood products to recombinant factor concentrates through the Recombinant Factor Consortium, with central purchasing by National Services Scotland, who then issued concentrates to Centre Blood Banks.

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

11.3. Efficacy, safety, availability and cost – the last two factors for Drs Davidson then Walker, in charge of the Blood Bank, to discuss with manufacturers.

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

11.4. I suggest you ask Professor Walker, I don't know.

d. What involvement did you have in these matters, (i) in the period before your promotion to consultant in October 1985, (ii) following your promotion to consultant in October 1985?

11.5. (i) None.

11.6. (ii) None, until I succeeded Dr Forbes as Centre Co-Director at the end of 1987. He and Drs McDonald, Davidson and Walker were experienced consultants who had trained at the Centre from the 1960s; and Dr Forbes was Chair of UKHCDO 1986-87. As noted above, from 1988 my involvement was discussion with my Co-Director (Dr McDonald, then Dr Walker) and Dr Davidson, who placed the orders. From 1996, Dr Walker was both my Co-Director and head of the Blood Bank and Blood Products Laboratory, and she placed the orders.

You may be assisted by considering your Comments on Professor Forbes' Evidence, 28 April 2011 [STHB0000828], and your C3A Statement (in particular §1.1 and §4.1) [PRSE0003462].

11.7. Comments on Professor Forbes' Evidence, 28 April 2011.

11.7.1. When he gave evidence to the Penrose Inquiry in 2011, Dr Forbes struggled when he was asked to recall the use of different blood products between 1975 and 1987, when he moved to Dundee as Professor of Medicine. I recall that he had not continued his involvement in haemophilia care in Dundee; and that by the time of the Penrose Inquiry, sadly, GRO-A GRO-A. As a result, the Central Legal Office in Edinburgh asked me if I could prepare these comments, from my recollections of possible reasons for their use over this time period, as well as the period 1988-1991 when I was Co-Director with Dr McDonald.

11.8. I confirm my evidence in STHB000828; and also my further statement in PRSE0001112 (your attached document 7), Para (3), that Dr Davidson's letter to Dr Mitchell of April 1985 would appear to clarify that his order of commercial FIX was for heat treated Factor IX, pending the introduction of heat-treated SNBTS Factor IX later that year.

11.9. I confirm my C3A statement (PRSE0003462), including $1.1 and $ 4.1.

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

12.1. Drs Davidson, then Walker, as successive heads of the Blood Products Laboratory would deal directly with these companies.

12.2. The only involvement I would have was, I recall, an occasional visit to the Centre from some representatives of these companies whose products the Laboratory was currently issuing, to review the latest information about their products with Centre medical and nursing staff, and answer any of our questions. We kept at the Centre all manufacturers' (including SNBTS's) current information sheets, and we would provide these to patients when discussing any changes of blood product, and on their request.

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

13.1. Initially, I recall that there was no organisation other than the GRI Blood Products Laboratory. With the development of the Coagulation Factor Working Party from 1988, I recall that a unified system was established for the purchase of commercial concentrates – as described in Professor Ludlam's document (WITN3496015) on the establishment of this Working Party, submitted to the Penrose Inquiry, then to the Infected Blood Inquiry.

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

14.1. I had no role until the end of 1987, see my answer to question 11, d.

14.2. After I succeeded Dr Forbes as Co-Director, I would discuss which products might be used in individual patients when I reviewed patients. For patients transferring to the Centre (for example from Yorkhill), I would review with the patient (and parents) their previous or current treatment, its efficacy, any adverse effects or risks, and discuss whether or not they would wish to continue with it, and if not what alternatives might be available. For patients registered at the Centre, these matters would also be discussed at their annual reviews.

14.3. Like my predecessors, Drs Douglas, McNicol, Prentice and Forbes, as the physicians in the Centre, we could not make the final choice of, and could not order, blood products. This could only be done by consultant haematologists in the GRI Blood Bank and Blood Products Laboratory – Dr Davidson until 1996, then Dr Walker.

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

15.1. For patients with mild severity haemophilia A or von Willebrand's Disease, these were desmopressin (DDAVP), if it was shown to be effective in, and also tolerated by, the individual patient; plus tranexamic acid in patients undergoing dental extractions. If not, cryoprecipitate was considered (see question 17). For patients with mild haemophilia B, this was fresh frozen plasma, plus tranexamic acid in patients undergoing dental extractions.

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

a. DDAVP (you may be assisted by your evidence to the Penrose Inquiry at Transcript, 13 October 2011, p.24 and following [PRSE0006054], and pp.68-73; and §2.1 of your C3A Statement)

16.1. I refer you to my evidence to the Penrose Inquiry at Transcript, 13 October 2011, p.24. I said that DDAVP (desmopressin) was the treatment of choice for mild haemophilia A, and for mild von Willebrand's disease; in conjunction with ancillary haemostatic measures, like tranexamic acid.

16.2. For treatment or prevention of a bleed in such patients, I said that the combination of desmopressin, and the response to injury (which also raises levels of Factor VIII / von Willebrand factor), often allowed us to not have to give blood products. In the event that somebody had a major bleed or major surgery, and this treatment was ineffective or not tolerated, a discussion would have to take place with the patient about the risks of blood product treatment. This discussion would involve explaining that a first exposure to concentrate (prior to August 1987 for SNBTS concentrates) or cryoprecipitate had a risk of transmission of non-A non-B hepatitis.

16.3. The disadvantages of desmopressin, reviewed in (22) are:

16.3.1. Individual response is variable, hence test doses are required.

16.3.2. Repeated infusions often result in a lower response (tachyphylaxis).

16.3.3. It is usually ineffective in severe von Willebrand's disease.

16.3.4. Even with slow intravenous infusion, it can cause vasodilatation with symptoms of flushing, rapid pulse rate, and faintness due to fall in blood pressure, which in some patients lead them to request stopping the infusion.

16.3.5. Because it is a derivative of vasopressin, an adverse effect is water retention and hyponatraemia, which can lead to neurological symptoms (such as headache, confusion and convulsions), which was first described by the Centre in 1977 (41).

16.3.6. The increase in high molecular weight von Willebrand factor multimers may increase platelet stickiness resulting in arterial thrombosis (heart attacks or strokes), hence UKHCDO guidelines caution against its use in patients aged 60 years or over.

b. Porcine Factor VIII (see §11 of your Comments on Professor Forbes' Evidence, 28 April 2011)

16.4. This is a factor concentrate, and is **not** an alternative to factor concentrates as the question implies.

16.5. I refer you to §11 of my Comments on Professor Forbes' Evidence, 28 April 2011 (STHB0000828). I recalled that this would be used by the Centre or by the Haematologists for treatment of patients with haemophilia A (and for treatment of patients with acquired inhibitors to factor VIII) who had developed Factor VIII inhibitors which were less inhibitory of porcine factor VIII than human factor VIII. I stated that porcine F VIII was never manufactured by SNBTS as far as I recalled.

16.6. Drs Davidson and Walker reported their use of porcine Factor VIII in patients with acquired haemophilia (that is, non-congenital haemophiliacs who develop factor VIII inhibitors) (15,16). They reported an anaphylactic reaction (16).

16.7. Porcine factor VIII has been used extensively in the treatment of haemophiliacs and non-haemophiliacs with anti-factor VIII antibodies. There is no virucidal step in the manufacture of this concentrate, but transmission of porcine viruses has not been reported in recipients (22).

16.8. In addition to reactions, I recall that a disadvantage of porcine Factor VIII was its high cost.

c. Proplex (see §12 of your Comments on Professor Forbes' Evidence, 28 April 2011)

d. FEIBA (see §3.4 of your C3A Statement).

16.9. These are factor concentrates, and are not alternatives to factor concentrates as the question implies.

16.10. For both Proplex and FEIBA, I refer you to §12 of my Comments on Professor Forbes' Evidence, 28 April 2011 (STHB0000828). I recalled that these were activated prothrombin complexes used for treatment of patients with haemophilia A who had factor VIII inhibitors, and for treatment of patients with acquired haemophilia with inhibitors to factor VIII. Such products were never manufactured by SNBTS as far as I recall.

16.11. I refer you to a review of their uses and disadvantages (42).

e. Tranexamic acid.

16.12. As discussed above (Questions 6-8, Development of the Centre 1950-1975), the GRI centre pioneered studies of the use of epsilon-aminocaproic acid, then tranexamic acid, to reduce blood product use and hepatitis risk in haemophilia between 1965 and 1972 (8,9). While ineffective for treatment of musculoskeletal bleeding, this antifibrinolytic therapy was shown to be effective in minimising plasma use (and hence reduce hepatitis risk) after dental extraction and other types of minor surgery in patients with mild or moderate haemophilia. John Bonnar, who trained at the Centre, subsequently as Professor of Obstetrics in Dublin showed that it also reduced menorrhagia, including in women with von Willebrand's disease. It was subsequently recommended in UK and international guidelines for treatment of haemophilia and von Willebrand's disease (43).

17. What was your/the Centre's policy and approach as regards the use of cryoprecipitate for the treatment of patients with bleeding disorders? Did that policy and approach change over time and if so how?

a. You may be assisted by your evidence to the Penrose Inquiry, Transcript 28 June 2011, p.164 and following [PRSE0006039]; and by §1.1 of your C3A Statement.

b. Please also see question 39 below.

17.1. As I have noted in Questions 6-8 above, the Centre in 1969 reported its experience with cryoprecipitate in 25 patients, and its advantages and complications - one of which was that viral hepatitis could occur following cryoprecipitate treatment (7). The Penrose Inquiry Preliminary Report (Appendix 1, pages 568-571) records UKHCDO data for GRI 1969-91 and includes use of cryoprecipitate 1969-1989; however, I understand that latterly its use was mostly out with the Centre (eg in cardiac surgery).

17.2. I recall that the Centre's policy and approach as regards the use of cryoprecipitate did change over time between 1975 and 1988.

17.3. I refer you to my evidence to the Penrose Inquiry, Transcript 28 June 2011, p.164 and following [PRSE0006039]. I recalled that my predecessor Centre Co-Directors prescribed cryoprecipitate for patients with mild or moderate severity Haemophilia A or von Willebrand's disease. This was consistent with UKHCDO guidance in May 1983 (Penrose Inquiry Preliminary Report, page 197).

17.4. As noted in Question 6-8, the Centre evaluated freeze-dried cryoprecipitate as a smaller-pool alternative treatment to factor concentrates (17). I recall it was not progressed, because of the risk of severe anaphylactic reactions which precluded home treatment on safety grounds; and as SNBTS prioritised Factor VIII concentrates, which had a lower risk of reactions, and could be virally inactivated by heat treatment.

17.5. In June 1985, Dr Forbes (Chair of UKHCDO AIDS Group) co-authored a letter in the Lancet with Drs Bloom (Chair UKHCDO) and Rizza (Secretary

UKHCDO), saying "... we no longer consider that cryoprecipitate or other non-heat treated concentrates is justified. ...All these considerations underline the need rapidly to introduce screening for HTLV-III antibody for all blood donations... When testing is fully implemented the role of single donor cryoprecipitate in the management of haemophilia can then be reassessed." (44).

17.6. I refer you to §1.1 of my C3A Statement (PRSE0003462). I recalled that from 1986 (I cannot recall which month) Dr Forbes informed me that the current SNBTS factor VIII concentrate (heat treated at 68 degrees) might not be effective against non A non B hepatitis. He informed me that, as all SNBTS blood donors had now been screened since 1985 without evidence of HIV transmission, he, Dr McDonald and Dr Davidson had decided to continue their policy to treat the small number of moderately severe patients with haemophilia A or von Willebrand's disease with cryoprecipitate, which had a smaller blood donor pool than factor concentrates, to reduce the risk of non A non B hepatitis. A prospective UK study of cryoprecipitate confirmed the absence of evidence of hepatitis or HIV infection in patients who had never received large pool concentrates (45).

17.7. When I gave evidence to the Penrose Inquiry at Transcript, 13 October 2011, p.24 (PRSE0006054), I said that I could not remember, at this time, ever having to make a decision about choice of cryoprecipitate (which might transmit HIV - although blood donors were tested for HIV from 1985), or of NHS (SNBTS) heat-treated Factor VIII which until mid-1987 was safe from HIV, but still carried a risk of non-A non-B hepatitis. When asked about what would have been my own choice as a patient after October 1985, when donors were HIV tested, I said I would take cryoprecipitate. I stated to the Penrose Inquiry my recollection that that would have been Dr Forbes's choice at that time, which I recall was also Dr Forbes's evidence to the Penrose Inquiry.

17.8. In my evidence to the Penrose Inquiry, Transcript 28 June 2011, p.164 and following [PRSE0006039], I recalled that the first UKHCDO guideline on

choice of blood products, issued in May 1988 (25), recommended that cryoprecipitate no longer be used for such patients, because by this time concentrates had been virally inactivated and were generally thought to be safer. My recollection is that from this time Drs McDonald, Davidson and I agreed that we should follow this advice.

17.9. By 1992, virally-inactivated von Willebrand factor concentrates (for example, BPL 8Y, Hyate C) were recommended for treatment of patients with von Willebrand's disease in the updated UKHCDO recommendations on choice of therapeutic products, instead of cryoprecipitate (46).

18. What was your/the Centre's policy and approach in relation to home treatment? When was home treatment introduced? Did the policy and approach towards home treatment change over time and if so how?

18.1. I recall that Drs Forbes was a member of the UKHCDO Working Group on Home Treatment in the 1970s; and that he and Dr Prentice initiated home treatment at the GRI Centre in 1979-1983, with patients (and relevant family members) being trained, and the programme monitored, by the Haemophilia Sister (Agnes Ward). I recall that the Centre used the book, Haemophilia Home Therapy, edited by Dr Peter Jones and endorsed by the Haemophilia Society, as an educational tool for staff, patients and family members (47). I recall that at the Yorkhill Centre, Dr Willoughby and the Haematology Staff Nurse also initiated home treatment about that time. The two Centres reported their joint experience in 1982 (21), which was very positive.

18.2. After I succeeded Dr Forbes as Co-Director, the GRI Centre usually continued home treatment for patients already receiving it (including patients transferred from Yorkhill), if indicated, and if the patient (and parents) wished. However, its use was monitored; discussed with our rheumatologist and physiotherapist colleagues, who were monitoring musculoskeletal bleeds and arthritis in our patients; and if appropriate it was stopped (47). I cannot recall if we started home treatment at GRI for the first time in any patient

between 1988 and 2009. If you wish to have this information, I suggest you ask the current Centre Directors.

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

19.1. I recall that the Centre's policy was to consider prophylaxis selectively if indicated, as per guidance (47). As prophylaxis was usually given to prevent musculoskeletal bleeds and progressive arthritis, decisions would be taken in consultation with our rheumatologist and physiotherapist colleagues, who were monitoring musculoskeletal bleeds and arthritis in our patients.

20. Did you/the Centre have a policy or approach in relation to the use of factor concentrates for children? If so, did that policy and approach change over time and if so how?

20.1. No, the GRI Centre did not treat children. Use of factor concentrates for children was regularly discussed at meetings of UKHCDO and SNIHDG.

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

21.1. I recall that the GRI Centre followed UKHCDO advice and guidelines for treatment – generally use of non-blood product treatments if appropriate (e.g. tranexamic acid, desmopressin); and if required plasma products from small blood donor pools (cryoprecipitate or plasma) were preferred at various times to minimise risk of hepatitis – until 1988 (see question 17). Concentrates would be used if such products were ineffective or contra-indicated.

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

22.1. I am not aware of any.

Section 3: Knowledge of, and response to, risk

General

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

23.1. When I began work in the Department of Medicine, as junior doctors we were taught by Drs Prentice and Forbes about haemophilia on ward 3 rounds, or visits to the adjacent Centre to see out-patients. They regularly emphasised to all staff that patients who had received blood products were at increased risk of viral hepatitis. When asked at the Penrose Inquiry on 28 June 2011 (transcript pages 160-164) [PRSE0006039], I recalled seeing prominent hepatitis warning signs at the Centre. I also stated that I knew Hepatitis B was a big issue in NHS Scotland in the early 1970s, Edinburgh having a serious outbreak in the early 1970s, in which junior doctors died, and a book "The Houseman's Tale" by Dr Colin Douglas was written about it. I recalled that multi-transfused patients in haemophilia units, kidney dialysis units and liver transplant units were regularly tested for hepatitis B and liver function tests. I also recalled that staff attending the Centre (including myself) were tested for hepatitis B for a few years. The Centre emphasised to patients (and staff) to be careful with needles and blood, disposing of all equipment.

23.2. As I stated at the Penrose Inquiry (transcript 16 December 2011 [PRSE0006080]), I recalled that routinely laboratory blood samples and request forms from patients who had received blood products had yellow "Dangerous Specimen" labels applied; also that Haemophilia Society information sheets and booklets (including on hepatitis) were displayed in the Centre for patients, relatives and staff.

23.3. My knowledge and understanding of the risks of infection associated with blood and blood products over time developed over time by reading the literature (including the British Medical Journal and Lancet which I subscribed to, which reviewed this topic regularly); and by regular updates to the Unit and Centre staff from Drs Prentice and Forbes from 1975 to 1987. From 1983 this would include risk of AIDS, and from 1984 risk of a virus, which became known later as HIV, as the postulated cause of AIDS.

23.4. Thereafter, as Centre Co-Director (1988-2009) I kept myself updated by reading the literature, and reports from UKHCDO and SNBTS.

23.5. I refer you to the detailed account of the emergence of knowledge in Scotland, the UK and internationally, from 1974 to 2009, in the Preliminary Report of the Penrose Inquiry (2010); and in its Final Report (2015), Volume 2: Knowledge of HIV/AIDS and Hepatitis C.

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

24.1. I recall that my predecessor Centre Co-Directors attended meetings from the 1970s of Scottish Haemophilia Centre Directors with SNBTS and the Scottish Home and Health Department (SHHD); and also meetings of UKHCDO. I understand that these bodies and their meetings regularly considered and assessed the risks of infection with the use of blood and blood products. UKHCDO monitored and regularly reported risks of hepatitis (B and NANB), then from the 1980s also AIDS and HIV. From 1983 UKHCDO provided regular guidance on appropriate selection of blood products or alternative treatments for haemophiliacs.

24.2. After I succeeded Dr Forbes as Centre Co-Director, I attended these meetings from 1988 with my Co-Directors. From 1988, the Factor VIII

Working Party (later renamed Coagulation Factor Working Party) monitored the development and safety of SNBTS blood products; and in due course arranged central purchasing of commercial blood products (WITN3496015). From 1996, the CFWP and the Recombinant Factor Consortium managed the transition from blood products to recombinant factor concentrates, achieved across NHS Scotland by 2002 for most patients with haemophilias.

25. What was your understanding of the relative risks of infection from (i) the use of commercially supplied blood products and (ii) the use of NHS/SNBTS blood products?

25.1. I recall that the Penrose Inquiry showed the World in Action television programme from December 1975, which raised concerns on the paid donors of some commercial blood products; and I recall that from that time there was general concern about possible greater risks of hepatitis transmission by such concentrates, relative to NHS/SNBTS blood products. However, as documented in detail by the Penrose Inquiry (Preliminary Report 2010; and Final Report 2015), it was known at that time that NHS/SNBTS plasma, cryoprecipitate and plasma factor concentrates also transmitted hepatitis.

25.2. In UKHCDO, I recall that Dr Craske monitored the UK situation, and Drs Prentice and Forbes would update ward and Centre staff on these risks, as assessed by his reports.

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

26.1. <u>1975-1987</u>

26.1.1. The Centre Co-Directors (Drs McDonald, Prentice and Forbes) and Dr Davidson minimised or reduced exposure to infection in several ways.

26.1.1.1. Use of non-plasma derived treatments (tranexamic acid, desmopressin) where possible, to minimise use of blood products. (See Questions 15 and 16).

26.1.1.2. Use of plasma or cryoprecipitate instead of factor concentrates, where appropriate (see Question 17).

26.1.1.3. Hepatitis B (HBV) vaccination of patients and Centre staff from 1985.

26.1.1.4. Use of virally-inactivated plasma factor concentrates from 1985, including SNBTS Factor VIII and Factor IX concentrates.

26.2. 1988-2009

26.2.1. The Centre Co-Directors (Drs McDonald, Walker, Tait and myself) and Dr Davidson further minimised or reduced exposure to infection in several ways.

26.2.1.1. Continued use of virally inactivated plasma factor concentrates, as recommended by UKHCDO guidance from May 1988 (25; 46; and thereafter).

26.2.1.2. Continued use of Hepatitis B vaccination; and from 1992 Hepatitis A (HAV) vaccination, as recommended by UKHCDO guidance.

26.2.1.3. The study of viral safety of SNBTS Factor VIII/IX concentrates in previously untreated patients was performed, and published in 1993 (28). No patient developed abnormal liver function tests, or antibody to HCV, HIV or HAV (28,29).

26.2.1.4. From 1997, progressive replacement of SNBTS plasma factor concentrates by recombinant (non-human-derived) factor concentrates. The great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK.

Hepatitis

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

27.1. As a clinical medical student 1970-1972, I was taught about hepatitis A and B. I recall that one of our questions in the final examination in medicine in 1972 was "Write an essay on hepatitis". As a house officer 1972-1974, I was taught the risks of transmission of hepatitis, including hepatitis B, from blood and blood products; and understood that SNBTS/NHS screened blood donors for HBV.

27.2. See also my answer to Question 23.

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

28.1. As I have noted in Questions 6-8 above, the Centre in 1969 reported its experience with cryoprecipitate in 25 patients, and its advantages and complications - one of which was that viral hepatitis could occur following plasma or cryoprecipitate treatment (7).

28.2. I recall that from the 1970s the Centre routinely monitored its patients who were treated with blood products for hepatitis. This included history of jaundice or other clinical symptoms of hepatitis, and testing of blood for liver function tests and hepatitis B antigen and antibody. As a notifiable disease, cases of jaundice and hepatitis B were reported to local Public Health and Infectious Diseases departments, who would follow up cases and contacts, including advice on preventing transmission. The GRI Blood Transfusion Laboratory were also informed, so that the West of Scotland and National SNBTS, or other manufacturers of relevant blood products, could trace possible infected blood or plasma donations and batches of blood products which should be withdrawn from stock.

28.3. I recall that from the 1970s the Centre routinely reported cases of jaundice and hepatitis B to the UKHCDO database, for collation, analysis and reporting at UK level by Dr Craske and the Hepatitis Working Party (48).

28.4. I note that the Edinburgh Centre reported in its patients, treated with SNBTS cryoprecipitate and factor concentrates, high prevalences of fluctuating liver function test abnormalities in 1981 (49); and of hepatitis B antigen and antibody in 1983 (50). In 1986, the GRI Centre also reported these in its patients (51). By this time, only virally-inactivated factor concentrates (from SNBTS and other manufacturers) were used by the Centre.

28.5. From 1991, when NHS Scotland introduced routine HCV screening of blood donors and recipients of blood products, the Centre routinely tested its patients, and reported HCV positivity and clinical liver disease to the UKHCDO Working Party for collation, analysis and reporting at UK level (52).

28.6. For the Penrose Inquiry 2010-2015, Haemophilia Centre Directors in Scotland and UKHCDO collated data on HCV. The Penrose Inquiry Final Report (2015) concluded that 478 people were infected with HCV in Scotland as a result of therapy for a bleeding disorder; and noted that Scottish Haemophilia Directors and UKHCDO continue to trace any further patients and to improve their estimates of the likely total number of patients infected,

particularly in relation to those patients treated with blood products other than concentrates (Executive Summary, page 8).

28.7. I understand that my successor Professor Tait has submitted to the Inquiry in March 2018 an update on these figures for NHS Scotland.

28.8. Investigations of outcomes of HCV infection in Scotland

28.8.1. In 2013, Haemophilia Centre Directors in Scotland reported a follow-up study of 455 patients with bleeding disorders estimated to be infected with HCV by coagulation factors provided by NHS Scotland (53). In 302 with documented HCV infection, rates of natural clearance (17%), genotype frequency (64% genotype 1), and responses to antiviral therapy (15% with monotherapy; 39% with combination therapy) were similar to those in other cohorts. Thirty-four liver biopsies were performed without adverse event; and liver transplantation was performed in 11 patients (7 for liver failure, 4 for hepatocellular carcinoma). These outcomes were similar to those reported from other cohorts.

28.8.2. In 2017, the Scottish Government asked Professor David Goldberg, Health Protection Scotland, to establish and preside over an expert group to assess the health and wellbeing of individuals, chronically infected with HCV through NHS blood transfusion / treatment with blood products, who had not progressed to advanced hepatitis C (previously often known as Skipton Fund "Stage Two".) The Group included Professor Tait from the Centre. Its report, published in 2018 (54) reviewed the increasing evidence on the spectrum of impact of HCV, clinical and non-clinical (e.g. employment, ambition, relationships); and recommended simplification and extension of application for a chronic HCV award in Scotland.

28.8.3. I refer you to Volume 5 (Information to Patients), of the Penrose Inquiry Final Report (2015), which reports in detail the Systems in Place in the UK and Scotland (including the GRI Centre) for informing patients about the risks. This includes reviews of the Ethical Context (Section 32) and hepatitis C (Section 34).

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

29.1. I repeat my answer to Question 26, with regard to **hepatitis** -

29.1.1. <u>1975-1987</u>

29.1.1.1. The Centre Co-Directors (Drs McDonald, Prentice and Forbes) and Dr Davidson minimised or reduced exposure to infection **with hepatitis** in several ways.

29.1.1.1.1. Use of non-plasma derived treatments (tranexamic acid, desmopressin) where possible, to minimise use of blood products. (See Questions 15 and 16).

29.1.1.1.2. Use of plasma or cryoprecipitate instead of factor concentrates, where appropriate (see Question 17). Evaluation of freeze-dried cryoprecipitate (17).

29.1.1.1.3. Hepatitis **B (HBV) vaccination of patients and Centre staff from 1985** (PRSE0003869, PEN.018.0649).

29.1.1.1.4. Use of virally-inactivated plasma factor concentrates from 1985, including SNBTS Factor VIII and Factor IX concentrates.

29.1.2. <u>1988-2009</u>

29.1.2.1. The Centre Co-Directors (Drs McDonald, Walker, Tait and myself) and Dr Davidson further minimised or reduced exposure to infection **with hepatitis** in several ways.

29.1.2.1.1. Continued use of virally inactivated plasma factor concentrates, as recommended by UKHCDO guidance from May 1988 (25).

29.1.2.1.2. Continued use of Hepatitis B vaccination; and from 1992 Hepatitis A (HAV) vaccination, as recommended by UKHCDO guidance (46).

29.1.2.1.3. The study of viral safety of SNBTS Factor VIII/IX concentrates was completed and published in 1993 (28). No patient developed abnormal liver function tests, or antibody to HCV, HIV (28) or HAV (29).

29.1.2.1.4. From 1997, progressive replacement of SNBTS plasma factor concentrates by recombinant (non-human-derived) factor concentrates. The priority was patients not previously exposed to factor concentrates. The great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK.

30. 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?

30.1. My understanding of the nature and severity of hepatitis B, A, NANB and C evolved over time, in parallel with the risks of transmission, as I described in Question 23 - by reading the literature (including the British Medical Journal and Lancet which I subscribed to, which reviewed this topic regularly); and

by regular updates to the Unit and Centre staff from Drs Prentice and Forbes from 1975 to 1987.

30.2. Thereafter, as Centre Co-Director (1988-2009) I kept myself updated by reading the literature, and reports from UKHCDO and SNBTS.

30.3. My recollection of the evolution of my understanding parallels the emergence of knowledge in Scotland, the UK and internationally, from 1974 to 2009, which has been detailed and summarised in the Preliminary Report of the Penrose Inquiry (2010), to which I refer you:

"By 1981, there was still very little evidence of the natural history of NANB hepatitis – whether arising post-transfusion, or among persons with haemophilia" (page 164).

"Positive developments included: recognition that there was a problem, i.e. that the vast majority of severe and moderately severe haemophilia patients receiving replacement therapy already had been exposed to NANB Hepatitis virus(es), and that many had chronic, although probably usually mild and asymptomatic, liver disease" (page 165).

30.4. The Inquiry report then reviews in detail the period 1981-1985, during which there was increasing information on the natural history of hepatitis, and ends by concluding:

"Thus, by the end of 1985:

- There was increasing concern about the potential seriousness of NANB Hepatitis,
- It was known that almost all haemophilia patients who regularly received treatment with concentrates were likely to develop the disease,
- First generation concentrates continued to transmit NANB Hepatitis, and
- The debate over the benefits and drawbacks of screening blood donors for surrogate markers of NANBH continued." (Page 185).

"Routine screening of blood donations for hepatitis C, and of patients with haemophilia who had received blood products, was introduced throughout the UK in September 1991, using second generation ELISA and RIBA tests. "(Page 320).

"The origin of the Factor VIII concentrate made no difference whatsoever to the risk of contracting hepatitis C or B." (Page 578).

a. In your oral evidence to the Penrose Inquiry (Transcript, 16 December 2011 [PRSE0006080], p.22) you stated that before circa 1985, "the general perception of [NANB hepatitis] among experts and haemophilia doctors was that very few patients were developing chronic liver disease" and that "it was thought to be a chronic but mild condition." What was the basis for this perception, given that, to adopt your words those were the "early days" of the disease as it had only been known about for ten years?

30.5. As I stated in my responses to Questions 6-8, I saw few patients with haemophilia between 1978 and 1984, which is why I concentrated, when giving my evidence to the Penrose Inquiry on 16th December 2011, on information given to patients from 1985, when I became an honorary NHS consultant in December and assisted Dr Forbes with consultant cover and patient reviews.

30.6. In my oral evidence to the Penrose Inquiry (Transcript, 16 December 2011 [PRSE0006080], p.21-22) I was talking about the period from the mid-1970s up to about 1985. I said, "the general feeling was that over that period of time very few patients with haemophilia had developed any clinical liver disease and that there were biopsy studies that showed that the changes in the liver tended to be relatively mild. So it was thought to be a chronic but mild condition." The basis for this perception is given in the literature review of hepatitis 1982-85 (pages 166-185) in the Penrose Inquiry Preliminary Report (2010), to which I refer you. This includes:

30.6.1. The UKHCDO report (1983) on the treatment of haemophilia 1976-1980 (48). "In view of the widespread concern about the transmission of hepatitis viruses by giving blood products it is interesting to note that only two deaths were attributed to hepatitis during the five year period. There have been several reports recently of persistently abnormal liver function values and abnormal histological findings in liver tissue from haemophiliacs treated with blood products. Most of these patients are asymptomatic but it remains to be seen how many will develop severe chronic liver disease with the passage of time." (page 174, 7.38).

30.6.2. The Mannucci et al liver biopsy paper (1982) "Non-progressive course of non-A, non-B chronic hepatitis in multitransfused haemophiliacs" (55). "This study suggests that in haemophiliacs with NANB chronic hepatitis, progressive disease is not the rule…It is remarkable…that only 2 of the entire series of 91 haemophiliacs followed since 1974 have died from cirrhosis and that both were [hepatitis B surface antigen] positive. Study of the serum and intrahepatic markers for hepatitis B and delta viruses suggest that chronic liver disease is non-progressive in hemophiliacs who have no intrahepatic markers." (page 170, 7.21,7.22).

30.6.3. The White et al liver biopsy paper (1982) "Chronic hepatitis in patients with hemophilia A: Histologic studies in patients with intermittently abnormal liver function tests" (56). "While some patients, primarily those with moderately severe and severe enzyme elevations, will have histologic evidence of chronic active hepatitis and/or cirrhosis, the results of the present study indicate that a larger proportion of patients will have milder degrees of enzyme abnormalities and predominantly chronic persistent hepatitis or milder forms of liver disease. Thus, for many transfusion-requiring hemophiliacs, the frequent exposure to

factor VIII concentrates is not accompanied by the development of the more severe forms of chronic liver disease." (page 171, 7.29).

30.6.4. The Stevens et al liver biopsy paper (1983). "Liver disease in haemophiliacs: an overstated problem?" (57). In 12 haemophilia patients with persistently abnormal liver function tests, one showed severe chronic active hepatitis with progression to cirrhosis, and four showed some evidence of mild chronic active hepatitis (page 173, 7.37). They quoted the Aledort paper (1981) "A study of liver disease among haemophiliacs" (58), of 115 biopsies worldwide, where the incidence of chronic active hepatitis and cirrhosis was 16% (page 174, 7.37).

30.6.5. The Hay et al liver biopsy paper (1985) "Progressive liver disease in haemophilia: an understated problem?" (59). In 79 haemophilia patients followed for eight years, 21% had evidence of chronic progressive liver disease (page 183-184, 7.78-7.80).

30.6.6. The Aledort et al liver biopsy paper (1985) "A study of liver biopsies and liver disease among haemophiliacs". (60). In 155 patients, 15% had cirrhosis and 7% chronic active hepatitis. No difference was observed between patients treated with large pool concentrates and patients treated principally with cryoprecipitate or plasma.

30.6.7. The Mannucci and Columbo discussion paper (1985) "Liver disease in haemophilia", (61) reviewing the papers of Hay et al, Aledort et al, and others including their own studies.

30.7. I note that the Final Report of the Penrose Inquiry (2015), Volume 2, Knowledge of AIDS/HIV and Hepatitis C, concludes - "There was no generally accepted view prior to 1985 that NANB Hepatitis had other than a generally benign prognosis. 1985 was a turning point: this was when

information began to emerge that would lead to changing views. From 1985 it became increasingly understood that NANB Hepatitis infection could be associated with serious disease, progressing to cirrhosis in a significant proportion of cases, and to liver failure and ultimately liver cancer, albeit rarely."

b. You referred in your evidence to the Penrose Inquiry (Transcript, 16 December 2011, p.22) to "biopsy studies that showed that the changes in the liver [with NANB hepatitis] tended to be relatively mild" . Which studies were these? Were you involved in any such biopsy studies?

30.8. I have detailed these studies above. In these papers, there was much discussion about discrepancies between studies, but there was clearly a trend in liver biopsy study reports from predominantly mild disease - "An overstated problem" (57) - to increasing severity and progression of changes - "An understated problem" (59) - between 1981 and 1985.

30.9. Neither the Centre, nor myself, was ever involved in research biopsy studies.

c. Do you consider that haemophilia doctors prior to circa 1985 adopted an unreasonable and/or over-optimistic view on the long-term risks of NANB hepatitis given the limited information that was available to them at that time?

30.10. As I was little involved with haemophilia care between 1978 and 1985, I do not think that I can give an informed opinion on this. It appears from the literature cited above that the long-term risks were evolving.

d. What information became available in or around 1985 that led to a change in attitude among "experts and haemophilia doctors" about the long term

consequences of NANB hepatitis? (You may be assisted by p.26 of the Transcript of 16 December 2011, and p.33 of the Transcript of 13 October 2011).

30.11. I recall it would be in particular the study of Hay et al (59) and discussion paper of Mannucci et al (61) published in the Lancet, which I recall reading at the time. I recall that Dr Forbes and I discussed this emerging evidence when I became honorary consultant in late 1985, and we were agreeing what updated information should be given to patients at reviews.

30.12. In addition, as I stated to the Penrose Inquiry (Transcript of 16 December 2011, pages 26-28 [PRSE0006080]), I recalled that our Centre had three or four patients who had developed cirrhosis, the majority of whom had either Hepatitis B or heavy alcohol use or both; and that it was not until about 1987 that we saw the first patient who had non-A non-B hepatitis, without heavy alcohol use, causing clinical evidence of early cirrhosis. That number of patients gradually increased over subsequent years.

HIV and AIDS

31. What was your knowledge and understanding of HIV (HTLV-III) and AIDS and in particular of the risks of transmission from blood and blood products? How did your knowledge and understanding develop over time?

31.1. As with hepatitis, my knowledge and understanding of the risks of HIV and AIDS and in particular of the risks of transmission from blood and blood products developed over time by reading the literature; and by regular updates to the Unit and Centre staff from about 1982 by Dr Prentice (until he moved to Leeds in 1983) and Dr Forbes who succeeded him as Centre Co-Director. From January 1985 Dr Forbes was chair of the UKHCDO AIDS Group; and founder and chair of the Greater Glasgow Health Board AIDS Information and Advisory Group. From 1986-87 he was UKHCDO Chair.

Therefore he was very well informed in this area, and very energetic from 1983 in researching it, and educating not only Unit and Centre staff and patients, but the whole UK.

31.2. After I succeeded Dr Forbes as Centre Co-Director (1988-2009) I kept myself updated by reading the literature and reports from UKHCDO and SNBTS; and (with my Co-Directors) attending meetings of UKHCDO, SNIHD and SNBTS.

31.3. My recollection of the evolution of my understanding parallels the emergence of knowledge in Scotland, the UK and internationally, from 1982, which has been detailed and summarised in the Preliminary Report of the Penrose Inquiry (2010), Chapter 8: HIV and AIDS; and in Volume 2 of the Final Report (2015).

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

32.1. I think this would be about late 1982, when Dr Forbes informed the Unit and Centre staff of this; and that he was initiating a study of immune abnormalities in patients with severe haemophilia attending the Centre, to see if they might be similar to those reported in the USA in patients with, or at risk of, AIDS.

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

33.1. I refer you to the written statement "the Immunological Testing Statement" which I gave to the Penrose Inquiry, which you sent me (PRSE0001561, PEN.012.1600). It lists several studies performed by Drs Forbes of the immune abnormalities in patients at the Centre, and their relationships to HIV seropositivity or seronegativity, with his colleagues in the Rheumatology

Section of the University Department of Medicine - Drs Sturrock, Froebel, Madhok, Lennie and others (62-70).

33.2. The statement includes a subsequent study by Dr Hay which was an indirect comparison of patients with haemophilia in England treated with monoclonally purified Factor VIII concentrate (Bioproducts Ltd., Elstree) and in patients in Scotland (Edinburgh and Glasgow Centres) treated with SNBTS Factor VIII concentrate which was heat treated (71). There were no significant differences in progression of HIV infection between these two groups of patients.

33.3. The statement also notes that from 1985 Dr Forbes arranged routine testing for anti-HTLV-III for all patients who had received blood products who were attending the Centre, as part of their clinical management, performed by Dr Follett at the Regional Virus Laboratory, Ruchill Hospital); and that data on clinical outcomes of HIV was included in UKHCDO UK reports (72).

33.4. I confirm this evidence that I gave to the Penrose Inquiry.

33.5. These studies are discussed further under Research (Question 77).

34. What if any actions did you and your colleagues take in light of your awareness of a possible association between AIDS and the use of blood products and/or to reduce the risk to your patients of being infected with HIV?

34.1. <u>1983-1987</u>

34.1.1. I recall that from 1983 NHS Scotland was mostly self-sufficient in SNBTS Factor VIII and IX concentrates, which were not associated with seroconversion for HTLV-III until late 1984; and that Drs Forbes, McDonald and Davidson continued to use these products at the Centre for most patients. Some patients required treatment with commercial concentrates, as detailed in the

Penrose Inquiry Preliminary Report (2010), Appendix 1; and discussed in my statement to the Penrose Inquiry, requested by the Central Legal Office, on possible reasons for their use (28 April 2011, STHB0000828) which you have sent to me.

34.1.2. I recall that they continued to use non-plasma derived treatments (tranexamic acid, desmopressin) where possible, to minimise use of blood products. (See Questions 15 and 16). This was recommended by UKHCDO in May 1983 (Penrose Inquiry Preliminary Report, page 197).

34.1.3. I recall that they continued to use plasma or cryoprecipitate instead of factor concentrates, where appropriate (see Question 17). This was recommended by UKHCDO in May 1983 (Penrose Inquiry Preliminary Report, page 197) for treatment of children, mildly affected patients or patients unexposed to imported concentrates.

34.1.4. Following the reports of HIV transmission by some SNBTS factor VIII and IX concentrates in late 1984, in some Glasgow Centre patients (63) and in some Edinburgh Centre patients (73), I recall that they used virally-inactivated plasma factor concentrates from 1985, including heat-treated SNBTS Factor VIII and Factor IX concentrates.

34.1.5. I note that the Penrose Inquiry Final Report (2015) concluded – "When the news came that HIV had entered the Scottish donor population, and that patients had acquired HIV from Scottish product, the PFC moved swiftly to introduce dry heat treatment and was able to provide the first comprehensive national supply of heat-treated Factor VIII in the world. The Inquiry has no criticism to make of those involved in viral inactivation in Scotland." (Executive Summary, page 22).

34.2. 1988-2009

34.2.1. The Centre Co-Directors (Drs McDonald, Walker, Tait and myself) and Dr Davidson continued use of virally inactivated plasma factor concentrates, as recommended by UKHCDO guidance from May 1988 (25).

34.2.2. The study of viral safety of SNBTS Factor VIII/IX concentrates was completed and published in 1993 (28). No patient developed hepatitis or seroconverted to HIV or HCV (28) or HAV (29).

34.2.3. From 1997, there was progressive replacement of SNBTS plasma factor concentrates by recombinant (non-human-derived) factor concentrates. The great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK.

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

35.1. From 1983-1987, I recall that Drs Forbes, Davidson and McDonald did continue to use factor concentrates, in patients for whom non-plasma derived treatments, plasma or cryoprecipitate were ineffective, as there was no alternative treatment. See answer to Question 34 above.

35.2. By the time that I became Co-Director in late 1987, all blood donors were tested for HIV, all factor concentrates were virally inactivated, and I recall that no further patients became HIV positive through treatment.

36. The Inquiry is aware of guidance being given on the use of blood products by the UK Haemophilia Centre Directors Organisation. In respect of guidance from this, or any other organisation, please answer the following questions.

a. From when did you become aware of such guidance, and how?

36.1. I refer you to my answer to Question 17. I recall that the Centre's policy and approach regarding the use of desmopressin (DDAVP) and cryoprecipitate as alternatives to factor concentrates changed over time between 1975 and 1988, according to guidance by UKHCDO.

b. What role did you play in responding to or implementing the guidance, (i) before your promotion to consultant in October 1985, (ii) between your promotion to consultant in October 1985 and your becoming a haemophilia centre director in late 1987, (iii) after becoming a haemophilia centre director in late 1987?

36.2. Before I was appointed honorary consultant in **December** 1985, as with other trainee doctors I followed the Centre's guidance which was based on UKHCDO guidelines. Between December 1985 and my succeeding Dr Forbes as Co-Director with Dr McDonald in late 1987, I continued to follow the Centre guidance. Thereafter, with my Co-Directors (Drs McDonald, Walker and Tait), we revised our Centre guidance in accordance with UKHCDO guidelines, from the first one in May 1988 (25). See below.

c. How did the guidance affect the policy and practice of the Centre's use of blood products in those periods? Was it always followed, or did the Centre depart from the guidance (and if so, why)?

36.3. I cannot recall any departure from UKHCDO guidance on use of blood products in those periods. Copies of current UKHCDO guidance were kept at the Centre, and all staff were asked to read them and follow them.

Response to risk

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

a. Please refer to the evidence that you gave to the Penrose Inquiry on these matters, including making any corrections, amendments or additions that you feel to be necessary.

37.1. I refer you to my statement to the Penrose Inquiry, which you have sent me (PRSE0002426); the Collective Response which you have also sent me (PRSE0003869); and the transcripts of my oral evidence (PRSE0006039 and PRSE0006080) which you have also sent me.

37.2. I also refer you to the Penrose Inquiry Final Report (2015), Volume 5: Information to patients, which details and discusses the written and oral evidence given to the Inquiry by Professor Forbes and myself.

37.3. **Hepatitis – The Practice at Glasgow Royal Infirmary, The evidence of clinicians: the use of blood products and information about the risk of infection with NANB Hepatitis/Hepatitis C (pages 1654-1663).**

37.3.1. Dr Forbes and I both gave evidence that from the 1970s, clinicians and patients at the Centre were aware of the adverse effects of blood and blood products, including hepatitis B and non-A non-B

hepatitis, for which patients were tested routinely (hepatitis B antibody and antigen, and liver function tests).

37.3.2. I recalled (PRSE0006039, Transcript 28 June 2011) that Centre staff in the mid-1970s were also tested for hepatitis B; that big red signs labelled "Hepatitis" were displayed in the Centre; and that medical and nursing staff and patients were reminded to be careful with needles and blood and on the disposal of all equipment. The Haemophilia Society issued booklets, pamphlets and Bulletins, displayed and given to patients, which included information on the risks of hepatitis, including an article by Dr Forbes in Bulletin 1 in 1980. Some of this material was collated for the Penrose Inquiry and submitted with the collated response (PRSE0003869, PEN.018.0649) on information given to patients about the risk of hepatitis, authored by present and past Haemophilia Centre directors in Scotland who were still alive and contactable in 2011. This built on their collective response, asked for by the previous Scottish Executive Health Department Inquiry into Hepatitis C and heat treatment of blood products for haemophiliacs in the mid 1980s (October 2000).

37.3.3. I recalled (PRSE0006080, Transcript 16 December) that patients at the Centre were routinely advised by medical and nursing staff of the risk of infection by the blood-borne hepatitis viruses (HBV and NANB Hepatitis). The risk was reinforced by precautions to avoid transmission during treatment (disposable gloves, careful disposal of needles, intravenous lines, and blood or blood product packs or vials); and by routine labelling of laboratory samples and request forms with yellow "Dangerous Specimen" labels, clearly visible to patients.

37.3.4. I recalled that patients, or their parents, who requested information about NHS or commercial clotting factor concentrates were given, and offered discussion on, the information leaflets

provided along with the concentrates themselves, which included details on the possibility that they might transmit hepatitis. From 1985 they were informed that concentrates were virally inactivated to reduce risk of hepatitis.

37.3.5. I recalled that vaccination was offered against HBV from 1985 to patients who lacked natural immunity; and against HAV from 1992; and also to parents who assisted with home treatment.

37.3.6. I recalled what information on risks, complications and prognosis of hepatitis (B, A and NANB) was given to patients, and how this changed over the years with emerging evidence.

37.3.7. I described that at routine reviews, patients were asked about jaundice and other symptoms of hepatitis, and examined for enlargement of liver and spleen, in addition to routine blood tests including HBV and liver function tests.

37.3.8. I described that HCV testing (antibody then antigen) was performed at the Centre from 1991, when reliable tests were available to NHS Scotland including the Regional Virus Laboratory, according to UKHCDO guidance from its Working Party on Hepatitis. Information on testing was given to patients and verbal consent obtained, as had been the case since the early 1970s for HBV. I agreed with Dr Hay's view, in his report to the Inquiry, that HIV-type pre-counselling was not required for HCV testing. I noted that I had also been advised of this in January 1990 by Dr Iain Simpson, Chief Executive of the Medical and Dental Defence Union of Scotland, at a meeting of UKHCDO; and discussed this with SNIHDs in February 1990.

37.3.9. I stated that information was supplemented by giving patients booklets on hepatitis from the Haemophilia Society or British Liver Trust. If a patient had a positive HCV test result, they would be

sent an early appointment for a clinic review and discussion of the implications of the result. Patients were advised that PCR results for the antigen documented that the patient was a carrier of the virus, and would be referred to the local liver clinic for monitoring, advice on precautions with regard to sexual intercourse, further investigation, and consideration for antiviral treatment.

37.3.10. I was surprised when Lord Penrose asked me not to discuss hepatitis B (page 49), but realised that it was omitted from his Inquiry's remit. I am surprised at this omission, given that hepatitis B was the first identified transfusion transmitted hepatitis virus; and that its management from 1970 (routine testing of blood donors and of frequent recipients of blood and blood products, and from 1985 vaccination; tracing and testing of contacts; and treatment of infected persons by specialists in infectious diseases / hepatology, including advice, support, monitoring and eventually antiviral drug therapy) established a precedent for management of transfusion transmitted HIV, HCV and HAV. This maxim of "test, trace and treat" for control of emerging infection pandemics resonates today in the COVID-19 era.

37.3.11. I note that the Penrose Inquiry Final Report (2015) concluded (page 1680): "Professor Lowe's evidence is accepted that, throughout his period at the GRI, clinicians discussed "hepatitis" with patients. Having regard to Professor Lowe's evidence, many patients attending the GRI throughout this period were informed of the risks of transmission of viral hepatitis associated with factor concentrate therapy, so far as it was understood. Review clinic practice appears to have been well adapted to provide opportunities for discussion and the provision of relevant information."

37.3.12. With Dr Walker as my co-Director from 1990; and with Dr Tait as our co-consultant from 1999 and our Co-Director from 2000; we

continued to provide information to patients at the Centre on the current state of risks of infection from treatments, especially factor concentrates. This would be during patient reviews, local meetings of the Haemophilia Society, and display and distribution of Haemophilia Society information leaflets and newsletters at the Centre. Patients were informed that Centre staff were expanding, with extra medical, nursing and social work/counselling staff; that the Centre was collaborating with colleagues in infectious diseases, sexually-transmitted diseases and hepatology; and were always willing to discuss risks of treatments, and their management, with patients, partners and families.

37.3.13. Such information would include: that only virally inactivated factor concentrates were used at the Centre; that UKHCDO was monitoring their safety at UK level (including their orange card reporting system for adverse events, established from 1989); that from 1989 the formal SNIHCD Group's viral safety study was under way, and by 1993 had established safety of SNBTS concentrates; and that from 1997 the Recombinant Factor Consortium and Coagulation Factor Working Party were progressively replacing plasma concentrates with recombinant (non-human) concentrates to remove all risk of human pathogens (including vCJD) - which was achieved for most patients in Scotland by 2002, several years before England.

37.4. **HIV/AIDS: The Practice at Glasgow Royal Infirmary (pages 1540-1543).**

37.4.1. In his evidence to the Penrose Inquiry in 2011, my predecessor Dr Forbes recalled the emergence of the risk of immune deficiency and AIDS, including in patients with haemophilia, from 1982. It was apparent to the Inquiry that he had a poor memory of this time and of his actions in 1983-1987, including details of treatments, with which the Central Legal Office asked me to help the Inquiry (STHB0000828). I recall that he had not been involved

with treatment of patients with haemophilia after moving to Dundee from 1987 onwards, and his health was deteriorating. The Inquiry therefore asked me about information given to Centre patients on AIDS and HIV between 1983 and 1985 (Transcript, 30 June 2011, PRSE0006040).

37.4.2. I told the inquiry that I had little involvement with in-patients with haemophilia in 1983-85, being attached to another medical unit. I only provided occasional assistance in clinical care of patients with haemophilia. I recalled increasing concern about AIDS in 1983 and 1984, but could not recall if I routinely raised the issue of AIDS, and did not recall any specific patients asking me about it. I recalled that information was being given out at the Centre from the Haemophilia Society's educational leaflets (Haemofact). These gave the consistent message that, while patients should balance the risks for themselves, Centre directors continued to recommend they continue their concentrate therapy; and stressed that patients should discuss their treatment with their haemophilia centre director. I was not doing any regular reviews with the patients, but told the Inquiry that in the event of a patient asking me about risk of AIDS, I would give them what information I could, including the Haemofact leaflets which were available in the Centre. I did not recall that Dr Forbes produced a protocol for initiating discussions with patients about the risk of AIDS.

37.4.3. I explained that if a patient had a concern about their treatment, I would have referred them to Dr Forbes, who was very knowledgeable about the risk of AIDS, and about any changes in treatment that should be considered – which would be a decision for him as consultant and as Co-Director of the Centre.

37.4.4. I provided a further written statement to the Inquiry a few days later (PRSE0001112, PEN.018.0559), expanding on the Haemofact factsheets and their messages.

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

38.1. I refer you to the Penrose Inquiry Preliminary Report (2010). In December 1984 SNBTS recalled non-heat-treated Factor VIII concentrate, and dry-heat treated all stocks (two hours at 68 degrees C) (Page 483). I presume that the Centre used these for all haemophilia A patients who required treatment with Factor VIII concentrates. SNBTS did not produce heat treated Factor IX concentrates until October 1985, and I recall that the Centre from April until that time used commercial heat-treated Immuno Factor IX (Appendix 1, page 570).

a. What role did you play in (i) the initial decision to use heat treated products, and (ii) any subsequent decisions on which products should be used?

38.2. None from 1985-87. From 1988, as Co-Director, I discussed with Drs McDonald and Davidson which products might be used in light of UKHCDO guidance from May 1988, and these were ordered by Dr Davidson.

b. Who was responsible for the decision on which products should be given to which patients?

38.3. As Co-Director, I would discuss these regularly with my Co-Directors (Dr McDonald from 1988, Dr Walker from 1990) and Dr Davidson, who did the ordering until 1996, which was then done by Dr Walker.

c. Please consider the list of commercially produced products referred to at §13, §15 and §17 of your Comments on Professor Forbes' Evidence. In respect of the

heat-treated products, why were specific products chosen (e.g. were they considered to be safer, more cost-effective, easier to use etc)?

38.4. I refer you to my answer to Question 11.

38.5. I presume that factors influencing choice included efficacy, safety, availability and cost – the last two factors were for Drs Davidson, then from 1996 Dr Walker, who were in charge of the Blood Bank and Blood Products laboratory, to discuss with manufacturers. I suggest you ask Dr Walker.

d. You refer at §17 to the recommendation by the UK Haemophilia Reference Centre Directors in May 1988 [PRSE0003484] to use Profilate. Why was this recommendation made? What role, if any, did you have in making the recommendation? Did you agree with it?

38.6. In these UKHCDO recommendations (25), page 3, 4,2,1, Profilate HT (Alpha) is described as a 2nd generation product with a full product licence, considered to have a negligible risk of HIV transmission, and a reduced risk of NANBH transmission in virgin patient studies. On page 6, 5.2.3, for patients in Scotland and Northern Ireland the recommendation is that NHS 8Y is not available and the recommendation is either Z8 (SNBTS) or the commercial products mentioned above in 5.2.1. In 5.2.1, Hemate P is the 2nd choice after 8Y, and Profilate is the 3rd choice.

38.7. As co-signatories to these recommendations, I recall that Dr McDonald and I agreed with the final version, after the drafts had been discussed by all signatories.

38.8. When SNBTS were unable, later in 1988, to produce sufficient Z8 to meet the needs of Haemophilia Centres in Scotland, the Centre had to order commercial product. I recall that Dr McDonald and I discussed the UKHCDO recommendations with Dr Davidson, who made enquiries with the

manufacturers of Hemate P (which was not available; see question 39 below) and of Profilate (which was available). We all agreed that Dr Davidson should therefore order Profilate. The agreed policy of Haemophilia Directors in Scotland and Northern Ireland at this time was that patients who had received only NHS (SNBTS) factor VIII should continue on Z8; so at the GRI Centre Profilate was substituted for treatment of patients with Factor VIII deficiency who had been previously treated with commercial Factor VIII concentrates. All such patients were informed of this change of treatment, and given full information on Profilate and the reason for change.

e. You state at §16 that the need for these products to be ordered "may have arisen for several reasons", which you then set out. Is this section of your evidence based on your direct knowledge? If not, what was the basis for your evidence in this paragraph?

38.9. I had **no** direct knowledge before I succeeded Dr Forbes as Co-Director at the end of 1987. Central Legal Office in 2011 asked me to recall from memory the possible reasons, and, to assist the Penrose Inquiry, I said what I could recall in general, thinking back to the period 1976-1993. Being retired, I had no access to patient records, which might record the reasons for these products to be used.

f. Are you aware of any of the patients at your centre being infected with HIV and/or HCV as a result of the use of a heat-treated product (either commercial or NHS/SBTS)? If so, how many such patients were infected, and by which products?

38.10. I am not aware of any GRI Centre patients being infected with HIV as a result of the use of a heat-treated product.

38.11. The Scottish Executive Health Department Inquiry into Hepatitis C and heat treatment of blood products for haemophiliacs in the mid 1980s (October 2000) raised the question of how many patients treated between September 1985 and December 1987 for the first time with the first SNBTS heat-treated factor concentrates (68 degrees C for 2 hours initially) subsequently seroconverted to HCV (74). I recall that GRI Centre staff identified that 2 such patients with Factor VIII deficiency seroconverted, of whom one also received cryoprecipitate. Further information may be available from current Centre Directors.

g. Were any commercial heat-treated products withdrawn from use at the Centre, and if so why? Were any such products considered with suspicion, and if so, why?

38.12. I do not recall withdrawal of any such products. Further information may be available from current Centre Directors.

i. You may be assisted by considering the 1st edition of the UK Regional Haemophilia Centre Directors' Committee Recommendation on Choice of Therapeutic Products, dated 16 May 1988 [PRSE0003484]. At p.3 of the document there is reference to all "1st generation" commercial dry heated products being withdrawn from the market, except Cutter's Koate HT.

ii. You are recorded as one of the authors of this guidance. What was your role in producing it?

38.13. As a new member of UKHCDO from 1988, I attended its Directors meeting at which Dr Peter Kernoff, who drafted these recommendations for discussion, presented the draft, and reviewed the evidence on which it was based. I recall that this review by Dr Kernoff, who had researched and published in this area extensively (23,75) was well researched and well

presented. I do not recall contributing to the discussion at this meeting, but following the meeting I did discuss it, and particularly the draft recommendations for patients in Scotland, with Dr McDonald, Dr Davidson and Dr Ludlam. I do not recall sending any comments to Dr Kernoff, and once the drafts were finalised Dr Ludlam, Dr McDonald and myself each approved it for NHS Scotland.

iii. What was meant by the references to "anecdotal reports" or "anecdotal evidence" in respect of infections caused, or suspected to be caused, by particular blood products (i.e. what did such evidence comprise of)? On what basis was such evidence "always disputed by manufacturers" (see reference at p.3).

38.14. An anecdote is a story or report by a person about an experience (for example, a doctor reporting a disease, a treatment, or in this case a complication of treatment), either at a meeting or in a publication. While an anecdote may be interesting, in medical science, and for evidence-based medical practice, it is the lowest level of evidence for reliability. Because of its unreliability as evidence, an anecdote would "always be disputed by manufacturers" who, as with all parties, would wish for additional, and if possible more reliable evidence to inform decisions. For example, a patient reported as seroconverting might also have received other blood products.

39. The Inquiry has obtained the minutes of the 30th meeting of the Haemophilia Reference Centre Directors' meeting held on 5 September 1988 [HCDO0000431]. The minutes (p.3) record a discussion in which "reservations were expressed about the Scottish factor VIII, 8Z [sic]." You are recorded as asking the English Haemophilia Centre Directors "if they were therefore prepared to make 8Y available for previously untransfused patients in Scotland. This was not accepted."

a. Please explain the background to this discussion, and your recollection of it.

39.1. This meeting was attended by, from Scotland, Dr Ludlam (Edinburgh), and for GRI Dr Walker (representing Dr McDonald) and myself.

39.2. On page 3, para 2, "Dr Kernoff said that he thought the original document should be revised, particularly in the light of the unavailability of Hemate P." I recall that this had been discovered by Dr Davidson in GRI when enquiring about availability of products recommended in the original document (see Question 38d above). Then, "Dr Ludlam raised the question of the position in Scotland where there was going to be a shortfall of 2 million units in the current year. SNBTS had announced that they were only capable of producing 7 million units because of a fall in donations and problems with stock control. This problem was likely to last for the next two years."

b. What reservations were expressed at this time about 8Z/Z8? Did you share those reservations?

39.3. I refer you to the minutes of the meeting of the Directors of SNBTS and Haemophilia Directors of 5th May 1988 (PRSE0003384, SGH.001.7505). It was reported that increasing confidence in its safety had led to a current surge in demand for Z8. Possible reasons included change from use of cryoprecipitate to factor concentrate - as recommended in evolving UKHCDO guidance (25); elective surgery previously postponed was now being performed; and I reported that some of my patients thought that heat treated factor VIII concentrates might be less effective than concentrates they previously used and were therefore using higher doses in home treatment.

39.4. Dr Ludlam and I pointed out the potential difficulty of low numbers of previously untreated patients in Scotland being available for testing of SNBTS heat treated factor concentrates for viral safety. Dr Ludlam was

invited to convene a small group to address this problem, which was the Factor VIII Working Party, subsequently renamed the Coagulation Factor Working Party (REF).

c. Did later evidence or studies affect the reservations that had been expressed? (The article that you co-authored in 1993, "Study of viral safety of Scottish National Blood Transfusion Service factor VIII/IX concentrate", B. Bennett et al, Transfusion Medicine 1993, 3, 395-298, may assist. [PRSE0000082])

39.5. Yes, it did. While I agreed with Dr Ludlam at the meeting on 5th May 1988 about the potential difficulty of low numbers of previously untreated patients in Scotland available for testing for viral safety, fortunately we did manage to enrol sufficient patients by 1993 to study this and to publish this report (28).

d. Did you seek the provision of 8Y for previously untreated Scottish patients at this meeting? If so, why?

39.6. Yes, I did. Discussions between Scottish Haemophilia Directors about the feasibility of a viral safety study of Z8 in previously untreated Scottish patients had included the question of having a "Plan B", in the event that early in such a study a seroconversion occurred. What product could then be used for such patients? Given the preliminary evidence of viral safety of 8Y, it seemed reasonable for us to raise this question as a possibility for a Plan B, which I did on behalf of Scottish Haemophilia Centre Directors.

e. What explanation was given for the apparent refusal of this request?

39.7. I recall it was because: "demand for NHS heat-treated product in England and Wales exceeded the supply of 8Y" (Penrose Inquiry, Final Report, 2015, Executive Summary, Page 20).

f. Are you aware of any other requests for 8Y being made at other times? If so, what was the outcome?

39.8. I was not aware of any other request at that time. However, the Penrose Inquiry established that on 1 August 1986, 50 vials were sent from the BPL; they were kept in Edinburgh. (Penrose Inquiry, Final Report, 2015, Executive Summary, Page 20).

40. Did you or your colleagues at the Centre 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?

a. You may be assisted by §1.1 of your C3A Statement and p.12, pp.18-19 and pp.27-31, p.53, and pp.59-67 of the Transcript of your evidence to Penrose Inquiry on 13 October 2011.

40.1. Yes, Dr Forbes and his colleagues did revert to treatment with cryoprecipitate at times - I refer you to my answer to Question 17 (cryoprecipitate) for the details.

40.2. As I said also in my answer to Question 17 –

40.2.1. In my evidence to the Penrose Inquiry, Transcript 28 June 2011, p.164 and following [PRSE0006039], I recalled that the first

UKHCDO guideline on choice of blood products came out in May 1988 (25) which recommended that cryoprecipitate no longer be used for such patients, because by this time concentrates had been virally inactivated and were generally thought to be safer. My recollection is that from this time Drs McDonald, Davidson and I agreed that we should follow this advice.

40.2.2. By 1992, virally-inactivated von Willebrand factor concentrates (for example, BPL 8Y, Hyate C) were recommended in the updated UKHCDO recommendations on choice of therapeutic products, instead of cryoprecipitate (46).

41. The Inquiry has obtained a copy of a letter that was sent in your name and that of Dr Forbes, dated 8 January 1985 [PRSE0000859]. You were asked about this letter during your evidence to the Penrose Inquiry (see, in particular, pp.29-46 of the Transcript of 30 June 2011 [PRSE0006040]), and subsequently provided a further statement about it ("the Further Statement re. June 2011 Evidence" [PRSE0001112]). Please answer the following questions about this letter, making reference to your previous evidence where appropriate.

a. What role did you play in drafting the letter?

41.1. None. As I said at the Penrose Inquiry on 30 June 2011 (Page 30 [PRSE0006040]), the letter was drafted entirely by Dr Forbes. When shown a copy by the Inquiry that day, I did not recall it at first, because I never had a copy of it in my files. I recall I had only been shown it briefly by Dr Forbes on 8 January 1985, which was my first day back in the Department of Medicine after my week of annual leave. I had to read through it slowly on 30 June at the Inquiry, and, with help from Mr Gardiner, work out that it had probably started as a form letter drafted by Dr Forbes with other Centre Directors in Scotland (PEN.012.0495, PRSE0002785), which Dr Forbes then

customised with his own heading to send to patients attending the GRI Centre. I requested to the Inquiry on 30 June 2011 that I be given a copy of the letter to consider, then send the Inquiry a further written statement.

41.2. A few days later, I sent this further statement (PRSE0001112, PEN.018.0559). I recalled that Dr Forbes drafted the letter, discussed it with myself and Sister Campbell, and asked if I could add my signature to it. The reason for this, Dr Forbes told me, was that, in the event that patients receiving it wished to discuss it prior to an appointment, and Dr Forbes was not available, I could be the alternative contact. I was happy to do this, added only my name and signature to Dr Forbes's draft, and gave it to the Unit Secretary, who retyped it for signing by Dr Forbes and myself. In this statement I presumed that the letter would then be sent out to patients with appointments by Sister Campbell.

41.3. I would add now that I see the written heading on this letter (AIDS Haem Directors W.P., Enclosure). This reminds me that Dr Forbes on 8 January wanted a draft of this draft letter quickly, to table and discuss at the first meeting of the UKHCDO AIDS Working Party which he was chairing on 11 January; and I wonder if this version of the letter was retrieved from these UKHCDO files.

b. Why were you the only co-signatory to the letter, given that in January 1985 you had not been promoted to consultant and that your principal position was within another medical unit at the Glasgow Royal Infirmary rather than the Haemophilia Centre?

41.4. The only reason I can think of is that Dr Forbes wanted me (as a junior doctor who had been around Wards 2 and 3 from 1975 to 1983 and might therefore be known to many patients at the Centre) to be an alternative contact, in the event that patients wished to discuss it prior to an appointment and Dr Forbes was not available. As a co-author of the recently published paper (63) whose

results for positive antibody tests are mentioned in the letter, I would have some knowledge of AIDS risk; and Dr Forbes informed me of the recent heat treatment of SNBTS factor concentrate also described in his letter.

c. Is there any significance to the fact that you are the first signatory to the letter, and Dr Forbes is the second?

41.5. I am surprised that my name appears first, and I wonder if the secretary had done this by mistake when she added my name to that of Dr Forbes who drafted it. The letter was entirely the work of Dr Forbes. He, as consultant, Centre Co-Director, Chair of the UKHCDO AIDS Working Party, and lead researcher of the epidemiological study which had recently identified that some Centre patients were HTLV-III antibody positive (63) was the doctor with all the relevant information who was going to review his patients at the appointments he made for them. I never saw any copy of this letter in Centre files or case records, and I wonder if it was in fact sent to patients in a different and more appropriate format. I do not recall ever being contacted by any patient to discuss this letter. I do not recall any patient that I subsequently reviewed at the clinic mentioning it or producing it.

41.6. Obviously, I could not discuss this with Professor Forbes during the Penrose Inquiry. After the Inquiry's Final Report was published in 2015, I visited him at his home for a social catch-up and to discuss the Report's conclusions and any matters arising, including this question. I recall that he told me that he thought he had modified the draft letter after discussion at the UKHCDO working party meeting on 11 April, putting his name first.

d. To which categories of patients was the letter sent? In particular, was it sent to patients assessed to have (i) mild, (ii) moderate, and/or (iii) severe haemophilia?

41.7. I do not know. I had no role in sending the letters.

e. What was the purpose of the letter?

41.8. It appears that Dr Forbes was informing his patients on the developments with AIDS. It was caused by a newly-discovered virus. Steps had been taken to reduce the risk of this virus (exclusion of blood donors at risk of AIDS; and heat treatment of factor VIII concentrates). A blood test for antibody to the virus had been developed. Recent studies in England had found that about half of regularly treated haemophiliacs had positive antibody tests. Dr Forbes and his colleagues (not including myself) had recently tested stored blood samples from many of his patients, of whom about 10% had positive antibody tests. He suggested that the lower level in his patients was probably due to the fact that the Centre had largely used Scottish concentrate in recent years rather than concentrate from the USA.

41.9. Dr Forbes enclosed an appointment to discuss these developments, and to arrange further blood tests to monitor virus exposure in all patients who had received factor concentrates. He advised that all patients should take precautions to reduce risk of transmission to other persons. He would be very happy to talk to wives / other family members / sexual partners about possible exposure to the virus; and invited patients to bring them along if they would like to do this.

41.10. I think that Dr Forbes' letter, which he drafted on 8 January, soon after the Scottish Office's news release on heat treatment of SNBTS Factor VIII concentrate etc (20 December 1984); and soon after the relevant study (63) was published in the Lancet (22/29 December 1984); was very prompt; and very honest and open with his patients and their families. This, I recall, was always his practice.

41.11. I refer you to my answers to Questions 50-52, which detail the procedures through which Drs Forbes and Wilkie counselled patients attending the clinic for the invited discussions; and pre-and post-counselled them about HIV testing using Dr Follett's Regional Virus Laboratory regulatory-approved tests. These were completed, and confirmed the results of the Melbye et al study (63), as reported by Dr Follett at the first meeting of the Greater Glasgow Health Board AIDS Information and Advisory Group on 31 May 1985 (SNB,004.9656).

f. Who was responsible for the advice: "The risk of the disease, AIDS, in haemophiliacs appears to be very small and less than the risks of bleeding. We therefore recommend that you should continue treatment with clotting factor concentrates"?

41.12. Dr Forbes. It was his letter.

g. On what basis was it said that the risk of AIDS in haemophiliacs appeared to be "very small and less than the risks of bleeding."

41.13. That would be Dr Forbes' opinion, but it appears to be also that of other UK, including Scottish, Centre Directors at that time.

41.14. I note that the last sentence of the form letter drafted by Dr Forbes with other Centre Directors in Scotland (PEN.012.0495, PRSE0002785) states:

"Remember that you must continue to treat yourself with the concentrates as the risks are much greater of bleeding than of contracting the rare disease of AIDS."

41.15. I recall that, in February 1985, the UK Haemophilia Society published the booklet "AIDS and the blood. A practical guide" (76), which Dr Forbes

and other doctors, nurses, paramedical staff and social workers, patients, mothers, laymen and secretaries helped Dr Peter Jones to prepare. Dr Forbes bought many copies of this from Centre funds, and sent them to patients registered at the GRI Centre in April 1985.

41.15.1. On page 7 it states:

"The present position.
Although it has attracted a great deal of media attention, the AIDS problem is still small compared with other diseases. By January 1985 there were 7981 cases in the United States. 59 of these were haemophiliacs and 112 were linked to blood transfusion. In the United Kingdom there were 118 cases of AIDS, principally among male homosexuals in London. Three people with haemophilia had Aids. The figures are shown in the table (3 adults with haemophilia out of the 4,500 UK haemophilic population."

h. Why was the advice given, and why was it given in those terms?

41.16. This advice was written by Dr Forbes; and is consistent with that in the form letter he drafted with other Scottish Centre Directors - see answer to (g) above.

41.17. I recall that the general advice given by UKHCDO, UK Haemophilia Directors and the UK Haemophilia Society in 1985 was that patients should not stop their haemophilia treatment of bleeds. For example, the UK Haemophilia Society booklet "AIDS and the blood. A practical guide" (76) states on page 25:

"SHOULD I STOP MY HAEMOPHILIA TREATMENT?
No. Bleeding causes more crippling and premature death in haemophilia than AIDS has or is ever likely to do."

i. In your view, and given the terms in which it is expressed, is that advice consistent with the principles of patient consent that were in place at the time?

41.18. I note that Dr Forbes in this letter was enclosing an appointment to discuss several matters, including the change in SNBTS factor concentrate to heat-treated concentrate to destroy the AIDS virus. This had been announced in a news release by the Scottish Office on 20th December 1984 (see Question 50). I recall that Dr Forbes told me on 8 January that, as was Centre policy, information on this proposed change in blood product treatment would be given to each patient; and that, after discussion, they would be asked to give express consent to its use. This procedure would also apply to all patients attending the Centre for treatment, or to collect home treatment supplies.

41.19. My understanding is that Dr Forbes's procedure was consistent with the principles of patient consent that were in place at the time. I recall that Dr Forbes as Centre Co-Director was always willing to discuss the balance of risks and benefits of their haemophilia treatment of bleeds with his patients; and respected patients' decisions to refuse treatment, or to stop using their home treatment.

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

42.1. I believe that the decisions and actions of my predecessor Centre Co-Directors, which I have described above, were adequate and appropriate.

42.2. I consider myself fortunate that, by the time I succeeded Dr Forbes as GRI Centre Co-Director in late 1987, all factor concentrates given at the Centre

were virally inactivated, sufficient to prevent infection with HIV and hepatitis (A, B and C). I consider that from that time the decisions and actions of my colleagues and myself in response to any known or suspected risks of infection were adequate and appropriate; including the achievement of replacing plasma factor concentrates with recombinant factor concentrates for most patients in Scotland by 2002.

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

43.1. I cannot recall any decisions or actions by my predecessor Co-Directors at the Centre which could or should have avoided, or brought to an end earlier, the use of infected blood products.

43.2. From the time I became Co-Director in late 1987, the Centre used only virally inactivated blood products (or recombinant, non-human factor concentrates), and I am not aware of any new infections from that time.

44. 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?

44.1. For NHS Scotland, I recall that the Penrose Inquiry investigated these matters thoroughly, and I do not recall that its reports indicated that anything could or should have been done differently which would have reduced the scale of infection.

44.2. I note that the Penrose Inquiry Final Report (2015), Executive Summary, states –

44.2.1. "When the news came that HIV had entered the Scottish donor population, and that patients had acquired HIV from Scottish product, the PFC moved swiftly to introduce dry heat treatment and was able to provide the first comprehensive national supply of heat-treated Factor VIII in the world. The Inquiry has no criticism to make of those involved in viral inactivation in Scotland. "(Page 22).

44.2.2. "The Inquiry notes that the PFC's success in being able from 1987 onwards to provide all Haemophilia A patients with a product that did not transmit HCV was a considerable achievement." (Page 24).

44.2.3. "The distribution of heat-treated Factor VIII concentrate from December 1984 and of heat-treated Factor IX from October 1985 ended the transmission of HIV by Scottish NHS blood products. Commercial products were also HIV-safe from that time." (Page 43).

44.2.4. "The heat treatment of NHS Factor IX introduced in Scotland in 1985 also rendered it safe against HCV. More severe heat treatment of Factor VIII introduced in 1987 inactivated HCV. (Page 43).

44.2.5. "Clotting factors are now artificially synthesised to produce drugs that do not carry a risk of viral transmission." (Page 43). I would add that transfer from human to recombinant factor concentrates in Scotland commenced in 1997 through the Recombinant Factor

Consortium and CFWP, resulting in provision for most patients with haemophilia in Scotland by 2002, several years before rUK.

45. Do you consider that greater efforts 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?

45.1. Prior to 1980 I was a junior doctor with only limited experience of haemophilia care; and therefore I cannot comment.

45.2. I note that the Penrose Inquiry Final Report (2015) reviewed the history from the 1970s of potential viral inactivation of blood products - in Scotland, the UK, and internationally; summarised in the Executive Summary (pages 20-24). For the period before 1980, it states - "Initial ideas centred on inactivation by heat, radiation or chemical treatment. Many different attempts had been made using specific techniques in these categories but none had succeeded in eliminating infectivity without unacceptable damage to product."

Section 4: Treatment of patients at the Centre

Please refer to the evidence that you gave to the Penrose Inquiry when answering the questions in this section, including making any corrections, amendments or additions that you feel to be necessary.

Provision of information to patients

46. What information did you provide or cause to be provided (or was, to your knowledge, provided by others at the Centre) to patients with a bleeding disorder about the risks of infection in consequence of treatment with blood

products (in particular, factor concentrates), prior to such treatment commencing? Please detail whether and if so how this changed over time.

46.1. I refer you to my answer to question 37, which summarises the evidence provided by the Centre in general to patients. I cannot recall myself giving information to any patients prior to their first treatment with blood products commencing. As GRI was an Adult Regional Reference Centre for the West of Scotland, many of its patients registered had been first treated with blood products at other hospitals in the West of Scotland, often as children – so especially at Yorkhill Hospital for Sick Children. See the Scottish Haemophilia Centre Directors' Collective Response to the Penrose Inquiry, on information given to patients on hepatitis (PRSE0003869).

46.2. After I succeeded Dr Forbes as Centre Co-Director in late 1987, I do not recall the Centre starting any patients on human factor concentrates for the first time. By that time, all human factor products were virally inactivated, and patients were informed of this, by myself, or my Co-Directors Drs Walker and Tait. If patients were transferred to a new type of human factor concentrate, they would be given information about it, including its safety for virus transmission.

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

47.1. I refer you to my answers to Questions 21, 16 and 17.

47.2. In Question 21 – Tranexamic acid, desmopressin, cryoprecipitate or plasma. Information on these alternative treatments would be given to appropriate patients.

47.3. I recall that the GRI Centre followed UKHCDO advice and guidelines for treatment – generally use of non-blood product treatments if appropriate (e.g.

tranexamic acid, desmopressin); and if required plasma products from small blood donor pools (cryoprecipitate or plasma) were preferred to minimise risk of hepatitis. Concentrates would be used if such products were ineffective or contra-indicated.

47.4. In Question 16 – Desmopressin. Information on this alternative treatment would be given to appropriate patients.

47.5. I refer you to my evidence to the Penrose Inquiry at Transcript, 13 October 2011, p.24 [PRSE0006054]. I said that DDAVP (desmopressin) was the treatment of choice for mild haemophilia, and for mild von Willebrand's disease; in conjunction with ancillary haemostatic measures, like tranexamic acid.

47.6. In Question 17- Cryoprecipitate. Information would be given on this to appropriate patients.

47.7. I refer you to my answer to Question 17.

48. What information did you provide or cause to be provided (or was, to your knowledge, provided by others at the Centre) to patients before they began home treatment?

48.1. I recall that most patients at the Centre were trained in home treatment between 1979 and 1983, by the Haemophilia Sister (Agnes Ward) and consultants Drs Prentice and Forbes. Dr Forbes was a member of the UKHCDO Working Party on home therapy. I was not involved in such training, but observed it occasionally, for example, when teaching students - if the patient agreed to a few of them observing this for a few minutes.

48.2. My recollection is that the Centre had copies of the book, "Haemophilia Home Therapy", edited by Dr Peter Jones (47), which the Centre used to train

patients and their family members who might assist them with home treatment. The Scottish Haemophilia Directors' Collective Response to the Penrose Inquiry, on information given to patients on hepatitis (PRSE0003869) noted that there are several references to risk of hepatitis in this book.

48.2.1. For example, pages 74- 75: "Every family knows that the use of human blood products carries the risk of hepatitis. They are aware that this risk has been linked particularly to commercial concentrates prepared from the blood of paid donors, and they know that these risks still exist despite the increased sensitivity of donor tests for hepatitis B. Families are taught the symptoms and signs of hepatitis, and asked to report to the centre immediately the affected member becomes jaundiced. Explicit instructions on the handling of equipment to eliminate the risk of accidental puncture with contaminated needles ('needle-stick') are given, and due attention paid to the careful disposal of used equipment in order to reduce the risk of hepatitis spread."

48.3. I would add that, when hepatitis B vaccination was available from 1985, I recall that all patients attending the Centre, and family members who assisted with home treatment, were tested for hepatitis B and advised vaccination if they were not naturally immune.

48.4. I cannot recall if the Centre started any patients on home treatment after 1983. As I stated in Questions 18 and 19, when patients from Yorkhill (or other Centres) transferred to the GRI Centre who were on home treatment, its need would be reviewed regularly, together with our rheumatologists, who were monitoring musculoskeletal bleeds and haemophilic arthritis.

HIV

49. When did you first discuss AIDS or HIV (HTLV-III) with any of the patients at the Centre? What did you tell them?

49.1. I refer you to my answer to Question 37.

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

50.1. I refer you to the Penrose Inquiry Final Report (2015) for an account of the development of HIV (anti-HTLV-III) testing of patients with haemophilia in the UK and in Scotland from 1984 (Volume 5, pages 1573-1637). UK Centre Directors were anxious to establish the prevalence of HIV exposure/infection in their patients, and its relationships to previous treatment with blood products (NHS and commercial), in order to guide identification of high risk products (and any specific batches of these for donor identification), and to guide development of viral inactivation of factor concentrates to reduce risk of future infections. Since the early 1970s such testing had been mandated for hepatitis B. UKHCDO advised that the only UK laboratory which could carry out testing (with a research assay) was that of Professor Tedder at the Middlesex Hospital, London; and Centres including Aberdeen, Cardiff, Edinburgh, London, Newcastle and Sheffield sent him a total of 584 stored serum samples for testing (73,77,78,79). 215 of 315 patients (68%) who received commercial concentrate for haemophilia A were seropositive, compared to 18 of 166 patients (11%) given British NHS concentrate alone (79).

50.2. At the GRI Centre, Drs Forbes and his colleagues in the Rheumatology Section of the University Department of Medicine, Drs Froebel and Madhok, selected 77 stored serum samples from their epidemiological studies of arthritis and immune abnormalities in patients at the Centre, and sent them to Dr Gallo's laboratory in Bethesda, USA for testing with another research assay of anti-HTLV-III (63). 12 samples were seropositive (16%); and the

results were combined with those of 22 samples from Dr Mads Melby, Aarhus, Denmark (59% seropositive). 23 of 58 patients (40%) who received commercial concentrate were seropositive, compared to 2 of 30 patients (7%) given local concentrate alone.

50.3. My evidence to the Penrose Inquiry was: I was not directly involved in this study, and recalled that my contribution as a co-author was (a) critical review of the manuscript, and (b) drafting the first paragraph of the results section which described a Scottish patient with haemophilia who developed AIDS – I had assisted Dr Forbes and doctors from the Infectious Diseases Department when Dr Forbes had recently admitted him for investigation of symptoms suggestive of the "AIDS-related complex". The investigators subsequently reported further data on the dates of seroconversion of the Scottish patients seropositive for HTLV-III antibody (64). I was not directly involved in this study, and I recall that my contribution as a co-author was critical review of the manuscript.

50.4. I recall first hearing about these results in late October 1984, when Dr Melbye visited the Department of Medicine and presented his draft paper for the Lancet to Drs Forbes, Froebel, Madhok and myself. I tabled the paragraph Dr Forbes had asked me to draft about the patient who developed AIDS. The results were discussed for Dr Melbye to finalise the paper, which was submitted to the Lancet and published in December 1984 (63).

50.5. When asked at the Penrose Inquiry about when patients were tested for HIV and informed of the results (Transcript of 30 June 2011, pages 52-53 [PRSE0006040]) I stated that, when the draft paper was discussed in October 1984 and Dr Froebel and I asked Dr Forbes "Well, what happens now?", he said "I will see the patients, I will speak to them and I will arrange counselling… I will discuss the results." I stated "I knew that he had reservations about whether the test was accurate or not" – as Dr Froebel pointed out in her statement to the Penrose Inquiry (PEN.012.1628, PRSE0002026), Dr Gallo's research HIV antibody test had not yet been approved by the regulatory body for clinical diagnosis in patients. I stated "I

do know that he was very keen that the situation now should be that we should have authoritative tests, licensed for advising and managing patients."

50.6. I was asked by the Penrose Inquiry about my knowledge of the evolution of events concerning HIV positivity in patients with haemophilia in Scotland during November-December 1984. These are summarised in the Penrose Inquiry Preliminary Report (2010), pages 216-219. On 29 November 1984, SNBTS and Haemophilia Centre Directors met. In patients at the Edinburgh Centre, Dr Ludlam reported that recipients of SNBTS PFC Factor VIII concentrate had developed antibodies to HTLV-III, measured at Dr Tedder's London laboratory as part of a UK-wide study of patients with haemophilia; Dr Forbes reported the Melbye study in Glasgow and Denmark; and Dr Gibson reported that 5 of 10 tested children at Yorkhill who had previously received imported Factor VIII concentrates were HTLV-III antibody positive. To reduce the risk of HTLV-III transmission, SNBTS proposed to replace unheated with heat-treated Factor VIII concentrate. On December 17, Dr Cash wrote to Scottish haemophilia directors announcing that delivery of heat treated Factor VIII was commencing. Drs Ludlam, Forbes and McLelland convened a meeting in Edinburgh on 19 December to inform patients of developments. On 20th December the Scottish Office issued a news release, announcing the change to heat-treated Factor VIII, and that a new letter had been issued to blood donors asking them to sign a statement that they were not in one of the risk groups. At the Penrose Inquiry, I recalled that I heard about some of these events from Dr Forbes around Christmas 1984. (Transcript 30 June pages 26-29 [PRSE0006040]).

50.7. As I stated to the Penrose Inquiry: following the letter Dr Forbes sent in January informing GRI Centre patients of these developments, providing advice on AIDS and risk reduction, and information on HIV testing; I recalled that he and Dr Patricia Wilkie commenced their appointments with patients to discuss HIV and testing and to counsel patients about this. I recalled that the focus was on the precautions to be taken by all patients; the likely availability soon of Dr Follett's Regional Virus Laboratory regulatory-

approved HIV testing and the implications of a positive test and a negative test. I confirmed that at this time I did not know the names of the patients with positive tests in the research study (63). At the time of my evidence to the Inquiry, I was uncertain about the date that Dr Follett's testing commenced. (Transcript of 30 June 2011, pages 42-47 [PRSE0006040]).

50.8. I confirm my evidence to the Penrose Inquiry; and would now add that the minutes of the first meeting of the Greater Glasgow Health Board AIDS Information and Advisory Group on 31 May 1985 (SNB.004.9656, PRSE0001606) record that Dr Follett had established his regulatory-approved tests, which confirmed the results of the Melbye Study that 12 patients were seropositive (63).

51. What if any arrangements were made at the Centre for pre-test counselling?

51.1. I recall that Dr Forbes appointed an experienced counsellor, Dr Patricia Wilkie, from January 1985 to December 1987, to perform both pre-and post-test counselling for HIV; as well as a research study to investigate how patients with haemophilia cope with information and knowledge about AIDS. From 1982 to 1988 she was a research fellow with Professor Ivanna Markova in the Department of Psychology at the University of Stirling, working in the GRI Department of Medicine, initially with Professor Arthur Kennedy on the genetic disorder polycystic kidney disease. Dr Forbes had worked with Professor Markova on the psychosocial problems of haemophilia and the effects of home treatment (19,21). He arranged with Professor Kennedy that at least part of Dr Wilkie's work be at the Haemophilia Centre from January 1985, assisting Dr Forbes in counselling initially the patients who were HIV positive in the Melbye Study (63). They also developed the grant application to the Scottish Home and Health Department, which was awarded in July 1985. Dr Wilkie provided a copy of the report of this study to the Penrose Inquiry. The latter part of Dr Wilkie's work in 1987 was funded by a grant from the Haemophilia Society.

51.2. Dr Wilkie was asked at the Penrose Inquiry (transcript 14 June, page 30) about her statement "My role as a counsellor gradually took over from my being a researcher. I met the patients both individually and with their partners, I would discuss the implications for testing for HIV with each of the patients. I would discuss the implications of being tested and there being a positive result and the implications of not taking a test."

51.3. Dr Wilkie, with Dr Forbes, also trained myself and other trainee doctors in pre-test counselling, which included checking that patients had received Dr Forbes's letters about AIDS, and/or the Haemophilia Society Booklet, AIDS and the Blood, which Dr Forbes had sent to patients registered at the Centre in April 1985 (76). If not, copies of the booklet were available at the Centre for patients to take away.

52. How and when were patients at the Centre told that they had been, or might have been, infected with HIV? Were they told in person, by letter or by telephone? Were patients seen individually or in groups?

52.1. My recollection is that Drs Forbes and Wilkie informed the patients who were HIV positive in the Melbye study (63) personally, by May 1985, after Dr Follett confirmed that they were HIV positive in his Regional Virus Laboratory (minutes of the first meeting of the Greater Glasgow Health Board AIDS Information and Advisory Group on 31 May 1985; SNB.004.9656, PRSE0001606).

52.2. When Dr Wilkie was asked at the Inquiry about her statement, "Almost all of the 20 or so patients I wrote to agree to meet me", she replied "These must be the patients who were HIV positive." (Transcript 14 June, page 29 [PRSE0006032]). On pages 35-36, Dr Wilkie stated that post-test interviews were in the clinic, usually with Dr Forbes.

52.3. Dr Wilkie recalled that on some occasions she may have been with myself when informing patients they were HIV positive. My recollection is that these latter occasions were in 1986-87, when I was a consultant, and they involved

not the Melbye study patients, but patients who transferred in 1986-87 to the GRI Centre from other Centres, who had been found to be tested at their previous Centre, then confirmed at GRI as HIV positive by Dr Follett (Transcript 30 June 2011, Page 59 [PRSE0006040])

52.4. Dr Forbes's supplementary statement to the Penrose Inquiry (Transcript 15 June, page 129 [PRSE0006033]), states: "The purpose of the study was to try and find out how many patients in our whole population of patients were HIV positive, although of course we did not get every patient that we did look after. The patients were aware that we were undertaking further studies of the infection, although specific details were not spelt out to them. At that time it was not the policy of the unit to specifically get informed consent for each study that was carried out. The patients in the course of time were all told of the result, of what had been found. In particular, those who were HIV positive were told and given specific instructions and counselling."

52.5. Dr Forbes described to the Penrose Inquiry how he informed the 12 patients who tested HIV positive after testing by Dr Melbye (pages 131-133 [PRSE0006033]). He said it would usually be himself (page 132), although he later stated that Dr Wilkie was certainly involved (page 133). He said that sometimes I would see the patients (page 132), but my recollection is that I did not review any of these patients until after I became a consultant in late 1985, by which time they had all been counselled and informed of their positive tests which had been confirmed in Dr Follett's laboratory, and I would just be confirming at their 3-monthly reviews that they remained HIV positive, and was reviewing their progress (Transcript 30 June, pages 61-66 [PRSE0006040]).

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

53.1. Dr Forbes, Dr Wilkie, and myself from when I became a consultant in late 1985, gave detailed oral and written information to patients who tested HIV positive on its significance. This included – the risks of developing clinical

symptoms of AIDS related complex or AIDS, and what these were; its potential transmission to others by sexual practices, blood and other bodily fluids and what precautions they should take; the need for regular (3 monthly) clinical review at the Centre together with Infectious Diseases consultants – initially Dr Dermot Kennedy or Dr Campbell Love.

53.2. I do not recall that patients were told to keep their infection a secret. We did discuss the current public concerns and fears about AIDS; who the patient might wish to discuss their diagnosis with (including family and partners), and the Centre's suggestion that their general practitioner be informed (in strict confidence), to ensure safe and coordinated clinical care. See the reviews in the Scottish Medical Journal, 1987, by Dr Kennedy (80), myself (81) and Dr Wilkie (82,83), and Dr Wilkie's Report to the Scottish Office on her research grant (which was sent to the Penrose Inquiry).

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

54.1. This was provided at the Centre initially by Dr Wilkie and Dr Forbes from January 1985, and described in detail by Dr Wilkie (82) and in her Report to the Scottish Office. After Dr Wilkie left in December 1988, this was provided by senior social worker Miriam Guthrie. We, and Dr Kennedy, could refer patients for counselling to Dr Kennedy's colleague Roger Wong, Consultant Psychologist in the AIDS service at Ruchill Hospital.

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

55.1. I recall Dr Forbes telling me that such discussions occurred at the UKHCDO meeting on 10 December 1984. When asked at the Penrose Inquiry about differences of opinion among UKHCDO members at this meeting Dr Forbes said: "And I personally took the view that it was only fair to tell people and

that there was no way of avoiding the telling of bad news and that was our policy." (Transcript 15 June 2011, Pages 140-141 [PRSE0006033]).

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

56.1. I recall that the Centre's policy was to recommend that patients discuss the risks of transmission with their partners / family members; and that the Centre staff were willing to discuss these with them and offer HIV testing after pre-counselling. If partners / family members then agreed to HIV testing, we could arrange testing at the Centre, or by referral to the Infectious Diseases or Sexually Transmitted Diseases Clinics (82). The Centre reported in 1986 that no household contact or recent sexual partner had tested positive for HIV antibody (84).

57. What if any information or advice did the Centre provide to partners or family members of people who were at risk of infection with HIV or were infected with HIV?

57.1. This was provided at the Centre by Dr Wilkie and Dr Forbes from January 1985, and described in detail by Dr Wilkie (82) and in her Report to the Scottish Office. After Dr Wilkie left in December 1988, this was provided by senior social worker Miriam Guthrie. Colleagues in Infectious Diseases (Dr Kennedy), Sexually Transmitted Diseases (Dr Sommerville), and Obstetrics and Gynaecology (Dr Hepburn) were also involved.

58. In his report, Lord Penrose found that 12 bleeding disorder patients at the GRI were found to be infected with HIV (Executive Summary, p.9). Do you consider that number to be correct (please provide reasons for your answer).

58.1. These data were collected for the Penrose Inquiry by Dr Tait who at that time was GRI Centre Co-Director (Transcript 30th March 2011).

58.2. I note that Dr Tait reported that 12 of 196 patients registered at the GRI Centre acquired HIV. I recall that this number refers to patients that he and Dr Chalmers, Yorkhill Director, judged had been infected with HIV by treatment at the GRI Centre. Subsequently, patients who were HIV positive through treatment at RHSC Yorkhill, or at other UK Centres, transferred to the GRI Centre, either after achieving adult age (Yorkhill), or moving to the West of Scotland (other Centres).

58.3. The Penrose Inquiry Preliminary Report (2010; pages 46-47, 3.60) reports UKHCDO data on the numbers of patients registered with Scottish Haemophilia Centres with all bleeding disorders who tested positive for HIV between 1982 and 1995. The total for Scotland was 72, of which 23 attended GRI, and 11 RHSC Yorkhill, (total for West of Scotland 34). The total number of patients registered at United Kingdom Centres out with Scotland who tested positive for HIV was 1,310. Scottish patients represented 5.2% of the United Kingdom total. The footnote on page 47 states "The Scottish Centre for Infection and Environmental Health data record 87 HIV+ve haemophiliac patients to 30 September 1999. The different reference periods may explain the difference."

58.4. If the Inquiry wishes further clarification on these numbers, I suggest it ask Professor David Goldberg, a member of its Clinical Groups on HIV and HCV, who assisted the Penrose Inquiry in clarifying numbers of HCV and HIV positive patients in Scotland.

Of those infected,

a. How many had severe haemophilia A?

58.5. I refer you to the Penrose Inquiry Report. Ten had haemophilia A – see page 18 of this Executive Summary. Nine had severe haemophilia A.

b. How many had moderate haemophilia A?

58.6. One.

c. How many had mild haemophilia A?

58.7. None.

d. How many had haemophilia B or von Willebrand's disease?

58.8. Two had haemophilia B – see page 18 of this Executive Summary.

e. Were any children?

58.9. None.

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

59.1. The Centre very rapidly investigated and published the time period during which patients seroconverted, which was between 1981 and 1984, suggesting that the virus was introduced into Scotland at about the same time as the onset of the AIDS epidemic (64).

60. What steps were taken to trace the source of infection of these patients, and with what success? Are you able to identify which products caused the infections?

60.1. See page 18-19 of the Penrose Inquiry Final Report Executive Summary. Three patients were apparently infected by commercial product and three by NHS (SNBTS) product. The remaining six patients had received treatment with both NHS and commercial product and it was not possible to ascertain which type of product caused their infection.

Hepatitis B

61. Were patients infected with hepatitis B informed of their infection and if so how?

61.1. I recall that in the period 1975-78 there were about 4 or 5 patients who were carriers of the hepatitis B virus attending the Centre, and they had all been informed of this by the Centre Co-Directors. I recall that a further patient was detected about 1984 and informed by Dr Forbes.

62. What information was provided to patients infected with hepatitis B about the infection, its significance, prognosis, treatment options and management?

62.1. I recall that all patients were given information, including the risk of transmission by blood or sexual intercourse, and risk of chronic liver disease (cirrhosis and cancer}; and were referred for follow-up by colleagues in Infectious Diseases or Hepatology Clinics, at which consultants would discuss prognosis, treatment options and management including prescription of antiviral drugs such as interferon.

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

63.1. As above, I recall about 4-5 initially, then I think another 1-2 transferred from Yorkhill or other Centres. The Penrose Inquiry did not collate this data, since HBV was not in its remit, but you could ask current Centre Directors.

NANB Hepatitis/Hepatitis C

64. Were patients infected with NANB hepatitis informed of their infection and if so how?

64.1. As I said in my answer to Question 28:

64.1.1. As I stated to the Penrose Inquiry (transcript 16 December 2011 [PRSE0006080]), the Centre routinely monitored patients receiving blood products for hepatitis, both clinically (for example, history of jaundice, signs of liver disease) and by laboratory tests for hepatitis (initially Hepatitis B, Hepatitis A and liver function tests; and from 1991 hepatitis C). Any patient developing clinical hepatitis was informed of the infection, and referred for investigation of blood products and other sources of infection (and tracing of contacts) to the local Infectious Diseases Department, and to the Haematology Department, who reported cases and blood product treatments to SNBTS or other manufacturers of factor concentrates. Cases of hepatitis were also reported to UKHCDO Secretariat, for collation and analysis in their annual reports.

64.2. I recall that patients suspected to have non-clinical NANB hepatitis (abnormal liver function tests) were informed and given the information described in the next section.

65. What information was provided to patients infected with NANB hepatitis about the infection, its significance, prognosis, treatment options and management?

65.1. I refer you to my evidence to the Penrose Inquiry (Transcript 16 December 2011 [PRSE0006080]). I recalled that Drs Prentice and Forbes would discuss these matters when they reviewed patients; as would I after I became a consultant in late 1985. By this time, patients were being advised to have

hepatitis B vaccination if they were not naturally immune; and in such discussions patients would be informed about NANB hepatitis which could not be prevented by vaccination against hepatitis B.

65.2. Patients were informed that there was increasing information from biopsy studies that an increasing percentage of patients with NANB hepatitis had progressive liver disease, with risks of subsequent cirrhosis, and in due course liver cancer, as with hepatitis B (reviewed in Question 30). And I recall from about 1987 we, and other UK Centres, started to see a few patients developing clinical features of cirrhosis. I stated that patients would be given information on its significance (risks of cirrhosis and possibly cancer), prognosis, and management which included the need for monitoring at clinic reviews, and minimising alcohol intake. There was no established drug treatment until hepatitis C was identified and trials of antiviral drugs began, starting with interferon. Patients would be given current information leaflets on hepatitis produced by the Haemophilia Society.

66. When did the Centre begin testing patients for hepatitis C? Over what period of time was testing for hepatitis C carried out after a test became available? How and when were patients told of their diagnosis of hepatitis C? Were they told in person, by letter or by phone?

66.1. I recall that Dr Walker and I began testing at our review clinic about October 1991, when the Regional Virus Laboratory routinely tested all patients at the Centre for HCV as well as HBV. Initially they used the antibody test; and later the RIBA-2 confirmatory test. Verbal informed consent was obtained, as for Hepatitis B. I stated to the Penrose Inquiry (Transcript 16 December 2011 [PRSE0006080]) that in 1990 Dr Iain Simpson, Chief Executive of the Medical and Dental Defence Union of Scotland, had advised UK Haemophilia Directors that Hepatitis C testing did not require HIV type counselling, because since the 1970s patients at Haemophilia Centres were routinely monitored for Hepatitis B and for post-transfusion hepatitis, and there was no case for changing the verbal consent policy for monitoring patients for post-transfusion hepatitis and its causal viruses. (See

Haemophilia Centre Staff in Scotland Collective Response to Penrose Inquiry on Topic C5; PRSE0003869)

66.2. I was asked by the Penrose Inquiry for my comments on whether or not I agreed or disagreed with Dr Charles Hay and with Dr Vivienne Nathanson about HCV testing and the provision of results. I agreed with Dr Hay that there is no comparison between HIV testing post-1985, and HCV testing in the 1990's with regard to the perceived poor prognosis, lack of effective treatment, and social stigma of HIV in the early years. I disagreed with Dr Nathanson in this respect. I pointed out that in the current SIGN guideline on hepatitis C, there is no mention of HIV-type counselling. (PRSE0000438; which you have sent me).

66.3. I stated to The Penrose Inquiry that patients were informed, in person, of their test results at the next clinic review, which would be scheduled for patients with a positive HCV tests in the next few weeks and the implications discussed. During that time the Centre would try to locate all the patient's previous case and treatment records, which could answer the patient's questions about when and where the infection might have occurred.

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

67.1. I stated to the Penrose Inquiry (Transcript 16 December 2011 [PRSE0006080]) that the patient would be told that a positive antibody test meant exposure to the virus; but that subsequent antigen tests would show whether the patient was a carrier of the virus, and hence at risk of chronic liver disease; or not. They would be informed of current knowledge about the risks of progression to chronic liver disease and cancer; and the current state of development of antiviral drugs. Patients were advised to keep their alcohol consumption low, and to continue the precautions with sexual intercourse and blood which the Centre had recommended from 1985 for patients who had received blood products, regardless of their HIV status. Patients were

advised to discuss this with their regular partners, who the Centre would be happy to see for discussion and counselling about testing for hepatitis C. Patients were given information leaflets on hepatitis from the Haemophilia Society or British Liver Trust.

The UKHCDO guidelines issued in 1995 (27) recommended that patients with positive HCV antigen tests be referred to hepatologists for management. The Centre referred them to Dr John Mackenzie's Gastroenterology Liver Clinic at GRI. This was being overwhelmed by not only our referrals, but also referrals of intravenous drug users; so Dr John Morris was appointed as consultant hepatologist and established by 1996 a joint Haemophilia/Hepatitis Clinic at the Haemophilia Centre, with his Hepatitis Specialist Nursing Sister Margaret Neilson, and Haemophilia Sister McDougall and Staff Nurse Little. Dr Morris and Sister Neilson provided detailed reports of their excellent service to the Penrose Inquiry (PEN.018.0874 [PRSE0003464]; PEN.018.0885 [PRSE0004589]).

68. How many patients at the Centre were infected with hepatitis C?

68.1. The Penrose Inquiry Preliminary Report (2010, page 46-47) records in Table 3.62 the UKHCDO data for patients registered at Scottish Centres. Total numbers of deceased and surviving Haemophilia A, Haemophilia B and von Willebrand's disease patients who tested positive for HCV in the period 1969-2010 were 494 (410 corrected for double counting). The comparable corrected total registered at non-Scottish Centres was 4,366. Scottish patients represented 9.4% of the United Kingdom total (3.63) which appears proportionate to their populations. Uncorrected for double counting, GRI had 166 patients, and Glasgow RHSC (Yorkhill) 62. The total for Glasgow was 228 patients (46% of Scottish uncorrected total), which appears proportionate to its population.

68.2. The Penrose Inquiry (Final Report 2015, Executive Summary, page 8) established that 478 patients in Scotland were infected with HCV as a result of therapy for a bleeding disorder. It did not report a breakdown of treatment

by Centres in Scotland. I would estimate that up to 50% of these would be patients in the West of Scotland, which contains about 50% of the population. This data was collated by the then current (2011) Centre Directors, Professor Campbell Tait (GRI) and Dr Elizabeth Chalmers (Yorkhill) for the West of Scotland; then with other Centre Directors in Scotland collated for the whole country.

68.3. I have asked Professor Tait if there has been any update for the IBI, and he informs me that he submitted to IBI an update for Scotland in 2018. Dr Tait and I suggest that if the IBI wishes further analysis by Centre, they could approach current Centre Directors in Scotland to ask if this could be performed.

Delay/public health/other information

69. 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.

69.1. As an honorary consultant from late 1985, I recall that the Centre's policy was to notify patients promptly – within weeks.

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

70.1. Centre staff thought it very important to notify communicable diseases (HBV, AIDS/HIV, HCV) to local departments of public health, and to local specialists in infectious diseases / gastroenterology or liver clinics, for follow-up; and to manufacturers of blood products (SNBTS or commercial) for tracing of donors and patient contacts.

70.2. Centre staff, and local specialist HIV and hepatitis clinics, routinely advised on precautions to minimise transmission to families and partners; including care of needles and equipment for patients on home treatment; protection of sexual intercourse (including provision of condoms); and social hygiene (80-82).

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

71.1. HIV positive patients were informed about risks of opportunistic infections, and monitored for these (80, 81).

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

72.1. HBV, HIV and HCV carriers were informed about current knowledge of infecting others; advised about precautions with sex and bodily fluids; and advised to discuss risk with wives or partners, who could be referred for counselling and testing.

Consent

73. How often were blood samples taken from patients attending the Centre? For what purposes were samples taken? What information was given to patients about the purposes for which blood samples were taken? Did the Centre obtain patients' informed consent to the storage and use of those samples?

73.1. Routine blood samples were taken at review clinics or ward admissions. Clinical appointments were sent at least annually for patients receiving blood products. Patients were informed that tests included -

73.1.1. Full blood count – to detect anaemia, low platelet count, etc.

73.1.2. Urea and electrolytes – to check kidney function

73.1.3. Liver function tests – to detect hepatitis, and alcohol or drug - induced liver disease

73.1.4. Hepatitis B virus (antibody and antigen) - from early 1970s

73.1.5. HIV antibody from 1985

73.1.6. Hepatitis C virus from 1991 (initially antibody, later antigen)

73.1.7. Hepatitis A from 1992

73.2. Verbal informed consent was sought, after explanation of what these tests were for. The Regional Virus Laboratory routinely stored serum after hepatitis B testing, and this was explained to patients. For patients recruited to their epidemiological studies of haemophilic arthritis and immunological abnormalities from 1982, I understand that Drs Forbes, Steven and Madhok stored samples in the Rheumatology Section of the University Department of Medicine research laboratory.

74. Were patients under the care of the Centre treated with factor concentrates or other blood products without their express and informed consent? If so, how and why did this occur? What was the approach to obtaining consent to treatment? If it is your position that patients did give express and informed consent to treatment with factor concentrates, please explain the basis for that position and set out the information that was provided to patients.

74.1. I recall that patients were treated with factor concentrates or other blood products by consultants Douglas, McDonald, McNicol, Prentice, Forbes, Davidson, and Walker in the 1970s and 1980s, before I became a Co-Director at the end 1987. As with other treatments with significant risks, I would expect that they would have sought express consent, and I recall observing Drs Prentice and Forbes do this on occasion, during ward rounds or teaching clinics. When Dr Walker and I became Co-Directors, we would review their current treatment and its risks at annual clinic reviews, discuss any changes of treatment with them (providing product information sheets) and obtain express and informed consent.

75. Were patients under the care of the Centre tested for HIV or for hepatitis or for any other purpose without their express and informed consent? If so, how and why did this occur? What was the approach to obtaining consent for testing?

75.1. See my answer to question 73 above – the Centre's policy was to seek verbal informed consent, after explanation. Pre-counselling and seeking of informed consent was standard before HIV testing performed as part of patients' clinical care, and is described in Question 51.

Dr Forbes gave evidence to the Penrose Inquiry that pre-counselling was not performed, and informed consent was not sought, before HIV testing, using a research test, in the epidemiological study that he performed with Dr Melbye and colleagues (63) (Transcript 15 June [PRSE0006033]). The Penrose Inquiry Final Report (2015; Volume 5, page 1636) concluded that "...Dr Forbes did not pass on the results of the Gallo (research) tests to his patients before confirmatory testing was undertaken by Dr Follett... "and the reservations he expressed about the reliability of the research assay provide both an explanation and a justification for that course of action. It cannot be concluded that that practice, in itself, involved any breach of the norms of ethical behaviour of the time."

75.2. I agree with the Report's conclusion. Dr Follett, reviewing the virology of HIV testing in 1987, stated "An HIV-1 positive test result has such traumatic consequences for the patient that the most sensitive and specific confirmatory test should be used. No positive result should be notified to a clinician before the result has been confirmed and a patient must not be informed of a positive finding based solely on an ELISA test result." (85). I note that Dr Gallo's laboratory's test was an ELISA, which had not been validated for clinical use (see Dr Froebel's statement, PEN.012.1628 [PRSE0002026]). In my opinion, the only ethical course for Dr Forbes was to arrange for patients who were seropositive by the Gallo research test in the epidemiological study (63) to have pre-counselling (with Dr Wilkie) then seeking of express consent for testing using a validated clinical test by Dr

Follett's laboratory. By May 1985, all 12 seropositive patients had been tested and confirmed by this due process (SNB.004.9656, PRSE0001606)

PUPS

76. 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).

76.1. The GRI Centre was an Adult Centre, and in my time as a Consultant (from late 1985) then Co-Director (from late 1987) there were few previously untreated patients. If such patients required treatment with factor concentrates, it would be explained to them that such concentrates were virally inactivated. From 1989 they would be invited to participate in the SNIHCD Group study of viral safety of SNBTS factor concentrates, which was published in 1993 and confirmed their lack of transmission of hepatitis, HCV and HIV (28). As a member of SNIHCD, I helped develop the protocol and co-authored this paper, but my recollection is that few such patients were available for this study in the GRI Centre. From 1996, such patients, as high priority, would be offered treatment with recombinant factor concentrates, organised by the Scottish Recombinant Factor Consortium.

<u>Research</u>

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

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 the steps taken to inform patients of their involvement and seek their informed consent; and

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

77.1. As I stated in Questions 6-8, most of the research studies in the Haemophilia and Thrombosis Centre that I was involved with (1975-2009) were in thrombosis and vascular disease. Few were in patients with haemophilia; some of which are relevant to the inquiry's remit of transfusion transmitted infections.

77.2. Publications on patients with haemophilia in which I was a co-author (including research studies; but also case reports or case series reports which are not research), which are **not relevant to the inquiry's remit of transfusion transmitted infections.**

77.2.1. 1976-1991. Publications with Drs Prentice and/or Forbes as lead consultants in Haemophilia Centre

77.2.1.1. Yates, A.J., Harvie, A., Lowe, G.D.O., Forbes, C.D., Prentice, C.R.M., Hamilton, D.N.H. Mandril-grown graft for vascular access in Christmas Disease. British Medical Journal 1976, ii (6044), 1108-1109. Case report.

77.2.1.2. Lowe, G.D.O., Harvie, A., Forbes, C.D., Prentice, C.R.M. Successful treatment with prothrombin complex concentrate of post-operative bleeding in a haemophiliac with a Factor VIII inhibitor. British Medical Journal, 1976, ii (6044), 1110-1111. Case report.

77.2.1.3. Forbes C.D., Lowe, G.D., Prentice, C.R.M. Ultrasonography in haemophilia. Lancet, 1977, i, (8020), 1064-5 (Letter). Case report.

77.2.1.4. Lowe, G.D.O., Pettigrew, A., Middleton, S., Forbes, C D., Prentice, C.R.M. DDAVP in haemophilia. Lancet, 1977, ii, 614 (Letter). Case report describing hyponatraemia as an adverse effect.

77.2.1.5. Harvie, A., Lowe, G.D.O., Forbes, C.D., Prentice, C.R.M., Turner, J. Intraspinal bleeding in haemophilia: successful treatment with Factor VIII concentrate. Journal of Neurology, Neurosurgery and Psychiatry, 1977, 40, 1220-1223. Case report.

77.2.1.6. Small, M., Lowe, G.D.O., Douglas, J.T., Forbes, C.D., Prentice, C.R.M. Factor IX thrombogenicity: *in vivo* effects on coagulation activation and a case report of disseminated intravascular coagulation. Thrombosis and Haemostasis, 1982, 48,76-7. Case report and research study of coagulation activation.

77.2.1.7. Small, M., Steven, M.M., Freeman, P.A., Lowe, G.D.O., Belch, J.J.F., Forbes, C.D., Prentice, C.R.M. Total knee arthroplasty in haemophilic arthritis. Journal of Bone and Joint Surgery, 1983, 65-B, 163-5. Case series report.

77.2.1.8. Greer, I.A., McLaren, M., Belch, J.J.F., Lowe, G.D.O., Forbes, C.D. Endothelial stimulation by DDAVP in von Willebrand's disease and haemophilia. Haemostasis, 1986. 16, 15-19. Research study.

77.2.1.9. Greer, I.A., Greaves, M., Madhok, R., McLoughlin, K., Porter, N., Lowe, G.D.O., Preston, F.E., Forbes, C.D. Effect of stanozolol on factors VIII and IX and serum aminotransferases in haemophilia. Thrombosis and Haemostasis, 1985, 53, 386-389. Research study (with

Sheffield Haemophilia Centre) to investigate its potential use as an alternative treatment to blood products (it was not effective).

77.2.1.10. Connor, J.M., Pettigrew, A.F., Hann, I.M., Forbes, C.D., Lowe, G.D.O., Affara, N.A. Application of an intragenic probe to genetic counselling for haemophilia B in the West of Scotland. Journal of Medical Genetics, 1985, 22, 441-446. Case series.

77.2.1.11. Connor, J.M., Pettigrew, A.F., Shiach, C., Hann, I.M., Lowe, G.D.O., Forbes, C.D. Application of three intragenic DNA polymorphisms for carrier detection in haemophilia B. Journal of Medical Genetics, 1986, 23, 300-309. Case series.

77.2.1.12. Greer, I.A., Lowe, G.D.O., Walker, J.J., Forbes, C.D. Haemorrhagic problems in obstetrics and gynaecology in patients with congenital coagulopathies. British Journal of Obstetrics & Gynaecology, 1991, 98, 909-918. Case series report.

77.2.2. 1991-2009 – studies with Dr Walker, then also Dr Tait, as Co-Directors and lead consultants.

77.2.2.1. Hampton, K.K., Preston, F.E., Lowe, G.D.O., Walker, I.D., Sampson, B. Reduced coagulation activation following infusion of a highly purified factor IX concentrate compared to a prothrombin complex concentrate. British Journal of Haematology, 1993, 84, 279-284. Research study (with Sheffield Haemophilia Centre) showing potential of high purity concentrate (Alpha Therapeutic UK) to reduce coagulation activation by prothrombin complex concentrate (Bio-Products Laboratory, Elstree). Written informed consent obtained from all subjects, and study approved by local hospital ethical committees.

77.2.2.2. Gallacher S.J., Deighan C., Wallace, A.M., Cowan, R.A., Fraser W.D., Fenner, J.A.K., Lowe, G.D.O., Boyle, I.T. Association of severe haemophilia A with osteoporosis: a densitometric and biochemical study. Quarterly Journal of Medicine, 1994, 87, 181-186. Case reports, and research study of this association. Study approved by local hospital ethical committee, and oral informed consent obtained from each patient and volunteer prior to assessment.

77.2.2.3. Bidichandani, S.I., Lanyon, W.G., Shiach, C.R., Lowe, G.D.O., Connor, J.M. Detection of mutations in ectopic factor VIII transcripts from nine haemophilia A patients and the correlation with phenotype. Human Genetics, 1995, 531-538. Case series report.

77.2.2.4. Ludlam, C.A., Lowe, G.D.O., Mayne, E.E., on behalf of the Haemophilia Directors for Scotland & Northern Ireland. A pharmacokinetic study of an ion-exchange solvent-detergent-treated high-purity factor VIII concentrate. Transfusion Medicine, 1995, 5, 289-292. Comparative pharmacokinetic study (with Coagulation Factor Working Party and Edinburgh and Belfast Centres) of SNBTS intermediate-purity concentrate (Z8) with SNBTS high-purity concentrate (Liberate), in volunteer patients, and followed published ISTH guidelines. SNBTS funding acknowledged.

77.2.2.5. Phillippou, H., Adami, A., Lane, D., McGregor, I., Tuddenham, E., Lowe, G.D.O., Rumley, A., Ludlam, C. High purity factor IX and prothrombin complex concentrate (PCC): pharmacokinetics and evidence that factor IXa is the thrombogenic trigger in PCC. Thrombosis and Haemostasis, 1996, 76, 23-28. Research study (with Edinburgh and London Centres) showing mechanism of coagulation activation by

virally inactivated SNBTS prothrombin complex concentrate (DEFIX) compared to virally inactivated SNBTS high purity factor IX concentrate (HP9). Study approved by local hospital ethical committees; conformed to recommendations of Declaration of Helsinki; and followed published ISTH guidelines.

77.2.2.6. Dykes AC, Walker ID, Lowe GDO, Tait RC. Combined prednisolone and intravenous immunoglobulin treatment for acquired factor VIII inhibitors: a 2-year review. Haemophilia, 2001; 7: 160-163. Case series report.

77.3. Publications in which I was a co-author (including research studies; but also case reports or case series reports which are not research), in patients with haemophilia, which are **relevant to the Inquiry's remit of transfusion transmitted infections.**

77.3.1. 1980-1991. Studies with Dr Forbes as lead consultant in Haemophilia Centre

77.3.1.1. These studies of immunological changes in patients with haemophilia (62-70, 86) were performed by Dr Forbes and his colleagues in the Rheumatology Section of the University Department of Medicine: Drs Roger Sturrock, senior lecturer and head of Section; Malcolm Steven, senior registrar; Rajan Madhok, registrar then Arthritis and Rheumatism Council Lecturer; Karin Froebel, immunologist, and Alastair Gracie, immunologist.

77.3.1.2. Drs Steven, Madhok, Forbes and Sturrock recruited a cohort of 139 patients attending the GRI Haemophilia Centre for an epidemiological study of haemophilic arthritis in patients with severe, moderate and mild haemophilia (Factor VIII and Factor IX deficiency) and von Willebrand's disease (87), in

which I was not involved. I understand that blood samples were taken as part of this study and stored in the Department's freezers in the rheumatology section of the laboratory, for investigation of immunological tests relevant to haemophilic arthritis; and tests relevant to the immunological changes reported in patients with AIDS or with haemophilia in the USA at this time.

77.3.1.3. These studies are described in my answer to Question 33; and in the written statement "the Immunological Testing Statement" which I gave to the Penrose Inquiry, which you have sent me with this Rule 9 request (PRSE0001561, PEN.012.1600).

77.3.1.4. a. The purpose of the research is stated in each of these publications. In general, they investigate the immunological changes in patients with haemophilia which had been previously reported in the early 1980s in patients in the USA; their relationships to previous treatments with blood products; and their relationships to HIV antibody positivity or negativity. I refer you to my written statement (PRSE0001561, PEN.012.1600) – "I am not an expert in immunology and cannot comment in any detail on the findings, but in general they appear to show a variety of immune abnormalities in patients with haemophilia who were HIV negative. The papers discuss the possibilities that these may be related to treatment with intermediate-purity clotting factor concentrate (SNBTS) or to liver disease."

77.3.1.5. b. Steps taken to obtain approval for the research. As I was not directly involved in these studies, I do not know, but I presume that Dr Forbes as Haemophilia Centre Co-Director and lead consultant would seek approval from the GRI Research Ethics Committee. The publication which involved

skin testing and biopsy (66) states "All subjects had volunteered to participate in the present study, which had been approved by the local ethics committee."

77.3.1.6. c. My involvement. I was not directly involved in these research studies, and as I stated in my written statement to the Penrose Inquiry (PRSE0001561, PEN.012.1600), and in my answer to Question 33, my contributions were (a) critical review of the draft manuscripts; and (b) for publication (63), drafting the first paragraph of the results section, which described a Scottish patient with haemophilia who developed AIDS. By 1982, as a Lecturer, I had completed a University of Glasgow course on research study design and statistical analysis; and I performed statistical analysis of my own studies in vascular disease and thrombosis, included those included in my MD thesis which I submitted in 1983. I therefore became the "go to" colleague in the Department of Medicine for fellow colleagues to request my critical review in their draft papers of their study design, analysis of results, and conclusions; which was often acknowledged by co-authorship in publications of studies in which I was not directly involved.

77.3.1.7. d. Other organisations or bodies involved are stated in some of these publications.

77.3.1.8. e. Research funding. Some of these publications record Dr Madhok's funding by the Arthritis and Rheumatism Council; part funding by a grant from the Scottish Hospital Endowments Research Trust; and part funding by the Haemophilia Society of Great Britain. One publication (69) reports provision for in vitro laboratory studies of factor VIII concentrates by SNBTS (intermediate purity concentrate) and by Armour Pharmaceuticals (Monoclate P).

77.3.1.9. f. The number of patients involved is stated in each publication.

77.3.1.10. g. Details of the steps taken to inform patients of their involvement and seek their informed consent.

77.3.1.10.1. I recall it was Dr Forbes' general policy to inform patients about research studies and to seek informed consent. The publication which involved skin testing and biopsy (66) states "All subjects had volunteered to participate in the present study, which had been approved by the local ethics committee."

77.3.1.11. h. The publications on non-epidemiological studies are –

77.3.1.11.1. (62) Froebel, K.S., Madhok, R., Forbes, C.D., Lennie, S., Lowe, G.D.O., Sturrock, R.S. Immunological abnormalities in haemophilia: are they caused by American factor VIII concentrate? British Medical Journal, 1983, 287, 1091-3. Blood samples taken from 19 patients with severe haemophilia, and age-matched healthy controls. Patients had reduced proportions of T helper cells, an increased proportion of T suppressor cells, and a reduced response to concanavilin A. Factor VIII concentrates from both USA and Scotland inhibited in vitro response to mitogens in patients and controls.

77.3.1.11.2. (86) Froebel KS, Lowe GDO, Madhok R, Forbes CD. AIDS and hepatitis B (letter). Lancet, 1984, i, 632. Letter reporting no association of immunological abnormalities in the 19 patients in study (62) with routinely performed liver function tests or hepatitis B surface antibody.

77.3.1.11.3. (64) Madhok, R., Gracie, A., Lowe, G.D.O., Burnett, A., Froebel, K., Follett, E., Forbes, C.D. Impaired cell mediated immunity in haemophilia in the absence of infection with human immunodeficiency virus. British Medical Journal, 1986, 293, 978-980. (59). Joint study with GRI Department of Haematology, and Regional Virus Laboratory. 29 patients with severe haemophilia had impaired cell mediated immunity in vivo by the dichlorobenzene skin test, whether or not they were HIV positive. There was an inverse correlation between skin response and exposure to clotting factor.

77.3.1.11.4. (65) Madhok, R., Lowe, G.D.O., Forbes, C.D., Stewart, C.J.R., Lee, F. Extranodal lymphoma in a haemophiliac negative for antibody to HIV. British Medical Journal, 1987, 294, 679-680. Case report of lymphoma, potentially relevant to reports of impaired cell mediated immunity.

77.3.1.11.5. (66) Lowe J.G., Swanson Beck, J., Madhok, R., Gracie, A., Gibbs, J.H., Potts, R.C., Lowe, G.D.O., Forbes, C.D. Histometric studies on cellular infiltrates of tuberculin tests in patients with haemophilia. Journal of Clinical Pathology, 1989, 42, 184-187. (60). Joint study with Department of Pathology, University of Dundee. 13 patients with severe haemophilia who had participated in study (64) volunteered to participate. Intradermal tuberculin skin test recorded, and small skin biopsy performed under clotting factor cover. Low preponderance of CD4 lymphocytes in diffuse infiltrate observed, possibly the earliest indicator of impending immunosuppression.

77.3.1.11.6. (67) Madhok, R., Gracie, A., Smith, J., Lowe, G.D.O., Forbes, C.D. Capacity to produce interleukin 2 is impaired

in haemophilia in the absence and presence of HIV-1 infection. British Journal of Haematology, 1990, 76, 70-74. (61). Blood samples taken from 46 patients with haemophilia and 30 age-matched healthy controls. Reduced interleukin 2 production in patients observed, independent of HIV-1 antibody status, mean annual dose of clotting factor concentrate used, and liver disease severity.

77.3.1.11.7. (68) Madhok, R., Gracie, J.A., Forbes, C.D., Lowe, G.D.O. B cell dysfunction in haemophilia in the absence and presence of HIV-I infection. Thrombosis and Haemostasis, 1991, 65, 7-10. (62). Blood samples taken from 56 patients with haemophilia and age-matched healthy controls for measurement of spontaneous and stimulated IgG and IgM production in vitro, HIV-1 infection was associated with increased spontaneous production and impaired responses to stimulation. In the absence of HIV-1 infection, there was a shift to a greater production of partially activated B cells in patients with greater evidence of liver disease.

77.3.1.11.8. (69) Madhok, R., Smith, J., Jenkins, A., Lowe, G.D.O. T cell sensitisation to factor VIII in haemophilia A? British Journal of Haematology, 1991, 79, 235-238. (63). Blood samples taken from 7 patients with severe haemophilia who were HIV-1 antibody negative. Addition of intermediate purity SNBTS concentrate in vitro inhibited peripheral mononuclear cell proliferation. Addition of high purity Armour factor VIII concentrate did not; and increased production of interleukin 2, suggesting the presence of a clone of T cells sensitized to factor VIII.

77.3.1.11.9. (70) Madhok, R., Cruickshank, A., Gracie, A.J., Shenkin, A., Lowe, G.D.O. Increased interleukin 6 concentrations in the absence and presence of HIV-1 infection in haemophilia. Journal of Clinical Pathology 1992, 4,: 766-769. (64). Joint study with Department of Biochemistry, GRI. Interleukin 6 concentrations were measured in stored serum samples from 60 patients with haemophilia, and were higher than in controls, independent of HIV-1 antibody status. There was a correlation of levels with IgG levels in patients who were HIV-1 antibody positive. There was no correlation with severity of liver disease.

Please provide the same details in relation to any epidemiological or similar studies which you undertook or in which you were involved (insofar as they are relevant to the Terms of Reference).

77.4. 1980-1991. Epidemiological studies of HIV, and of liver function tests, with Dr Forbes as lead consultant in Haemophilia Centre

77.4.1. Two further, epidemiological, HIV studies are also described in my answer to Question 33; and in the written statement "the Immunological Testing Statement" which I gave to the Penrose Inquiry, which you have sent me with this Rule 9 request (PRSE0001561, PEN.012.1600).

77.4.1.1. (63). Melbye, M., Froebel, K.S., Madhok, R., Biggar, R.J., Sarin, P.S., Stenbjerg, S., Lowe, G.D.O., Forbes, C.D., Goedert, J.J., Gallo, R.C., Ebbesen, P. HTLV-III seropositivity in European haemophiliacs exposed to factor VIII concentrate imported from the U.S.A. Lancet, 1984, ii, 1444-1446. (57)

77.4.1.1.1. Collaboration with Dr Mads Melbye in Aarhus, Denmark, and Dr Robert Gallo in Bethesda, USA, to investigate prevalence of HTLV-III seropositivity (in stored blood samples) among European patients; and if this was correlated with treatment with commercial clotting factor concentrates from United States donors. The findings of the study were that it was.

77.4.1.1.2. I was not directly involved in this study, and recalled that my contribution as a co-author was (a) critical review of the manuscript, and (b) at Dr Forbes's request, drafting the first paragraph of the results section which described a Scottish patient with haemophilia who developed AIDS - I had assisted Dr Forbes and doctors from the Infectious Diseases Department when Dr Forbes had recently admitted him for investigation of symptoms suggestive of the "AIDS-related complex". I was not involved in study approval, funding, or consent.

77.4.1.2. (64). Madhok, R., Melbye, M., Lowe, G.D.O., Forbes, C.D., Froebel, K.S., Bodner, A.J., Biggar, R.J. HTLV-III antibody in sequential plasma samples from haemophiliacs 1974-1984. Lancet, 1985, i, 524-525 (letter). (58).

77.4.1.2.1. The same investigators subsequently reported further data on the dates of seroconversion of the patients seropositive for HTLV-III antibody. I recall that my contribution as a co-author was critical review of the manuscript. I was not involved in study approval, funding, or consent.

77.4.2. There are two further publications of epidemiological studies, one on HIV transmission, and one on prevalence of liver function test abnormalities:

77.4.2.1. (88). Madhok, R, Gracie, J.A., Lowe, G.D.O, Forbes, C.D. Lack of HIV transmission by casual contact. Lancet, 1986, ii, 863. (letter). (84).

77.4.2.1.1. Report commenting on recent Lancet paper demonstrating lack of HIV transmission via casual contact from patients with haemophilia. Confirms that in routine testing (after pre-counselling and informed consent) of 23 household contacts associated with 10 HIV antibody positive patients at the Haemophilia Centre, none were positive on HIV antibody screening; 8 recent sexual partners of 7 positive patients were also negative. Also reports data on serum beta-2-microglobulin levels in 76 patients with haemophilia, which did not correlate with symptoms or laboratory abnormalities suggestive of HIV-related disease, nor with concentrate use, but were correlated with serum transaminase levels. I recall that my contribution as a co-author was critical review of the manuscript.

77.4.2.2. (51). Steven MM, Small M, Pettigrew A, Lowe GDO, Sturrock RD, Follett EA, Forbes CD. Liver dysfunction in haemophilia. Scottish Medical Journal, 1986, 31, 103-108.

77.4.2.2.1. This was a joint epidemiological study with Dr Follett of the Regional Virus Laboratory, and a spin-off study from Dr Steven's epidemiological study of haemophilic arthritis in 139 patients (76), in which I was not involved. Dr Steven reviewed case records for routinely collected data, including clinical information on previous hepatitis or jaundice; evidence of past or present hepatitis B infection (HBsAG, HBsAb, HBcAb) by Dr Follett's Regional Virus Laboratory; and liver function tests. He analysed these

and compared them with possible non-infectious causes for liver dysfunction, including extensive immunological testing and drugs such as methyldopa. The prevalence of clinical, biochemical and virological features of liver dysfunction in this study were consistent with previous reports from other haemophilia centres. As a co-author to this study, in which I was not directly involved, my contribution was again critical review of the manuscript. I was not involved in study approval, funding, or consent.

77.5. 1990-2009 – studies with Dr Walker, then also Dr Tait, as Co-Directors and lead consultants

77.5.1. Together with other Haemophilia Centre Directors in Scotland, and the Coagulation Factor Working Party (CFWP), Dr Walker and I participated in the clinical trials monitoring efficacy and safety of SNBTS factor VIII and IX concentrates; of initially intermediate purity, then high purity. These are summarised in Professor Ludlam's CFWP development document (WITN3496015) on the establishment of this Working Party, submitted to the Penrose Inquiry, then to the Infected Blood Inquiry. These were approved by the local Research Ethics Committees. Patients were given full information sheets on these studies (including on compensation from the Scottish Home and Health Department for any adverse effects), and signed written consent obtained. The Centre received some SNBTS funding for the additional work which these studies required from its Clinical Assistant and its Secretary; their funding was subsequently continued by the GRI and Greater Glasgow Health Board. The final high purity Factor IX study was discontinued after reports of protein precipitation in the vials after the diluent was added. There were no reports of clinical adverse effects in this study, and the Scottish Home and Health Department arranged that Centres used instead licensed commercial virally inactivated high purity

Factor IX concentrate, until this was replaced by recombinant Factor IX concentrates.

77.5.2. Publications

77.5.2.1. (28). Bennett, B., Dawson, A.A., Gibson, B S., Hepplestone, A., Lowe, G D.O., Ludlam, C.A., Mayne, E.E., Taylor, T. Study of viral safety of Scottish National Blood Transfusion Service factor VIII/IX concentrate. Transfusion Medicine, 1993, 3, 295-298.

77.5.2.1.1. 13 previously untreated or minimally treated (a few donations of cryoprecipitate or red cells) patients completed after treatment with dry heat treated SNBTS Factor VIIII or Factor IX concentrates a 6-month study of fortnightly then monthly liver function tests and testing for HIV and HCV. None developed hepatitis or seroconversion to HIV or HCV.

77.5.2.2. (29). Clark, P., Cameron, S.O., Walker, I.D., Lowe, G.D.O. Seroprevalence of total antibodies to hepatitis A virus in haemophiliacs in the West of Scotland. Haemophilia, 1995, 1, 194-195. (29).

77.5.2.2.1. Epidemiological study, following UKHCDO recommendation that patients with haemophilia be tested for anti-HAV and vaccinated if not immune. 73 Centre patients were tested for anti-HAV at Regional Virus Laboratory. 40% were antibody positive, similar to local population prevalence. 30 patients subsequently treated with SNBTS high purity Factor VIII concentrate were re-tested after a median of 5 months; no cases of seroconversion occurred.

77.5.2.3. (88). Roy, K.M., Bagg, J., Follett, E.A., Brewer, A., Lowe, G.D.O. Hepatitis C virus in saliva of haemophiliac patients attending an oral surgery unit. British Journal of Oral and Maxillofacial Surgery, 1996, 34, 162-165.

77.5.2.3.1. Epidemiological study of frequency of detectable HCV in saliva by colleagues performing oral and dental care in 21 HCV seropositive Centre patients at the Glasgow Dental Hospital Oral Surgery Unit, with Dr Follett of the Regional Virology Laboratory. HCV detected in saliva in 10 patients. Concluded that further epidemiological studies are required to determine whether some cases of sporadic HCV could be explained by salivary transmission.

77.5.2.4. (71) Hay, C.R.M., Ludlam, C.A., Lowe, G.D.O., Mayne, E.E., Lee, R.J., Prescott, R.J., Lee, C.A. The effect of monoclonal or ion-exchange purified factor VIII concentrate on HIV disease progression: a prospective cohort comparison. British Journal of Haematology, 1998, 101, 632-637. (65)

77.5.2.4.1. In my statement to the Penrose Inquiry (PRSE0001561, PEN.012.1600), I noted that Dr Hay, together with Dr Ludlam, myself and colleagues, published an indirect comparison of HIV infection in patients in England treated with monoclonally purified Factor VIII concentrate (Bioproducts Ltd., Elstree) and in patients in Scotland (Edinburgh and Glasgow) treated with SNBTS Factor VIII concentrate. This epidemiological study used routinely collected data on the patients in Scotland. There were no significant differences in progression of HIV infection between these two groups of patients.

77.5.2.5. (89). Ludlam C.A., Lee R.J., Prescott R.J., Andrews J., Kirke E., Thomas A.E., Chalmers E.A., Lowe G.D.O. Haemophilia Care in Central Scotland 1980-1994. I. Demographic characteristics, hospital admissions and causes of death. Haemophilia, 2000; 6: 494-503.

77.5.2.5.1. Epidemiological / heathcare planning study on haemophilia care in central Scotland, 1980-1994; using routinely collected data on demographic characteristics, hospital admissions and causes of death. Collaboration with Directors at the Yorkhill and Edinburgh Centres, and the Department of Public Health, University of Edinburgh. Life expectancy was generally increasing, although HIV and HCV caused increasing mortality and morbidity (hospital admissions). Hospital bed usage for treatment of acute bleeds continued to be required, but fluctuated greatly. The admission rate was significant lower for haemophilia B than haemophilia A, and was similar for all degrees of severity of the disorder. This study was funded by a grant from the Chief Scientist Office, Scottish Office Health Department; and was useful in planning for haemophilia care from 2000 onwards.

77.5.2.6. (53). Khan MM, Tait RC, Kerr R, Ludlam CA, Lowe GD, Murray W, et al. Hepatitis C infection and outcomes in the Scottish haemophilia population. Haemophilia 2013: 19: 870-875.

77.5.2.6.1. This epidemiological study on routinely collected data is described in Question 28.

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

78.1. I have read the Infected Blood Inquiry's Expert Group on Ethics Report (Section 4, Research) which I think is generally an accurate history of the development of ethical principles that should guide research, in the UK and internationally, from the 1960s to the present day.

78.2. I support the suggestion by the Expert Group on Ethics that patients be viewed as partners with healthcare professionals in research, rather than subjects of research. I recall that the GRI Centre staff and patients took this view; and that its patients (realising mutual benefit to their care) participated willingly in both clinical teaching, and in research, performed by Centre staff.

78.3. The Group also discusses the ethical overlaps between clinical research, clinical audit, and clinical standards. I believe that clinical audit, clinical standards, and clinical guidelines should also be partnerships between patients and healthcare professionals. I promoted such partnerships when developing and organising (see Question 3) –

78.3.1. SNIHCD and UKHCDO national audits of haemophilia centres, Scottish then UK, 1992-2000;

78.3.2. GRI hospital audits (member of audit committee), and NHS Scotland national audits (member of CRAG and its Clinical Outcomes subcommittee), 1996-2002

78.3.3. UK Consensus Conferences, as Deputy Assessor, RCPE, 1993-1999

78.3.4. NHS Scotland national clinical guidelines produced by SIGN, 1993-2007, chairing two of these, as RCPE member of Council, then as Chair of Council (90).

78.4. When I joined the GRI Department of Medicine and started participation in its research in 1975, I recall that its clinical research proposals were drafted

by the relevant lead consultant and submitted to the hospital's local Research Ethics Committee for consideration and approval. These proposals included the purpose of the study, procedures, information to be given to participants, and procedure for obtaining express consent (verbal or written). When I was lead consultant for clinical research studies in which I was involved from 1986, I submitted these proposals to the Research Ethics Committee for approval, and followed their rulings on information given to patients, and on the required form of express patient consent.

78.5. I refer you to the Penrose Inquiry Final Report (2015), Volume 5: Information to Patients. 32, An investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context (pages 1489-1536). For each of HIV/AIDS and Hepatitis C, these topics were defined:

78.5.1. The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products.

78.5.2. The tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products.

78.5.3. The information given to patients who might have been infected, or who were found to be infected, and their families.

78.6. This investigation included the ethical principles of medical research, and in particular the research studies of the epidemiology of HIV and HCV, conducted by Dr Ludlam in the Edinburgh Centre, and Dr Forbes in the GRI Centre, in stored blood samples.

78.7. The Penrose Inquiry was assisted in this investigation by two experts, Professor Vivienne Nathanson, Director of Professional Activities at the British Medical Association (BMA) for 16 years; and Dr Charles Hay, Chairman of UKHCDO, an experienced haemophilia clinician with a long and distinguished career in haemophilia care (including researches on hepatitis and HIV) (page 1491).

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

79.1. Dr Forbes was asked at the Penrose Inquiry if he sought consent from patients at the GRI Centre for use of stored samples, taken for immunological studies, for HTLV-III testing by Dr Gallo's laboratory in the epidemiological study he performed as co-investigator with Dr Melbye (63). I recall that his evidence was they were not, as it was an epidemiological / public health investigation, to be published without patient identification.

79.2. The Penrose Inquiry Final Report (2015; Executive Summary, page 37) noted that specific consent was obtained for immunological investigations in Glasgow; and goes on to say, for Scotland as a whole:

"The Inquiry concludes that it was in the best interests of patients to conduct such studies of immune function. There was, however, no structured or systematic approach to providing relevant information to patients. The studies lay on the boundary between treatment and research. While aspects of the conceptualisation and implementation of the study could have been handled better, there was at that time no fixed rule which would have required consent from patients, and it is not therefore possible to say that breach of any ethical rule occurred. The same conclusion was reached in relation to the publication of the results of these studies in the Lancet; the data were fully anonymised and there was no likelihood of individuals being identified."

79.3. See also Question 50.

79.4. For studies in patients with haemophilia from 1990 onwards, when Dr Walker, Dr Tait and I were Co-Directors, I do not recall that any patients were involved without express consent.

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

80.1. See my answer to Question 79.

81. Was patient data (anonymised, de-identified or otherwise) shared with third parties (e.g. to UKHCDO or to Dr Craske of the Public Health Laboratory in Manchester)? If so how and why did this occur and what information was provided and to whom?

81.1. I understand that, from the 1970s, the GRI Centre, like other Haemophilia Centres in the UK, provided data to UKHCDO Secretariat which it requested annually from all Centres. UKHCDO Secretariat maintained a database of all patients registered at UK Centres, including names, type and severity of bleeding disorder, annual treatments given, and complications including death and cause, development of factor inhibitors, thrombosis, hepatitis, HIV and vCJD. The rationale for UKHCDO surveillance; the benefits of its national reports for information on numbers of patients, their treatments and their safety – provided annually to patients (e.g. via the Haemophilia Society), Centre Directors, suppliers of treatments, NHS and UK Government haemophilia care planners, and the UK public; and its procedures to ensure confidentiality; were reviewed in 1997 (48). No information regarding individual patients or Centres was disclosed to third parties without the consent of the Centre concerned (48).

81.2. I note Dr Colvin's written evidence to the Inquiry (WITN3343007) includes his recollection that while he was UKHCDO Chair 1993-1996, an information sheet was sent to all patients informing them of the database and inviting them to request the removal of their names and data should they wish it.

81.3. When the UKHCDO database was updated in 2002, its data protection issues were reviewed for NHS Scotland by the SNIHCD Group and the Scottish Department of Health. As Scottish Law differed from English Law,

they ensured that the proposed information sheet was in accordance with Scottish Law (Minutes of SNIHDG, 14 June 2002 [LOTH0000082_017])

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

82.1. None.

a. You may be assisted by the following evidence that you gave to the Penrose Inquiry: the Immunological Testing Statement (and the papers referred to within it) [PRSE0001561]; Transcript 28 June 2011, pp.167-170; Transcript 30 June 2011, pp.24-26; Transcript 13 October 2011, pp.48-49 (your article, "Haemophilia, Blood Products and HIV Infection" is provided with this letter [PRSE0003040]).

82.2. This statement and these studies are described in Question 77.

Treatment of patients who were infected with HIV and/or hepatitis

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

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

83.1. From 1984, when the first patient with haemophilia and suspected AIDS was identified after he returned to his family in Glasgow (63), Dr Forbes arranged that all patients at the Centre who were HIV positive, including those who developed AIDS, were managed jointly with local consultants in infectious diseases, based at Ruchill Hospital, about 1.5 miles from GRI. Initially these consultants were Drs Dermot Kennedy and Campbell Love; then Dr Alan Pithie; then Dr Andrew Seaton. Initially, patients were reviewed jointly at the GRI Haemophilia Centre by a haemophilia consultant (Dr Forbes, myself or

Dr Walker) together with an infectious disease consultant (Dr Kennedy, Dr Love or Dr Pithie). Individual management plans were agreed with haemophilia and infectious diseases specialist nurses, and other staff from the developing West of Scotland Health Boards' AIDS/HIV Services.

83.2. Dr Forbes was very pro-active in addressing the emerging challenge of HIV infection and AIDS in patients with haemophilia (he chaired the UKHCDO AIDS Advisory Group from 1985), drug users, and other at-risk groups in Glasgow and the West of Scotland. He established and chaired the Greater Glasgow Health Board's AIDS Information and Advisory Group, which met first on 31 May 1985 in GRI (SNB.004.9656, PRSE0001606). By that time, Dr Forbes had written to Centre patients with information on AIDS and HIV testing (including the Haemophilia Society booklet, AIDS and the blood") (76) and with appointments to all patients registered at the GRI Centre. He and Dr Patricia Wilkie had counselled all HIV positive patients at the Centre, and continued this until end 1987; he and Dr Follett were monitoring HIV testing at the Regional Virus Laboratory; and he and Dr Kennedy had arranged joint clinic reviews at GRI, and hospital admission policies at GRI and at the infectious diseases wards at Ruchill Hospital, with close liaison.

83.3. In 1987, Dr Forbes as editor of the Scottish Medical Journal, published reviews, for general medical and surgical practitioners in Scotland, of current HIV management in NHS Scotland. These included clinical manifestations (Dr Kennedy) (80), haemophilia and blood products (myself, on behalf of Dr Forbes) (81), virology of HIV testing (Dr Follett) (85), counselling in HIV infection (Dr Wilkie) (82) and life assurance (Dr Wilkie) (83).

83.4. In 1997, the Infectious Diseases Department and Wards moved from Ruchill Hospital to the new Brownlee Unit at Gartnavel General Hospital. From that time Dr Seaton reviewed all HIV patients at his clinic there, which was more accessible to the HIV support services based at that site. He developed dual and triple antiviral therapies to control HIV infection.

83.5. Dr Kennedy and Professor James McEwen have recently reviewed the developments of Infectious Diseases and of Public Health in Glasgow (1). These include: the management of HIV and hepatitis B and C; and Glasgow's achievements with Public Health control of these infections by Drs Lawrence Gruer (who introduced needle exchange services in 1987); and in their monitoring and epidemiology by Professor Dan Reid, then in Health Protection Scotland by Professor David Goldberg (a member of the Inquiry's Clinical Groups on HIV and Hepatitis).

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

83.6. All antimicrobial drugs and other treatments were prescribed and monitored by the consultants, nurse specialists and pharmacists in the West of Scotland's Health Boards' infectious diseases HIV/AIDS Services. I recall that initially these included zidovudine, and inhaled pentamidine as prophylaxis of Pneumocystis pneumoniae until it was replaced by oral co-trimoxazole. Details of the emerging treatments including triple therapy from the 1990's to date can be obtained from Dr Seaton if required.

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

83.7. This was provided by the consultants in infectious diseases and other staff from the developing Health Boards' AIDS/HIV Services who provided specific treatments; supported by Haemophilia Centre staff. Details can be obtained from Dr Seaton if required.

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

84.1. This was provided by the consultants in infectious diseases and other staff from the developing Health Boards' AIDS/HIV Services; supported by Haemophilia Centre staff... Details can be obtained from Dr Seaton if required.

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

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

85.1. I recall that the few carriers of hepatitis B were referred for specialist care to the local Infectious Diseases clinics or Liver clinics.

b. What treatment options were offered over the years?

85.2. I recall that such clinics could prescribe antiviral drugs, starting with interferon, and possibly liver transplantation, but I cannot recall the details of these.

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

85.3. This would be given at the specialist clinics.

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

86.1. This would be arranged at the specialist clinics. Details of the emerging treatments offered from 1990 to date can be obtained from Dr Seaton (who managed patients co-infected with HIV), or hepatologists Dr John Morris, Professor Peter Mills, or Dr Ewen Forrest if required.

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

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

87.1. Patients were referred for specialist care to the local Infectious Diseases clinics or Liver clinics.

b. What treatment options were offered over the years?

87.2. Prior to identification of hepatitis C, I do not recall that patients were prescribed specific treatments for NANB hepatitis, such as interferon, at these clinics.

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

87.3. These would be provided at the local Infectious Diseases clinics or Liver clinics.

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

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

88.1. All patients found to be carriers of HCV (positive antigen tests) were referred to Dr John Mackenzie's GRI liver clinic for specialist care. This clinic was being overwhelmed with referrals of not only patients with haemophilia, but the many local drug users found to be HCV positive. As a result, Dr John Morris was appointed Consultant Hepatologist and from 1996 established a joint hepatitis / haemophilia clinic at the Haemophilia Centre.

b. What treatment options were offered over the years?

88.2. I refer you to the reports to the Penrose Inquiry of Dr Morris [PEN0180874, PRSE0003464] and Sister Neilson [PEN0180885, PRSE0004589].

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

88.3. I refer you to the reports to the Penrose Inquiry of Dr Morris and Sister Neilson.

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

89.1. I refer you to the reports to the Penrose Inquiry of Dr Morris and Sister Neilson.

90. What if any involvement did you and/or colleagues at the Centre have with any clinical trials in relation to treatments for HIV and hepatitis C? Please provide details.

90.1. I do not recall any such involvement in trials. You could ask Dr Seaton (HIV) or Dr Morris (HCV).

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

91.1. No children were treated at the GRI Centre.

92. What if any arrangements were made at or through the Centre (if relevant) to provide patients of children infected through blood products with

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

92.1. Assuming you mean **parents** of younger patients, I recall that when they were transferred from Yorkhill to GRI, it was routine to involve their parents at clinic reviews in discussions about arrangements for treatment. For their children infected with HIV or hepatitis, these discussions (with colleagues in infectious diseases or hepatology as appropriate) would include provision of local counselling, psychological or social work support.

93. Was the Centre provided with any funding (whether from central government or otherwise) to help with counselling of patients infected with HIV? If so please provide details of the funding. What kind of counselling was provided to such patients?

93.1. I refer you to my answer to Question 31. Drs Forbes and Professor Markova in 1985 developed a grant application to the Scottish Home and Health Department, which was awarded in July 1985. This funded most of the work of Dr Patricia Wilkie, who along with her researches, provided both pre- and post-counselling at the Centre from January 1985 to December 1987. She provided a copy of the report of this study to the Penrose Inquiry. The latter part of Dr Wilkie's work in 1987 was funded by a grant from the Haemophilia Society. She described her counselling work to the Penrose Inquiry in written and oral evidence, and in a copy of her grant report. She also described it in her Scottish Medical Journal article in 1987 (82). From 1988, counselling at the Centre was provided by Mrs Miriam Guthrie, senior social worker. Counselling was also available through the Infectious Diseases Department at Ruchill Hospital, then the Brownlee Centre.

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

94.1. I do not recall any such difficulties. You could ask Dr Seaton (HIV) or Dr Morris (HCV).

Records

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

95.1. Most patients infected with HIV or hepatitis died not in GRI, but at home, or in other hospitals (for example, the infectious diseases wards); so death certificates would be completed by the patient's general practitioner or by staff in other hospitals.

95.2. I recall that when patients or relatives were concerned about confidentiality of a certificate containing information on AIDS, HIV or hepatitis, practitioners completing the certificate could ring the Procurator Fiscal's office to discuss these issues. The Centre's and Health Board's policy was to inform patients, relatives and their doctors about this.

96. What were the retention policies of the Centre in regards to medical records?

96.1. As congenital bleeding disorders are genetic diseases, the Centre's policy was to retain medical records long-term after the patient's death, in case future generations including potential female carriers contacted the Centre for information on the type and severity of haemophilia in the family, for counselling on the risks of having a child with a bleeding disorder.

96.2. Accordingly, the Centre agreed with the GRI Medical Records Department that case records should be labelled "Do not Destroy: Return to Haemophilia Centre"; and retained at the Centre after the patient's death in its secure storage cupboard.

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

97.1. No.

98. 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 Centre? If so, why, what information and where is that information held now?

98.1. No.

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

99.1. No.

Section 5: Self-sufficiency

100. In December 1974 the Department of Health announced additional funding with the primary aim of making the NHS self-sufficient in Factor VIII blood products within two to three years.

a. Were you aware of this announcement at that time? (The Inquiry understands that this was a month after you joined the GRI as a Registrar in the University Medical Unit.)

100.1. No. I had just moved to Glasgow after being appointed as a junior doctor training in general medicine, was settling in at the Department of Medicine, was buying a house, and was not involved in the Haemophilia Centre.

100.2. Which of the 4 UK Departments of Health are you referring to - England?

100.3. When I became involved in haemophilia as a trainee at the GRI Centre in 1976, I understood that the Department of Health in Scotland had a policy of self-sufficiency, and that SNBTS supplied most of the treatments given, including plasma, cryoprecipitate and Factor VIII and Factor IX concentrates. At that time I recall that commercial products were required only occasionally (for example, treatment of patients with Factor VIII inhibitors).

b. What role, if any, did you play in any arrangements made in the Centre in which you worked at the time, or subsequently in any other organisation, in response to that announcement?

100.4. None in 1974. When I succeeded Dr Forbes as Centre Co-Director 14 years later, in 1988, I worked with my Co-Directors, and with other Haemophilia Centres in Scotland and Northern Ireland, SNBTS, and the Scottish Department of Health to maintain self-sufficiency for NHS Scotland, as far as that was possible. This was managed from 1988 through the Factor VIII Working Party, subsequently renamed the Coagulation Factor Working Party.

101. What, if any, understanding did you have of the term "self-sufficiency" to mean in 1974/1975? In particular, did you understand it to mean self-sufficiency in providing Factor VIII blood products prophylactically, or solely in response to bleeding incidents?

101.1. None at that time. When I succeeded Dr Forbes as Centre Co-Director in 1988, I recall that in NHS Scotland, "self-sufficiency "meant in providing from blood donors in Scotland coagulation factor concentrates (Factor VIII and Factor IX), for prompt treatment of bleeding (by both home and hospital treatment), and prophylaxis where indicated, as far as that was possible.

101.2. By that time, I was well aware that the concept of self-sufficiency was increasingly challenged in Scotland by unpredictable fluctuations in demand.

Patients with haemophilia do not "bleed to order". Factor VIII inhibitors can suddenly appear, in more than one individual at a time, requiring very large doses of Factor VIII concentrate. This demand was balanced by the need to frequently purchase commercial factor concentrates such as porcine Factor VIII, activated prothrombin factor concentrates, or recombinant Factor VIII concentrates, none of which could be manufactured by SNBTS. Other fluctuations included: need for urgent major surgery (requiring thousands of units of Factor VIII concentrates); and peak holiday time when patients required to take adequate supplies of their assigned SNBTS concentrate to other countries in the UK and abroad.

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

102.1. The major change was that from 1996 the question was becoming irrelevant, given (a) the UK decision to cease use of UK donor plasma due to the risk of VCJD; and (b) the UKHCDO recommendation to progressively replace human blood donor concentrates with recombinant factor concentrates, to eliminate transmission of all past and future human infections. This was progressed in NHS Scotland and largely achieved by 2002.

103. What was your understanding of how others defined "self-sufficiency"? Please answer by reference to (i) those involved in the supply of plasma, (ii) those involved in the production of blood products, (iii) clinicians prescribing blood products, (iv) patients using blood products (and their families), and (v) those responsible for managing relevant health authorities and bodies.

103.1. Within NHS Scotland, I recall that from the early 1980s, haemophilia care was co-ordinated by regular meetings between managers (Scottish Home and Health Department, SHHD, which represented Scottish Health Boards, which were quite different from Health Authorities in England and Wales); SNBTS as suppliers of plasma, and production of most blood products;

Centre Co-Directors prescribing them; and patients and their families using them – through their feedback to Scottish Centres and from the Scottish branch(es) of the Haemophilia Society. I recall that we all shared the view that self-sufficiency meant, for all treatment and prophylaxis – which was almost achieved in Scotland by 1983.

103.2. I do not recall that I had much knowledge of the interactions of these bodies within the other countries of the UK, so I cannot comment on these.

104. What, if any, efforts were made to ensure that all of the groups mentioned in the previous question shared a common understanding of what "self-sufficiency" meant?

104.1. See my answer to Question 103. We all worked together in Scotland, together with Northern Ireland, which SNBTS also supplied with factor concentrates. Co-ordination was greatly facilitated by the formation of the NHS Scotland Factor VIII Working Partly (later renamed the Coagulation Factor Working Party (CFWP) from May 1988, which continued until 2008 when SNBTS had ceased production of concentrates. The CFWP was ably chaired by Dr Ludlam, who provided a report to the Penrose Inquiry (WITN3496015), which has been provided to the Infected Blood Inquiry.

105. Insofar as it is within your knowledge and experience, how were estimates made of how much Factor VIII blood product would be required for use (i) in Scotland, (ii) in England and Wales and/or (iii) in the United Kingdom. In particular:

a. What was your role in making such estimates, and how did this change over time?

105.1. My role, from when I succeeded Dr Forbes as Co-Director from 1988, was to continue, together with my GRI Centre Co-Directors, to provide annual estimates of the Centre's requirements to meetings of Scottish Centre

Directors, SNBTS, and the Scottish Home and Health Department. Co-ordination was greatly facilitated by the CFWP. As Professor Ludlam's CFWP document (WITN3496015) records, clotting factor usage was collected monthly from each Centre and collated by the CFWP Secretary. SNBTS issues from its Protein Fractionation Centre (PFC) were reviewed and collated. Future projected concentrate requirement was kept under regular review. Distribution of PFC concentrate between Centres was agreed by CFWP. A unified system was established for the purchase of commercial concentrates. The demographic distribution of patients was considered.

105.2. It was never my role to presume to make estimates for England and Wales, or for the UK.

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

105.3. Because NHS Scotland had its own coordination systems from the 1980s, I recall that the UKHCDO did not have a significant role in Scotland, apart from its UK level professional guidance being relayed to partners in Scotland through Scottish Centre Directors. A good example is the UKHCDO guidance from 1996, that because of the risk of vCJD, human blood donor concentrates should be progressively replaced by recombinant factor concentrates. Accordingly, Professor Ludlam (who was UKHCDO chair at this time) and I met with the Chief Medical Officer, SNBTS and NHS Scotland managers to request this. As a result, recombinant factor concentrates replaced human factor concentrates for treatment of most patients in Scotland by 2002, some years before England.

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

105.4. As I have said above, the assumption in NHS Scotland that self-sufficiency meant: for treatment of bleeding episodes both in home and hospital treatment; and for prophylaxis where indicated.

105.5. The pattern of usage across Centres in Scotland in recent years.

105.6. Changing professional practice, for example as recommended by UKHCDO guidance.

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

105.7. See my answers above.

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

105.8. See my answers above.

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

105.9. See my answers above.

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

106.1. See my answers to Question 105 above.

a. What was your role in providing such figures, and how did this change over time?

106.2. See my answers to Question 105 above.

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

106.3. While NHS Scotland collated its own data, UKHCDO reports permitted comparison of Scotland with the UK.

106.4. As noted in Question 105c - changing UKHCDO guidance could influence professional practice, notably its recommendation from 1996 to progressively replace human with recombinant factor concentrates.

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

106.5. See my answer to Question 105c above.

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

106.6. See my answer to Question 105c above.

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

106.7. See my answer to Question 105a above. Scotland co-ordinated itself efficiently.

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

106.8. I recall that CFWP reports were shared with relevant UK parties. I suggest you could ask Professor Ludlam as CFWP Chair.

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

106.9. See Professor Ludlam's document on CRWP development (WITN3496015).

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

107.1. Yes. Unpredictability of patient demand, product manufacture, and professional practice. See my answers to Question 105 above.

108. You have stated in your Comments on Professor Forbes' Evidence (§7) that "it therefore seems clear that Scotland was rarely, if ever, 'self-sufficient' in clotting factor concentrates for treatment of patients with haemophilia. The Scottish National Blood Transfusion Service appeared unable to meet the needs of patients, as noted by Professor Forbes on page 113 of the transcript." Please explain:

a. Your reasons for this conclusion.

108.1. Please read the two sentences which precede this conclusion in this statement (STHB0000828, page 2, item 7). "I recall that commercial clotting factor concentrates had to be used in most years from 1976 to 1991, as recorded in Appendix 1 of the Penrose Inquiry's Preliminary Report. I note that this also applied to Aberdeen, Edinburgh (from 1980) and Glasgow Royal Hospital for Sick Children (until 1986)."

b. Why, in your opinion, self-sufficiency was not achieved in Scotland.

108.2. I recall that SNBTS **was** able to produce sufficient Factor VIII and Factor IX concentrates to meet the needs of **most of** the patients in NHS Scotland from about **1983 until about mid-1988** (see question (c) below).

c. Any particular years or periods in which there were particular problems with self-sufficiency.

108.3. I recall that in 1988-1990 SNBTS could not maintain NHS Scotland's self-sufficiency in factor VIII concentrate - see my evidence to the Penrose Inquiry (STHB0000828, page 4, item 17).

108.4. The minutes of the meeting of the Directors of SNBTS and Haemophilia Directors, 5 May 1988 (SGH.001.7505, PRSE0003384) record that the input of plasma to PFC had fallen for the first time since 1974; and also that there was a surge in use of factor VIII concentrates for several reasons, discussed by myself and Dr Ludlam.

108.5. The minutes of the 30th meeting of UKHCDO Directors on 5th September 1988 (HCDO0000431; page 3, item 4) record that "Dr Ludlam raised the question of the position in Scotland where there was going to be a shortfall of 2 million units in the current year. The Scottish Blood Transfusion Service had announced that they were only capable of producing 7 million units because of a fall in donations and problems with stock control. This problem was likely to last for the next two years."

d. Any particular products or types of products which gave rise to particular problems with self-sufficiency.

108.6. I refer you to my evidence to the Penrose Inquiry (STHB0000828), page 3, item 16).

108.6.1. SNBTS never manufactured products for treatment of patients with factor VIII inhibitors, such as activated prothrombin complex concentrates, porcine factor VIII, or FEIBA. For the GRI Centre, these had to be purchased by Drs Davidson or Walker from commercial manufacturers.

108.6.2. As with any other factor concentrate, some patients had allergic reactions to SNBTS concentrates; and if this was a recurrent problem, patients would be offered alternative, commercial, factor concentrates.

108.6.3. Inability of SNBTS to provide sufficient quantity of factor VIII concentrate at particular times – e.g. several patients having inhibitors or major bleeds, major surgery (e.g. knee joint replacement).

e. The reasons why clinicians in Scotland did, or may have, preferred to continue to use imported blood products.

108.7. I refer you to my evidence to the Penrose Inquiry (STHB0000828, page 3, item 16).

108.7.1. Treatment of patients with factor VIII inhibitors (either congenital or acquired haemophilia).

108.7.2. Treatment of patients who were intolerant of SNBTS factor VIII concentrates, e.g. allergic reactions.

108.7.3. Inability of SNBTS to provide sufficient quantity of factor VIII concentrate at particular times – e.g. several patients having inhibitors or major bleeds, major surgery (e.g. knee joint replacement)

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

109.1. I do not know the answers to any of these questions, and I refer you to colleagues in England and Wales.

110. What knowledge do you have of whether and if so when Northern Ireland achieved self-sufficiency in blood products (accepting that the plasma was fractionated in Scotland rather than Northern Ireland)?

110.1. I do not have any knowledge of this, and I refer you to colleagues in Northern Ireland.

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

111.1. In NHS Scotland, I cannot speak for my predecessor Co-Directors. In the GRI Centre, I believe that I and my colleague Co-Directors 1988-2009 did our best to provide such estimates, and to identify foreseeable increase in use. The formation of the Coagulation Factor Working Party from 1988, under the very capable chairmanship of Dr Ludlam, played a major role in coordinating these activities across NHS Scotland (WITN3496015).

112. If full self-sufficiency had been achieved in Factor VIII and Factor IX products in Scotland what, in your view, would have been the effect on the numbers of patients infected with (i) HBV, (ii) HCV, and (iii) HIV? Please comment, if you are able to, on when self-sufficiency would have needed to be achieved (in your view) in order for any material difference to have been made in respect of each of these viruses.

112.1. (i) HBV. No effect. HBV was present in blood donor populations worldwide, including Scotland, where studies in the Edinburgh and Glasgow Haemophilia Centres showed a high prevalence of HBV exposure (50,51)

112.2. (ii) HCV. No effect. HCV was present in blood donor populations worldwide, including Scotland - as assessed by prevalence of abnormal liver function tests in studies in Edinburgh and Glasgow Haemophilia Centres (49,51). When HCV antibody tests became available from 1990, estimates of prevalence of HCV were found to be approximately 1 in 300 UK blood donors. Hence a single dose of NHS factor concentrate, prepared from over 1000 donors, would be sufficient to transmit HCV.

112.3. (iii) HIV. I believe that the achievement by SNBTS of near-self-sufficiency by 1983 did have an effect of reducing the numbers of the patients in NHS Scotland infected with HIV, which appear lower than in the UK as a whole (81; and Penrose Inquiry Preliminary Report, 2010, page 47, 3.61). This Penrose report data shows that among UK patients who tested positive for HIV, Scottish patients represented 5.2% of the total, whereas on a population basis 9-10% might be expected. This lower prevalence of HIV presumably reflects a lower prevalence of HIV at that time in the donor population in Scotland than in the USA, from where commercial factor VIII concentrates (used less commonly in Scotland than in the rest of the UK) were purchased.

112.4. The Melbye et al study in 1984 of patients at the GRI Centre showed a higher incidence of HIV-1 antibody positivity in patients with haemophilia who had received also commercial Factor VIII concentrates, compared to those who had received only SNBTS concentrates; two of the 12 patients had received only SNBTS concentrates (63). At this time, Dr Ludlam and colleagues at the Edinburgh Centre also reported that some batches of SNBTS concentrates transmitted HIV (73, 77-79). From the follow-up report of dates of seroconversion in Glasgow Centre patients (64), it appears likely that a further reduction in the numbers of patients in Scotland might have been achieved, had self-sufficiency been achieved by 1980.

112.5. The Penrose Inquiry Final report (2015) concluded: "Other than by a general cessation of therapy with concentrates, the infection of haemophilia patients with HIV over the period 1980 to 1984 could not have been

prevented. Moreover, the earliest infections in Scotland occurred before 1 January 1981, meaning that any such general cessation would have needed to occur before AIDS itself had been reported." It also reported that 28 patients in Scotland were infected by HIV from treatment with SNBTS concentrates, and 31 patients received also, or only, commercial factor concentrates (Executive Summary, pages 18-19).

113. If self-sufficiency had been achieved in Factor VIII products in England and Wales, what, in your view and in light of the experience in Scotland, would have been the effect on the numbers of patients infected with (i) HBV, (ii) HCV, and (iii) HIV? Please comment, if you are able to, on when self-sufficiency would have needed to be achieved (in your view) in order for any material difference to have been made in respect of each of these viruses.

a. You may be assisted in answering this question by consideration of your 1987 article, "Haemophilia, Blood Products and HIV Infection" (p.110), where you compare the number of HIV antibody positive haemophilia patients in England and Wales to the number in Scotland. The same article also comments on the prevalence of HCV infection among those who used blood products.

113.1. First, I stated in my 1987 review (81) (PRSE0003040) "By the end of March 1987, 1025 UK haemophiliacs had been reported as HIV-antibody positive to surveillance centres: 950 in England and Wales, and 75 in Scotland. The prevalence in Scottish haemophiliacs is somewhat lower than expected. This is probably due to the commendable efficiency of the Scottish National Blood Transfusion Service in achieving near self-sufficiency in production of clotting factor concentrate from Scottish donors in the early 1980s, whereas in England and Wales haemophilia centres had to use significant quantities of imported commercial concentrate from the USA during this period." As I state in Question 112 (iii), the Penrose Inquiry Preliminary Report, (2010, page 47. 3.61) confirms that the prevalence in patients with haemophilia in Scotland is lower than expected.

113.2. However, I added: "Unfortunately, a number of East of Scotland haemophiliacs were infected by a batch of HIV-contaminated SNBTS factor VIII concentrate (81) ".

113.3. You misquote my 1987 review article as saying "The same article also comments on the prevalence of HCV infection among those who used blood products". I reviewed the risk of viral hepatitis (usually non-A, non-B) following the introduction of clotting factor concentrates in the mid-1970s. The HCV virus was only identified in 1989, two years after my article was published.

113.4. (i) HBV. No effect. HBV was present in blood donor populations worldwide.

113.5. (ii) HCV. No effect. HCV was present in blood donor populations worldwide.

113.6. (iii) HIV. As appears to have happened in Scotland, I think that self-sufficiency might have reduced the number of patients infected in England and Wales. However, I think that this would have needed to occur by 1981-1983 to have a significant effect, as the prevalence of HIV in UK blood donors was probably increasing over time. As in Scotland, commercial blood products (such as activated prothrombin complexes) would still have been required for treatment of patients with Factor VIII inhibitors.

113.7. In Scotland, I understand that the achievement of self-sufficiency in factor VIII concentrates by 1983 required an increase in the number of blood donors, in excess of the number traditionally required for whole blood or red cell transfusions. Is it possible that a similar increase in donor numbers would have been required in England and Wales for self-sufficiency?

113.8. A 1986 report from Dr Tedder's laboratory, which performed epidemiological studies of HIV-1 positivity across several UK Centres, stated that "In 1984 the greatest burden of infection was borne by patients who had

received commercial factor concentrate in the preceding five years. Roughly two thirds of such patients were seropositive. By contrast, only 18 of 166 patients who had received British Factor VIII exclusively were seropositive. At the time of study 15 of these cases were accounted for by infections arising in a group of 33 Scottish haemophiliacs given a uniquely infectious batch of British concentrate." (73, 79). As a result, there appeared in Scotland to be no significant difference in the risks of HIV infection between these two groups of patients with haemophilia: 28 patients in Scotland were infected by HIV from treatment with SNBTS concentrates, and 31 patients received also, or only, commercial factor concentrates (Penrose inquiry Final Report 2015, Executive Summary, pages 18-19). I suggest the Inquiry Consult Professor David Goldberg, a member of its Clinical Groups on HIV and HCV, who collated data on HIV and HCV for the Penrose Inquiry, about analysing this data to verify if this is the case.

113.9. I suggest also that the Inquiry could ask its Expert Group on Statistics to model the scenario that, if England and Wales had become near-self-sufficient in factor concentrate production at the same time as Scotland (1983), would there have been any material difference to the numbers of patients infected with HIV? Given that one or more blood donors in Scotland provided "a uniquely infectious batch of British concentrate" (73, 79); is it possible that increasing the number of England and Wales blood donors to achieve self-sufficiency might have increased the number of such donors contributing to uniquely infectious batches, thus reducing the difference in HIV infection rates between patients treated with commercial versus NHS concentrates, as appears to have happened in Scotland?

Section 6: Scottish National Blood Transfusion Service

114. Please set out the interactions and dealings you had in relation to SNBTS as the director of the Centre, insofar as relevant to the Inquiry's Terms of Reference. (If you had relevant dealings and interactions with any other national or regional blood service within the UK, please also provide

information about those and answer the questions set out below in relation to other national or regional blood services as well as SNBTS).

114.1. As Co-Director of the GRI Centre from 1988, I joined other Haemophilia Directors in Scotland in their annual meetings with SNBTS and the SHHD. I recall that I attended this meeting first in May 1988, when Dr Ludlam was asked to convene a Factor VIII Working Party. Together with my Co-Directors (Dr McDonald, then Dr Walker) I attended meetings of this working party, as well as the annual meetings. The remit of the working party was to coordinate the development and testing of new SNBTS Factor VIII concentrates, and to improve prediction of future demand which needed "real-time "usage" statistics. The remit subsequently broadened to include other coagulation factor concentrates (Factor IX, fibrinogen, etc); hence it was renamed the Coagulation Factor Working Party (CFWP). Professor Ludlam drafted a report on the CFWP for the Penrose Inquiry in 2011 (WITN3496015) which has been submitted to the Inquiry.

114.2. Like my predecessor honorary consultant physicians in the University of Medicine (Drs Douglas, McNicol, Prentice and Forbes), I did not participate in ordering SNBTS products (or any coagulation factor products) for treatment of patients at the Centre; this was the sole responsibility of our colleagues in the NHS Department of Haematology and its Blood and Blood Products Laboratory (Drs McDonald, Davidson, Walker and Tait).

114.3. In 1992 Dr Ian Franklin, a consultant haematologist who had worked in the Birmingham Haemophilia Centre, was appointed Bone Marrow Transplant Director in the GRI Haematology Department, succeeding Dr Alan Burnett. In 1996 he was appointed as Regional Director of the West of Scotland Blood Transfusion Service; and Professor of Transfusion Medicine in the University of Glasgow's GRI Department of Medicine (under Professor James McKillop), as was his Senior Lecturer Dr Tessa Holyoake; and therefore they became my research and teaching colleagues in this Department. Professor Franklin offered to participate in patient care at the GRI Haemophilia Centre, in view of his previous experience in Birmingham.

However, Professor McKillop, Dr Davidson, Dr Walker and I agreed that this would be a potential conflict of interest, as SNBTS was a manufacturer of blood products, so his offer was politely declined. He and Dr Holyoake continued their clinical and research activities in haematological malignancies, achieving international recognition in this field (1).

114.4. I had no dealings with any other national or regional blood service.

115. What consideration was given to increasing production of cryoprecipitate, or producing a product with lower risk, in response to the risks associated with factor products, and what if any involvement did you have with SNBTS in relation to this?

115.1. By the time I was involved with SNBTS as Co-Director from 1988, UKHCDO guidance was that cryoprecipitate should no longer be used for treatment of patients with haemophilia or von Willebrand's disease, unless concentrates did not contain sufficient VWF levels for effective treatment of some individual patients with VWD (25). By this time, all factor concentrates were virally inactivated and believed to be safer regarding transmission of HIV and hepatitis. There was therefore no need to increase production of cryoprecipitate for use in Haemophilia Centres in Scotland.

115.2. The responsibilities of the CFWP (WITN3496015) included development of higher purity SNBTS factor VIII concentrates, with transitions from the current product Z8 to Liberate, in collaboration with the French national fractionation facility in Lille. Together with other Scottish Haemophilia Centre Directors, Dr Walker and I worked constructively with SNBTS colleagues in initial pharmacokinetic assessment; then formal clinical trials of efficacy and safety (with ethical approval and written patient consent). A previously untreated patient (PUP) study was completed to assess viral safety (28).

116. What discussions or meetings or interactions did you have with SNBTS in relation to:

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

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

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

116.1. See my answer to Question 115 -

116.1.1. By the time I was involved with SNBTS as a Co-Director in 1988, all factor concentrates were virally inactivated and believed to be safer regarding transmission of HIV and hepatitis.

116.1.2. Formal clinical trials of efficacy and safety of concentrates (with ethical approval and written patient consent) were performed.

116.2. A previously untreated patient (PUP) study was completed to assess viral safety (28); as was a study of HAV safety (29).

117. What involvement did you have with any decisions or actions taken by SNBTS in response to the risks arising from blood and blood products?

117.1. See my answers to 115-116 above.

118. What system was followed for keeping records of the blood or blood products used in Scotland (both in relation to source and use)?

118.1. This was another important role of the CFWP from 1988, described in (WITN3496015).

118.1.1. Clotting factor usage was collected monthly from each haemophilia centre, and collated by the Secretary.

118.1.2. Clotting factor concentrate issues from PFC were reviewed and collated.

118.1.3. The future projected concentrates requirement was kept under regular review.

118.1.4. CFWP agreed how PFC concentrate should be distributed between haemophilia centres.

118.1.5. A unified system was established for the purchase of commercial concentrates.

118.1.6. The demographic distribution of patients was considered.

119. Why was the Factor 8 Working Party for Scotland and North Ireland established, and what was your role within it?

119.1. See my answers to 114-118 above. I was a member, as were Drs Gibson, Walker, Chalmers and Tait.

120. Have you held any positions at the Scottish National Blood Transfusion Service (SNBTS), and if so what were your role and responsibilities in any such positions?

120.1. None in SNBTS.

120.2. I was a member for a few years in the 1990s (I can't remember exact dates, as I have no records of its meetings) of the independent Scottish National Blood Transfusion Association (SNBTA), which represents the interests of blood donors, and was chaired by Professor R H Girdwood.

Section 7: UKHCDO

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

121.1. After I succeeded Dr Forbes as GRI Centre Co-Director at the end of 1987, I joined Dr McDonald (then Drs Walker and Tait) as a steering committee / executive committee member, and at least one of us would try to attend its committee and annual general meetings. After Dr Tait became a Centre Co-Director in 2001, I attended fewer of its meetings because I was involved with other administrative duties in RCPE, ISTH, SIGN, and Quality Improvement Scotland (see Question 3).

121.2. I was never a member of any of its working parties.

121.3. My main contribution, apart from being a committee member, was in proposing to UKHCDO from 1990 that it should develop National UK Clinical Audit of haemophilia centres. After a pilot study of all Centres in Scotland and Northern Ireland with Dr Ludlam, Edinburgh, and Dr Mayne, Belfast; this was initiated across the UK Comprehensive Care Centres in 1992, with a triennial inspection and report by a haemophilia director from another UK Centre (30). Its development was enthusiastically supported by Drs Mayne, Colvin then Ludlam, as successive chairs of UKHCDO. Initially, audit visits were conducted by a Director from another Centre; and included anonymous patient feedback. The audit was educational for all Centre staff (and the auditor); encouraged service improvements to be made (and often funded by hospital managers). I coordinated the audit until 2000, then was succeeded by Dr Jonathan Wilde, Birmingham (31). The audit was expanded to include a haemophilia nurse specialist, and a patient representative, from other haemophilia centres. It continues to this day.

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

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

122.1. I refer you to the full description of UKHCDO given by Rosemary Spooner and Dr Charles Rizza, in the textbook on haemophilia which Dr Rizza and I co-edited in 1997 (48). This applies to my involvement with UKHCDO from 1988 when I became a member, until 1997. After 2000, due to my increasing administrative commitments with RCPE, SIGN and ISTH, I attended fewer meetings of UKHCDO and was happy for my Co-Directors Professor Walker and Dr Tait attend these instead.

122.2. The purposes, functions and responsibilities of UKHCDO from its foundation in 1968 were (48) –

122.2.1. Meetings of Haemophilia Centre Directors at least once a year to discuss matters specifically of interest in the management of haemophilia and to review the results of their surveys.

122.2.2. An Executive Committee, made up of the Reference Centre Directors (including Glasgow) met at least twice a year. This was replaced in the mid-1990s by Comprehensive Care Centre Directors.

122.2.3. The Oxford Haemophilia Centre acted as the Secretariat for UKHCDO since 1968, arranging meetings, circulating information of interest to all Directors, and providing annual reports on the data collated and analysed on behalf of the UKHCDO. This was later transferred to Manchester.

122.2.4. From 1968, annual surveys collated information on patients with haemophilia A and haemophilia B. These recorded personal details including name, date of birth, sex,

coagulation defect and its severity, date of death, type and amount of materials received each time patients were treated, reason for treatment, details of incidence of jaundice, and presence of antibodies (inhibitors) to Factor VIII or Factor IX. Confidentiality was maintained by identification of each individual patient by a diagnostic code number, so that patients' names and Centre location were used as little as possible.

122.2.5. In 1976 the Department of Health, after discussion with UKHCDO, issued a circular -HC(76)4 – setting out the revised criteria for the designation of Haemophilia Centres and the services they were expected to provide for the patients.

122.2.6. From 1976 Directors agreed to continue to send information as above to the Oxford Secretariat regarding all haemophilia A and haemophilia B patients they knew (including patients who were not treated with blood products), and also from 1976 details of treated patients with von Willebrand's disease, carriers of haemophilia A and B, acquired haemophilia A, and other rarer congenital blood coagulation defects.

122.2.7. Data collection was transferred from manual to computer register from 1977, after approval by the Haemophilia Society whose members were particularly concerned about confidentiality of a centrally-held register. Rigid security arrangements were set up to protect confidentiality.

122.2.8. In 1988 arrangements were made with the Office of Population Censuses and Surveys (OCPS, and the General Register Offices in Edinburgh and Belfast,) for the Secretariat to obtain, in confidence, copies of UK death certificates.

122.2.9. In 1991 a Constitution for UKHCDO was drawn up; and in 1993 the NHS.Management Executive, after discussion with UKHCDO Steering Committee and the Haemophilia Society, issued new Guidelines – HSG(93)30 – on provision of haemophilia treatment and care. The previous system of Haemophilia Reference Centres, Centres and Associate Centres was replaced by Comprehensive Care Centres (including Glasgow), and Centres.

122.3. The UKCHDO database has been of great value to NHS haemophilia centre staff, their patients and families, and healthcare managers and planners (Including providers of treatment products, including both human and recombinant factor concentrates). Its published surveys have accurately documented the numbers of patients, treatments given, and their complications including transfusion transmitted infections, development of inhibitors, allergic reactions, and the thrombotic complications of Factor IX concentrates. Details are given in (48).

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

122.4. In addition to the Meetings of Centre Directors and the Steering Committee, Working Parties were established from 1977. These included – hepatitis, home treatment, and the treatment of patients who had factor VIII antibodies; and from 1989 adverse events (48). For the latter, an orange card system to report these complications was introduced, to complement the Committee on Safety of Medicine's yellow card system.

c. the relationships between UKHCDO and pharmaceutical companies;

122.5. I do not know details of these, and suggest you ask the UKHCDO secretariat.

d. how decisions were taken by UKHCDO;

122.6. I recall these were usually made by the Executive Committee, and discussed and approved by all members at annual meetings of all Centre Directors. I suggest you ask the UKHCO secretariat.

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

122.7. I recall that this was disseminated in letters, publications in scientific and medical journals; and at Open Scientific Meetings (initiated in Glasgow in 1980 by my predecessors), which I recall representatives of the Haemophilia Society, manufacturers of blood products, and Haemophilia Centre nursing, physiotherapy, social work and data manager staff could attend. Also by publications including guidance, articles, newsletters and books (many with the Haemophilia Society); and latterly through its website. I suggest you ask the UKHCO secretariat.

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;

122.8. I discussed and was a co-author of the first UKHCDO guideline on selection of therapeutic products in 1988 (25).

ii. the manufacture of blood products;

122.9. None.

iii. self-sufficiency;

122.10. None.

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

122.11. None, apart from 1988 guidance (25).

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

122.12. This is mentioned in 1988 guidance (25).

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

122.13. None.

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

122.14. None.

viii. heat treatment;

122.15. This is mentioned in 1988 guidance (25).

ix. other measures to reduce risk;

122.16. None.

x. vCJD exposure; and

122.17. None.

xi. treatments for HIV and hepatitis C.

122.18. None.

Section 8: Pharmaceutical companies/medical research/clinical trials

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

123.1. No.

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

124.1. No.

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

125.1. No.

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

126.1. No.

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

127.1. No.

128. 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.

128.1. No.

129. What regulations or requirements or guidelines were in place at the time concerning declaratory procedures for involvement with a pharmaceutical company? If you were so involved, did you follow these regulations, requirements and guidelines and what steps did you take to comply with them?

129.1. From late 1985, as a Senior Lecturer and Honorary NHS consultant, I performed research studies with University and NHS colleagues, administered through the University of Glasgow's Research, Personnel and Finance Offices (see Questions 6-8). Most of these studies were collaborative UK epidemiological studies of the associations of haemostatic and rheological variables, measured in my University research laboratory, with cardiovascular diseases. These were funded by Government (e.g. Scottish Home and Health Department Chief Scientist Office; European Concerted Action on Thrombosis, ECAT), NHS (e.g. Scottish Hospitals Education and Research Trust, SHERT); or Charitable Bodies (e.g. Chest Heart and Stroke Scotland, British Heart Foundation). Some were studies involving pharmaceutical companies developing several vasoactive and/or antithrombotic drugs for prevention and treatment of cardiovascular disorders. Regulations, requirements and guidelines for the latter developed

between 1988 and 2009. I believe I complied with these, including annual declarations of interest to my employers; but cannot recall the details.

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

130.1. See question 77 for a list of studies with the CFWP of SNBTS blood products. SNBTS was a manufacturer of blood products, but was part of NHS Scotland and was not a pharmaceutical company. One research study, with Sheffield Haemophilia Centre, comparing coagulation activation of high purity Factor IX concentrate (Alpha Therapeutic UK) with prothrombin complex concentrate (Bio-Products Laboratory) (Hampton et al, 1993).

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

131.1. See question 130 (paper of Hampton et al, 1993).

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

132.1. All my proposed medical research projects with pharmaceutical companies were referred to the University of Glasgow, as my employer, to administer. I also notified them to the Head of the Glasgow Royal Infirmary Department of Medicine (and of the Department of Medicine's NHS Clinical Unit, including the Haemophilia and Thrombosis Centre).

Section 9: vCJD

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

133.1. To help answer your questions in this section, I have requested from the Central Legal Office, Edinburgh, copies of relevant documents retained at the GRI Haemophilia Centre; and what is currently available to them from SNBTS and Lothian Health Board archives. I believe this may be incomplete, so the Central Legal Office advises me to state as a caveat that there are documents that I still wish to see to allow this response to be complete and accurate, but which the CLO has been unable to provide to me at present. Accordingly, I may wish to modify this draft statement if I obtain access to relevant documents which provide additional information to those which I have access to at the present time.

133.2. I recall that in December 1997 Professor Ludlam, Chairman of UKHCDO, on behalf of the Executive Committee of UKHCDO, published a position paper (Ludlam, CA. New-variant Creutzfeldt-Jakob disease and treatment of haemophilia. Lancet 1997; 350; ii, 1704). This expressed concern about the possibility that blood products might transmit the agent responsible for vCJD; and noted that two batches of factor VIII concentrate had been withdrawn in the UK by the manufacturer because they were produced from plasma containing donations from individuals who subsequently developed vCJD. It noted that in 1996 UKHCDO recommended that recombinant factor VIII concentrate was the treatment of choice for patients with haemophilia A. The Executive Committee therefore recommended that patients should be treated as soon as possible with recombinant factor VIII. made without the use of bovine proteins or human albumin. Patients for whom recombinant factor VIII was not available would need treatment with plasma derived products. The committee stated that it was likely that any risk of transmission would be reduced by using concentrates prepared from donor plasma collected in countries other than the UK, e.g. the USA, where there were no recorded cases of vCJD or BSE.

133.3. On 26 November 1997 Professor Ludlam copied this letter to NHS Scotland managers, recommending that, unless they wished to authorise that all patients should receive recombinant Factor VIII, patients who did not should receive concentrates prepared from plasma collected in the USA rather than the UK. Drs Walker, Chalmers and myself as West of Scotland Co-Directors supported this request.

133.4. On 16 January 1998 the CFWP discussed this matter.

133.5. I recall that in 1998, UK Government stopped the use of UK plasma in the manufacture of blood products, and required BPL to source plasma instead from the USA; in Scotland SNBTS sourced plasma from the USA and Germany.

133.6. On 6 February 1988 the NHS England Director of Health Services circulated a letter on what patients who had received nvCJD-implicated blood components or products should be told. The advice the Department of Health received from ethics experts and other advisory bodies was that there was no need to inform patients, because it was thought unlikely that nvCJD would be transmitted in this way; that there was no diagnostic test for nvCJD; and that even if a test was available, there was no preventive treatment that could be offered. The letter stated – "In deciding whether or not to inform a particular patient, the benefit/harm balance for their individual situation must be carefully considered. In communicating with patients who have received implicated products, it is therefore for individual clinicians to decide whether to follow this general advice."

133.7. On 23 April 1998 the Chief Medical Officer circulated this letter in NHS Scotland, endorsing this view.

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

134.1. During 2001 and 2002, there were two incidents of possible exposure of UK patients to risk of vCJD.

134.2. In January 2001, UK Haemophilia Centre Directors were informed by the Bio-Products Laboratory (BPL) in England that a blood donor had recently been found to have vCJD and had donated plasma in 1996 and 1997 and was used to make clotting factor concentrates. The products made were 8Y, Replenate, Replenine-VF and antithrombin III. In NHS Scotland, SNBTS supplied some of these products to clinical users; and confirmed to Scottish Haemophilia Centre Directors that none of these products were involved in the recent notification from BPL.

134.3. Dr Hill, Chairman of UKHCDO, drafted a letter to UK patients for Centres to send to their patients, informing them of this incident. On behalf of Scottish Haemophilia Centre Directors, Professor Ludlam made minor changes, which were discussed at the Scotland and Northern Ireland Haemophilia Directors Group on 28 January. Each Centre then sent the letter to all patients with haemophilia and related disorders in Scotland (or parents of affected children). I recall that the copy GRI letter you sent me (GGCL 0000148_001) was sent to patients.

135. When and how were patients told of possible exposure to vCJD?

135.1. Patients and parents were sent this letter in February 2001.

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

136.1. This information is contained in this letter.

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

137.1. Patients (or parents) were asked to complete and return the attached reply sheet to indicate that they had received this letter and so that the Centre knew whether or not they would like to discuss the issues further. A follow-up form was sent on 2 April to those who did had not replied. Those who wished to discuss the issues were sent an appointment to meet with one of the Co-Directors who would provide advice, support, and if indicated referral for counselling.

138. You were the author of a letter dated 25 October 2002 to Dr E M Armstrong, Chief Medical Officer [GGCL0000152_001]. This letter refers to Haemophilia Directors in Scotland and Northern Ireland learning that a donor who had subsequently died of vCJD had contributed to batches of SNBTS coagulation factor concentrates. The letter states that the Directors had subsequently prepared information sheets, but there had then been an eight month delay during which time there had been "an absence of any comment from the Banner committee." The letter goes on to inform Dr Armstrong of the steps that the Haemophilia Directors intend to take to inform patients. See also: the attached "potential statement" to be issued by an NHS Trust: [GGCL0000152_002]; and the attached proposed letter to patients dated 31 October 2002: [GGCL0000152_003]; the response to your letter of 25 October 2002 from Dr A Keel (response dated 29 October 2002): [GGCL0000152_004]; a related template letter concerning the discovery of a blood donor with vCJD whose plasma was used to make factor concentrate products in England [GGCL0000148_001].

a. Please explain the background to this correspondence and the views expressed within it, and the reference to the absence of any comments from the Banner committee.

138.1. I recall that the second incident, in November 2001, of possible exposure of UK patients to risk of vCJD was notified by SNBTS to Scottish Executive Health Department (SEHD), the CJD Clinical Incidents Panel (Banner Committee), and SNIHD, informing that a donor of blood products had

recently been found to have vCJD (WITN3496016). These concentrates (Factor VIII, Z8; and Factor IX, DEFIX) were used for treatment between 1987 and 1989.

138.2. This matter was discussed at the meetings of SNIHD on 28 January 2002; and at the CFWP on 7 February 2002. At this meeting on 28 January, Professor Ludlam reported that he had written to the Banner Committee requesting advice about contacting patients exposed to implicated batches of plasma derived products; and that the reply was awaited. SNIHD proposed to draft letters to patients with some urgency; and to construct lists of patients treated in this window from their own records and from the UKHCDO database. SNIHDs and SNBTS would prepare press responses and information for Trusts.

138.3. SNIHD met on 14 June 2002. Advice from the vCJD Incident Panel clearly stated that patients should not be contacted until the panel had advised on their individual risks. This required anonymous data on the numbers of vials received being forwarded to the Panel. The SNBTS statement was awaited; meanwhile a press statement from the Scotland and Northern Ireland Haemophilia Directors Group had been drafted. It was agreed that no letters should be sent to patients at present. pending response from the vCJD Panel.

138.4. The annual meeting of SNIHD, SNBTS Directors, and Scottish Executive Health Department was held later on 14 June, chaired by Chief Medical Officer, Scottish Executive, Dr E M Armstrong, who agreed to raise the matter at the next meeting of UK Chief Medical Officers, and to put questions to the Incidents Panel.

138.5. At the SNIHD meeting on 23 September, no advice had been received from the Incidents Panel following details sent to them from Glasgow, Edinburgh and Aberdeen. It was agreed to be proactive, and a draft letter to Dr Armstrong was discussed.

138.6. At the UKHCDO Annual Meeting in Liverpool on 10 October, SNIHD met and agreed to proceed to discuss a draft information letter for circulation to their patients at their annual meeting with the Haemophilia Society (Scotland and UK) on 4 November; then send to relevant patients. A letter to Dr Armstrong was drafted, and having consulted my GRI Medical Director Dr Anderson who agreed that GRI Centre Directors should inform their patients, I sent this to Dr Armstrong on 25 October (GGCL0000152_001), enclosing a draft potential statement to be issued by NHS Scotland Trusts with Haemophilia Centres (GGCL0000152_002), and a draft letter to patients (GGCL0000152_003). Dr Aileen Keel, Deputy Chief Medical Officer, replied on 29 October on Dr Armstrong's behalf as he was on leave. She had discussed the matter with Professor Ludlam. Her advice was that Haemophilia Directors should proceed to inform their patients, with appropriate counselling. She recommended that Trust statements were not necessary. (GGCL0000152_004).

138.7. At the SNIHD meeting on 4 November 2002, it was agreed to make minor modifications to the letter and circulate for final approval. A policy for notification of patients who had moved either to other Scottish Haemophilia Centres or to Haemophilia Centres in England was agreed. Professor Ludlam would inform Dr Frank Hill as Chairman of UKHCDO. It was agreed that Haemophilia Directors would undertake patient counselling unless the numbers became very large.

b. Was the proposed statement from the Trust made, and was the proposed letter sent to patients?

138.8. The proposed letter was sent to patients on 26 November 2002. The Trust statements were not issued, as per Dr Keel's instruction. The Scottish Executive Health Department, Haemophilia Centres in Scotland, and SNBTS issued a Press Briefing on 27 November 2002 (WITN3496016).

c. Why, to the best of your knowledge, was there such a delay between the production of the information sheets and a final decision on whether or not they should be published?

138.9. See (a) above. Advice from the vCJD Incident Panel clearly stated that patients should not be contacted until the panel had advised on their individual risks. This required anonymous data on the numbers of vials received being forwarded to the Panel. By 10 October SNIHDs found the delay unacceptable, and informed the Scottish Chief Medical Officer and Chair of UKHCDO that they would proceed to discuss the matter and the draft information sheet at their next meeting with the Haemophilia Society (Scotland and UK) on 4 November, and thereafter send it to relevant patients. Like SNBTS, they considered that openness in these matters is important in maintaining confidence in blood transfusion (WITN3496016).

138.10. Finally, I would add that all UK Haemophilia Directors were asked by all the UK Departments of Health to send a further letter and information in September 2004 to all patients with haemophilia born with bleeding disorders (haemophilia, or von Willebrand's disease) currently registered at their Centre, advising that ALL who have received clotting factors derived from UK-sourced plasma between 1980 and 2001 are considered "At-risk" of vCJD for public health purposes.

d. Are you aware of any patients from the Centre subsequently being diagnosed with vCJD? If so, was the source of the infection established (and if so, what was it)?

i. You may be assisted by a template letter (seemingly for distribution across the UK) dated February 2009 that informs patients that a person with haemophilia had been found to have evidence of the infection that causes vCJD [GGCL0000157].

138.11. I am not aware of any UK patient with haemophilia subsequently being diagnosed with vCJD. The patient described in GGCL0000157 did not die of VCJD, and never had any symptoms of this disease when he was alive. He was found to have evidence of the infection that causes vCJD in his spleen at post mortem.

Section 10: Financial Support Schemes

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

139.1. As Centre Co-Directors, I, Dr Walker and Dr Tait provided documents to support applications of our patients for assistance from the Macfarlane Trust, and from the Skipton Fund

140. To the extent that you had any involvement with the trusts or funds or with the applications made by patients for assistance, please answer the following questions:

a. To what extent did the Centre and its staff (including you) inform patients about these different trusts or funds?

140.1. Our Centre staff routinely informed patients about these trusts and funds, and we encouraged and supported their applications for assistance.

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

140.2. See (a) above.

c. What kind of information did the Centre (whether through you or otherwise) provide to the trusts and funds about or on behalf of patients who were seeking assistance from the trusts and funds?

140.3. We gave requested information on behalf of our patients when sought.

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

140.4. We completed the necessary forms on such matters on behalf of our patients when sought.

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

140.5. I have no recall of any such involvement.

f. Based on your own dealings with any of the trusts or funds and/or based on your knowledge of the experiences of the Centre's 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?

140.6. I do not recall any shortcomings during my time as a Centre Co-Director. I refer the Inquiry to the Scottish Government 2018 report, which recommended that in NHS Scotland the application process for persons infected with HCV should be modified and simplified (54). I suggest that the

Inquiry might consider whether this process modification might be a useful recommendation by the Inquiry to the rest of the UK.

Section 11: Other issues

141. 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.

a. The Inquiry is aware of one complaint made to the General Medical Council about you in 2003, concerning allegations about the testing of a patient for HCV in 1991 and the information that was subsequently provided to him in 1992. The Inquiry is also aware that in April 2005 the General Medical Council informed you that its Case Examiners had concluded that there was insufficient evidence to support the allegations and that no action would be taken on your registration.

141.1. I do not recall any other complaints.

142. Please explain, in as much detail as you are able to, any other issues that you believe may be of relevance to the Infected Blood Inquiry.

142.1. **The International Dimension**

142.1.1. It was known internationally since the 1940s that the only available treatment for haemophilia and von Willebrand's disease was replacement of the missing coagulation factor by transfusion of blood. HBV, HIV, HCV were global pandemics affecting all blood donor populations, and were transmitted globally to patients requiring blood and

blood products, before these viruses could be identified for screening and exclusion of infected blood donors. Viral inactivation of factor concentrates was challenging, but finally successful in ending transmission by about 1987. From 1997 treatment with recombinant factors progressed, ending transmission of all human pathogens including vCJD,

142.1.2. The current global pandemic of COVID-19 has highlighted different approaches to its control internationally, and between the devolved nations of the UK. I suggest that the Inquiry consider taking evidence from relevant experts in other countries, for example mainland Europe, and seeking their judgement on procedures to minimise transfusion transmitted infections and outcomes in the UK. An example was set by the Penrose Inquiry for Scotland, which in 2011 invited Professor van Aken from the Netherlands to review the development of viral inactivation procedures by the Scottish National Blood Transfusion Service. At that time, Scottish Haemophilia Centre Directors suggested to the Penrose Inquiry that it should likewise invite a mainland European expert to review their actions in management of transfusion transmitted infections, but this suggestion was refused.

142.2. The Scottish Dimension

142.2.1. I and my former colleagues in haemophilia care in NHS Scotland understand from the NHS Scotland Central Legal Office that the UK Infected Blood Inquiry may wish to consider the Scottish dimension of its remit; and to compare the organisation,

procedures and contributions of the Scottish Home and Health Department / Scottish Government, NHS Scotland (Health Boards and their Haemophilia Centres; and Scottish National Blood Transfusion Service), and Scottish Royal Medical Colleges and Universities to their equivalents in the rest of the UK (rUK). We are currently drafting a Collective Document on these matters, which we plan to submit to the Inquiry by the end of October.

142.3. The UK Volunteer Blood Donors

142.3.1. Those affected by the tragedy of infected blood include: patients, families and loved ones; and the Haemophilia Centre staff who cared for them (Penrose Inquiry Final Report 2015; Volume 1; page x). The millions of UK volunteer blood donors required to meet the UK's aim for self-sufficiency in factor VIII concentrates from the 1970s (achieved in Scotland by 1983) should not be forgotten. The UK Haemophilia Society's symbol is a white figure (representing patients requiring replacement of a missing blood component for treatment) being supported by a red figure (representing the donor). The gift of blood donors saved many patients with haemophilia from death and disability (physical and psychosocial); and it is a tragedy that the evolution of pandemic viruses did not spare blood donors, some of whom were diagnosed as carriers by donor testing. As I have discussed above (Questions 108 and 112), achievement of near-self-sufficiency in Scotland probably reduced the prevalence of HIV infection compared to the rest of the UK. Sadly, the prevalences of HBV and HCV were not reduced by near-self-sufficiency in Scotland, due to their higher prevalence in UK volunteer blood donors.

142.4. The GRI Haemophilia Centre

142.4.1. UK Haemophilia Centres from the 1970s were one of the medical specialties pioneering the concept of comprehensive care by

multidisciplinary teams. From the 1980s, with the evolution of HBV, HIV and HCV, these teams expanded to include specialists in hepatology, infectious diseases, counselling and psychosocial support. In this statement I have reviewed the achievements of my predecessors at the GRI Centre in promoting knowledge, teaching, and developing multidisciplinary care of haemophilias; and also the efforts of my colleagues and myself to develop the Centre and its staff from the late 1980s, to address the progressive challenges of HIV, HCV, and finally the potential risk of vCJD. We worked closely with the Children's Centre at Yorkhill Hospital; with our colleagues in East of Scotland Haemophilia Centres; and with SNBTS and Scottish Government to coordinate care across NHS Scotland.

142.4.2. I believe that, from its formation in the 1950s by Professor Stuart Douglas, the staff at our Centre - at the heart of our friendly hospital, at the centre of the friendly City of Glasgow - aimed for partnership and friendship with our West of Scotland patients and their families. I cherish my 2009 retirement card, which says "with grateful thanks for your years of dedicated service to the haemophilia and bleeding disorders community. From the staff, trustees and members of the Haemophilia Society."

Statement of Truth

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

Signed GRO-C

Dated 29 October 2020

Table of exhibits:

Date	Notes/ Description	Exhibit number
30 September 2020	Organisation of haemophilia care in Scotland	WITN3496014
	Ludlam, C.A, Establishment of the Factor VIII Working Party for Scotland and Northern Ireland, later to become the Coagulation Factor Working Party for Scotland and Northern Ireland.	WITN3496015
27 November 2002	Press Statement. Blood transfusion, Clotting Factor Concentrates and variant Creutzfeld-Jacob Disease (CJD)	WITN3496016

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