INFECTED BLOOOD INQUIRY

WITNESS STATEMENT OF
DOCTOR BRIAN TREVOR COLVIN

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 2 March 2020

I, Dr Brian Trevor Colvin, will say as follows:-

SECTION 1: INTRODUCTION

1. Dr Brian Colvin (My address is known to the Inquiry)

   Date of Birth: GRO-C 1946

   Qualifications: MA MB BChir FRCP FRCPath

2. **Employment History** (Curriculum vitae attached)

   The London Hospital 1969 – 1975

   Junior posts in general medicine, orthopaedics, cardiology and haematology

   The London Hospital 1977-2007

   (from 1990 The Royal London Hospital- from 1996 Barts and The London NHS Trust)

   Honorary Consultant Haematologist

   This was a part time post in general haematology, with increasing specialisation in haemostasis and thrombosis, especially after haematological oncology was moved to St Bartholomew's Hospital following the 1996 merger.

   Haemophilia Centre Director circa 1977-2007

   On appointment to an honorary consultant post in 1977 I was given responsibility for the haemophilia service, although Professor Jenkins remained Director of the Haemophilia Centre. I do not believe that this arrangement was ever formally changed and the Haemophilia Centre note paper still carried his name in 1985.

Head of Oncology Services Unit The Royal London Hospital 1992-1994

Administrative responsibility for coordinating all oncology services leading up to merger with St Bartholomew's Hospital.

Director of Postgraduate Medical and Dental Education The Royal London Hospital 1996-1999

Responsibility for all postgraduate education in the new Barts and The London NHS Trust

Associate Medical Director Barts and The London NHS Trust 1997-1999

Associate Medical Directors were appointed by the Trust to assist the Medical Director.

Chairman Clinical Ethics Committee Barts and The London NHS Trust 1997-2007

The Clinical Ethics Committee was not a Research Ethics Committee. We considered matters of ethical interest and importance arising within the Trust, both clinical individual and organisational.

Chairman Steering Committee Human Tissue Resource Centre 2005-2008 Barts and The London NHS Trust

The committee managed implementation of The Human Tissue Act 2004.

(See also curriculum vitae)

The London Hospital Medical College

Lecturer in Haematology 1975-1977

Senior Lecturer The London Hospital Medical College – (later Barts and The London School of Medicine and Dentistry) 1977-2008

Medical Postgraduate Sub-Dean 1987-1995

Responsibility for all preregistration appointments and their administration at the Medical School

Queen Mary's School of Medicine and Dentistry

Sub-Dean for Postgraduate Medical Education 1995 – 1996

Assistant Warden (Student Affairs), later re-titled Dean for Student Affairs 1998 – 2008.

The academic roles in the School(s) of Medicine and Dentistry were principally educational and administrative. The post of Dean for Student Affairs was to provide overall support to the Warden, Professor Sir Nicholas Wright, especially in the field of Student Support and Guidance.

3. **Memberships**

Member United Kingdom Haemophilia Centre Doctors (formerly Directors) Organisation (UKHCDO) 1975 (approximately) - present

Chairman UKHCDO 1993-1996

Honorary Membership UKHCDO awarded 2009

Member Haemophilia Society 1970s – Present

Chairman Ethics Committee The Royal College of Pathologists (2003-2008)

I set up this committee at the request of the President of the College and was its first chairman. We considered all matters of ethical interest to the College.

4. **Investigations and Inquiries**

I was involved in the defence of approximately 30 law suits submitted to The London Hospital in 1990 relating to the campaign for compensation concerning the HIV infection of blood products.

I gave evidence to the Lindsay Tribunal. Papers relating to this have been provided by the Inquiry.

I gave evidence to the Archer Inquiry and my papers relating to this have been provided by the Inquiry.

I gave evidence to the Penrose Inquiry and the Inquiry has copies.

I was a witness at the Inquest on Mr. GRO-A and the Inquiry has supplied evidence of this to me.

SECTION 2: STATEMENTS PROVIDED TO PREVIOUS INQUIRIES AND INVESTIGATIONS

5. – 9. **Statements provided**

I have no record of anything that was said or written in the 1990 litigation.

I have no reason to believe that the evidence I gave to the Lindsay Tribunal or the contents of the reports or evidence to the Archer Inquiry, the Penrose Inquiry or the GRO-A Inquest were anything other than true and accurate.

SECTION 3: DECISIONS AND ACTIONS OF THE ROYAL LONDON HAEMOPHILIA CENTRE ("THE CENTRE") AND YOUR DECISIONS AND ACTIONS AT THE CENTRE

10. and 12. **The Royal London Hospital and The London Hospital Medical College**

I was appointed to The London Hospital Medical College as Senior Lecturer (Honorary Consultant Haematologist) at The London Hospital in 1977. At that time the haemophilia centre was small and in its infancy. Dr, later Professor, George Jenkins (now in his 90s), was nominally Haemophilia Centre Director but I was effectively in charge. In 1977 the Centre had no physical or administrative structure, no nursing service or other dedicated services from professions allied to medicine, such as physiotherapy, and I developed it from a small unit into one of the major Haemophilia Centres in the UK, although dedicated space was never provided in my time. I was effectively single handed and was on call at all times until Professor John Pasi was appointed as a second consultant in 2003. On retirement from the NHS between 2007 and 2009, my half time post was replaced by three (and now four) consultant appointments.

On taking up the post, I realised there was a gap in the care we provided to the community and I therefore established a series of outreach clinics in Essex to identify people with haemophilia. We also achieved the appointment of a Domiciliary Nursing Sister in 1977, linked to The Royal Free Hospital within the old North East Metropolitan Region. I then developed the registration of our patients, a home treatment programme (initially using cryoprecipitate), regular review and elective surgery, as concentrate supply improved. I set up multidisciplinary clinics, especially in paediatrics and rheumatology to provide, in one consultation, the best possible all-round care and access to those services which patients might need. I attended all of these clinics myself. When prophylaxis became a realistic option, I began to treat patients with severe haemophilia with prophylaxis, although concentrate availability limited this approach until the 1990s. Dedicated nurse specialists were appointed and I was involved in early work to enable nurse prescribing at the hospital.

When HIV was recognised, I set up a counselling service with a social worker and a review clinic with colleagues in the Graham Hayton Unit (STD centre) where expertise in HIV related illness

was available. Later I introduced a specialised liver disease clinic within my own clinic arrangements, which was attended by a hepatologist.

Prophylaxis for severely affected patients was developed in the 1990s, as product supply allowed, which enabled patients better to control their lives, including one of my patients, born in the 1980s, who was enabled to become a world champion cyclist.

I was responsible for all clinical development at The London but received excellent support from the consultants and staff at The Royal Free Hospital Haemophilia Centre.

The Inquiry has provided a document (BART0002284) which gives a snapshot of Haemophilia Services in the North East Thames Region in August 1983 and demonstrates the level of regional cooperation between The Royal Free and The Royal London hospitals at the time.

In 1993 I was appointed Chairman of UKHCDO, an organisation of which I had always been a member, although I was not a Reference Centre Director. These Directors had formed an effective Executive Committee for many years. From this point the Centre at The London Hospital was recognised as a Comprehensive Care Centre, as the status of centres was revised and accredited. As Chairman I introduced a system of National Audit and also began the process of making UKHCDO compliant with data protection legislation.

In 1996 I passed the Chairmanship of UKHCDO to Professor Christopher Ludlam and supported him through the difficult management of the nvCJD crisis, which was a significant third challenge after the HIV and HCV crises, both at a local and a national level.

At The London I combined directorship of the Haemophilia Centre with my role as a consultant general haematologist, managing haematological malignancies, haemoglobinopathies and general haematology at the outset of my career but later I focused on haemostasis and thrombosis, including the management of thromboembolism, the use of anticoagulants and the care of haemophilia and allied disorders.

Throughout, I was heavily engaged with quality assurance in laboratory medicine at a local and national level (See CV).

My interest in Law and Ethics resulted in my appointment as Chairman of The London Hospital's Clinical Ethics Committee and I was appointed as the first Chairman of the Ethics Committee of The Royal College of Pathologists.

11. **Senior colleagues at The London**

Department of Haematology (consultants)

Professor George Jenkins

Head of Department and general haematologist

Dr Adam Turnbull (deceased)

Consultant physician and clinical haematologist (inpatient care and general clinical service)

Professor Adrian Newland

Consultant clinical haematologist (principally oncology and immuno-haematology)

Dr Peter McCallum after 1996

Consultant haematologist (almost exclusively thrombosis and haemostasis but not haemophilia)

Professor John Pasi after 2003

Consultant haematologist (haemophilia and allied disorders, thrombosis and haemostasis – Director of Haemophilia Centre from 2007)

Haemophilia Centre

Key nursing and administrative staff are not mentioned by name, but they were critical to the work of the Centre and patient care.

Department of Paediatrics

Dr Graeme Snodgrass (deceased)

Consultant paediatrician (shared children's clinics and inpatient advice)

Dr Roger Harris

Consultant paediatrician (shared children's clinics and inpatient advice)

Dr (now Professor) Elizabeth Davenport - Children's Dentistry

Consultant in Child Dental Health (attended children's clinics and coordinated children's dentistry)

Department of Rheumatology

Dr Colin Barnes

Consultant rheumatologist (attended joint rheumatology clinics and gave rheumatological advice)

Dr David Perry

Consultant rheumatologist (attended joint rheumatology clinics following Dr Barnes' retirement)

Graham Hayton Unit

Dr Guy Baily

HIV consultant (attended joint HIV clinics and gave advice on patient care)

Dr Celia Skinner

HIV consultant (attended joint HIV clinics and gave advice on patient care)

Virology

Professor Leslie Collier (deceased)

Consultant virologist (gave advice on all virological matters)

Professor Donald Jeffries (deceased)

Consultant virologist (gave advice on all virological matters following Professor Collier's retirement)

Hepatology

Dr Paul Swain

Consultant gastroenterologist and hepatologist (attended joint hepatology clinics and gave advice on liver disease)

Professor Graham Foster

Consultant gastroenterologist and hepatologist (attended joint hepatology clinics and gave advice on liver disease)

Psychiatry

Dr Colin Murray Parkes (deceased)

Consultant psychiatrist (gave advice on psychiatric care for patients and psychological support for staff)

Social work

Mr Nigel Harvey

Social Worker with expertise in HIV counselling and care (attended joint HIV clinics and undertook individual follow-up counselling)

Senior colleagues at The Royal Free Hospital

Dr Peter Kernoff (deceased)

Consultant physician (provision of general advice and support, especially on hepatitis and HIV until his illness)

Professor Christine Lee

Consultant haematologist (provision of general advice and support, especially on hepatitis and HIV following Dr Kernoff's illness)

Professor Geoffrey Dusheiko

Consultant hepatologist (gave advice on specialist hepatological matters on request)

13. **Patient Numbers**

In 1977 there was a small base of patients who had attended The London for many years under the care of Dr John Perrin (deceased). Dr Frank Boulton had begun to organise the Centre before he left for a post in Liverpool in the mid-1970s.

The Inquiry has provided evidence of the register for 1983 at BART0002284. This shows a total of 338 patients: haemophilia A 201; haemophilia B 28; von Willebrand's disease 109. By 1993 there were, perhaps 500 patients on the register and over 100 patients attended regularly, so that there were enough severely affected patients to qualify for our application for Comprehensive Care Centre (CCC) status. (The World Federation of Haemophilia recommendation number is 40).

It was policy to see all children regularly and the average clinic interval was three to six months. As the average clinic size was about 10 the number of children under my regular care would therefore have been about 50.

More accurate and detailed numbers for The London Hospital register, treatment profile and age range might be available from the UKHCDO database and/or Mrs Heather Williams at the Haemophilia Centre.

14. **Importation, manufacture and use of blood products**

I have been a life-long supporter of the NHS, but commercial products were used at The London from the early 1970s when I was still a junior doctor, because of a shortage of supply of NHS concentrate.

It was my policy to use cryoprecipitate for children, where possible, into the 1980s but this was very difficult, because of a) cryoprecipitate allergy, b) problems with venous access, c) cryoprecipitate use was impossible to sustain in home treatment d) serious bleeding unsuitable

for cryoprecipitate therapy, e) the need for surgery, f) the development of inhibitors and g) treatment given in other centres.

As our experience developed and home treatment (or even prophylaxis) became an option, we tried to reserve NHS concentrate for children who were not on cryoprecipitate, or for the home treatment programme. The reason for this was partly safety but was also related to trying to allocate our limited supplies of NHS concentrate in a useful, efficient and predictable way.

We did our best to protect small children seen in the hospital by using cryoprecipitate but very sadly, a number of my young patients died of HIV infection [see a) to g) above].

15. **Responsibility for the selection of blood products**

I was in charge of the selection of blood products for patients under my care from the late 1970s until national tendering was introduced in 2005. I believe that NHS products were mostly provided by the Brentwood Blood Transfusion Service without charge. The London Hospital Pharmacy must have purchased commercial concentrates, as appropriate, and on the Centre's behalf, but I have no record or memory of the detail of the process that was used. I recall that, at some time, a nominal "charge" was introduced for NHS products, but I was aware that these financial arrangements were not the same as applied for the purchase of commercial products. I believe that UKHCDO will have a record of the usage of all products during the whole of the period.

BART0002284 gives evidence of cooperation between The Royal Free and The London hospitals in 1983, when estimated concentrate usage at The London was, cryoprecipitate 0.05 million units; NHS concentrate 0.9 million units; Commercial concentrate 0.85 million units. Our preference was always for NHS sourced products, but supplies did not meet demand, as can be seen from the graph at the end of the paper.

Products used included:

Fresh frozen plasma (FFP) [NHS]

Cryoprecipitate [NHS]

Factor VIII, [NHS and commercial]

Factor IX, [NHS and commercial]

Factor Eight Inhibitor Bypassing Fraction (FEIBA) from the 1970s [commercial]

Desmopressin (DDAVP) + tranexamic acid from the late 1970s [pharmaceutical]

Porcine factor VIII in the 1980s [commercial]

Virally inactivated concentrate VIII and IX concentrates, [NHS and commercial]

Recombinant Factor VIIa from the late 1980s [commercial]

Recombinant factors VIII and IX, introduced in the 1990s [commercial]

My decisions on product use were made on the basis of clinical need, suitability of the product for the individual patient and their particular problem at the time, availability, and cost.

16. **Pharmaceutical Companies**

I would receive regular visits from pharmaceutical companies. These visits did not influence my choice of products and my decisions were made on my own assessment of clinical indication.

Inhibitor management

For the management of inhibitors, the choice of products lay between Factor Eight Inhibitor Bypassing Fraction (FEIBA) from the 1970s and Recombinant Factor VIIa from the late 1980s. Product selection was based on clinical indication, concentrate availability and, to some degree, cost.

Porcine factor VIII was available for the management of selected patients with inhibitors to factor VIII in the 1980s. Product selection was on the basis of clinical need, laboratory results, suitability of the product for the individual patient and their particular problem at the time, availability, and cost.

17. **Responsibility**

See answer to 15.

18. **Choice**

It is difficult to answer a question which covers my 30 years as Director of the Haemophilia Centre but, in summary:

Children

I aimed to give cryoprecipitate to small children seen in the hospital until NHS heat treated concentrate became available in 1985. This policy was very difficult to achieve because of:

a) cryoprecipitate allergy, b) difficulty with venous access, c) cryoprecipitate use was impossible to sustain in home treatment d) serious bleeding unsuitable for cryoprecipitate therapy, e) the need for surgery, f) the development of inhibitors and g) treatment given in other centres.

I can offer no specific examples and many of my children were infected by HIV and HCV.

Home treatment (adults and children)

We began the home treatment programme using cryoprecipitate, but this was not realistic because of logistic difficulties and concentrates were used from an early stage.

I attempted to reserve NHS concentrate for the home treatment programme, but I cannot say that commercial concentrates were not used in this context, especially for severely affected patients.

Everyday use (adults)

I do not recall precisely how much we tried to give NHS concentrates to casual attenders, as this might depend on a number of factors, including the severity of the illness or injury. The record will show that the majority of my patients who suffered HIV infection were people severely affected by haemophilia and at least two of my patients were infected with HIV by treatment with UK sourced NHS concentrate, (one being a severely affected patient and one being a mildly affected patient, who I think had suffered an injury).

Surgery

For surgical procedures, especially in times of shortage of product, it was essential to use commercial product in order to maintain the use of NHS product for regularly treated patients, especially those on the home treatment programme. This meant that some very difficult choices had to be made, in discussion with the patient and I referred to this dilemma in my evidence to the Archer Inquiry.

Inhibitors

Inhibitor development makes haemophilia care extremely difficult and large amounts of blood products may be required, often with little clinical effect. Inhibitors may develop in both moderately and mildly affected patients. In these circumstances, large quantities of commercial products of various kinds were often used. (see q.16)

There were occasions when patients were given a choice of how to proceed but, in general, I made the decision on which product to use. I gave clear instructions on product use which were understood and supported by doctors and nursing staff in the Haemophilia Centre.

19. **Alternative products**

1. The main alternative product for people with bleeding disorders was desmopressin (DDAVP). Its use was first published in 1977 but it was only suitable for the occasional treatment of people with mild haemophilia or heterozygous von Willebrand disease (vWD), especially for dental extraction or minor bleeding. In my view it was not suitable for any serious bleeding or surgery because its effect was not reliable and because the effect tended to "wear off" (tachyphylaxis) after two or three doses.

The use of DDAVP was often accompanied by the antifibrinolytic agent tranexamic acid but this agent had little, if any, efficacy when used alone, save perhaps in the context of excessive menstrual bleeding in women with bleeding disorders.

2. Hormone therapy was often used to regulate menstrual loss in women with heritable bleeding disorders.

3. After the HIV/HCV infection period recombinant factor VIIa was introduced, almost exclusively for the management of inhibitors to factor VIII or IX.

4. Recombinant factors VIII and IX were introduced in the 1990s but early factor rVIII concentrates contained human albumen and therefore remained essentially "blood products". The cost of recombinant products was regarded as prohibitive until the nvCJD crisis brought their use into regular practice. Technical developments in manufacture later resulted in the production of factors free from all biological material in the new millennium.

20. **Value of alternative treatments**

Alternative treatments were of limited use as follows:

DDAVP (desmopressin) and tranexamic acid were extremely valuable for people with mild haemophilia and heterozygous vWD in selected cases, especially dentistry. DDAVP was not effective in haemophilia B, severely or moderately severely affected patients with haemophilia A or patients with conditions needing treatment for more than a few days or for most types of surgery.

Hormone therapy was valuable for menstrual disorders in women with bleeding disorders.

Recombinant VIIa was generally only suitable for the management of inhibitors to factors VIII or IX. Its effectiveness was very variable and difficult to measure and its cost was very high.

FEIBA is an activated form of factor IX, available commercially from Baxter since the 1970s, and has been used in the management of inhibitors to factors VIII and IX.

Porcine factor VIII was not a human blood product but was prepared from pigs' blood by Speywood. It was useful in the management of some patients with weak inhibitors to factor VIII. Its main side effects were allergy and thrombocytopenia. It was withdrawn because of anxiety concerning the possible transmission of porcine parvovirus.

21. **Cryoprecipitate**

We began the home treatment programme using cryoprecipitate for some patients in the late 1970s, but the material is really too difficult for patients or their relatives to use at home.

I aimed to use cryoprecipitate for children who were seen in the hospital with minor or moderate bleeding until the advent of the heat-treated NHS 8Y concentrate in 1985. For reasons cited above (q18) this policy was very difficult to achieve.

Cryoprecipitate is difficult to handle and it is difficult to calculate the correct dose. Allergic reactions are common and can be severe. It has never been virally inactivated and if an infected donation is transfused, infection will follow.

22. **Home Treatment (see qs 10 and 12, 14, 18 and 21 above)**

The Centre's home treatment programme was introduced in the late 1970s under my direction and was much assisted by the appointment of a domiciliary nursing sister in 1977. Subsequent haemophilia nurse specialist appointments enabled the training of patients, parents and children in venepuncture techniques.

We began by using cryoprecipitate, but freeze-dried concentrates were preferable as they could be kept in a refrigerator, as opposed to a freezer, and were much easier to make up. More and more patients, including small children, were introduced to home treatment over the years and I aimed to allocate my NHS supplies to the home treatment programme, whenever possible.

23. **Product choice**

The policy to use NHS concentrates, when available, for the home treatment programme and commercial products for disasters and surgery was to make efficient and appropriate use of available resources.

Predictable product volume for the home treatment programme (and for occasional use for minor problems, especially for moderately affected patients who were rarely treated and for those unsuitable for DDAVP and tranexamic acid) gave clarity to product selection. The policy was difficult to implement and only partially successful, for reasons already explained.

The result of product selection was that some patients escaped infection, as demonstrated by my published work, but the result was also that I was able, in retrospect, to know when individual patients became infected with HIV.

The policy did not produce useful statistics because some patients were infected at other hospitals and at least two of my patients became HIV positive as a result of NHS concentrate administration alone.

24. **Prophylaxis**

In the early days of concentrate use there was insufficient material available to offer prophylaxis for haemophilia A in the United Kingdom.

By 1988 there was a world shortage of all forms of factor VIII which was partly created by a reduction in "yield" from plasma donations, caused by the loss of activity during viral inactivation. Therefore, prophylaxis could only be used in the 1990s and beyond, starting with modest dosage regimens, especially in younger patients. This produced a generation of young people with severe or moderate haemophilia who reached adult life in good health but with some arthropathy, especially in the ankles.

I do not recall when prophylaxis for haemophilia B was introduced but its provision was not nearly as challenging because of the smaller number of patients (UK self-sufficiency in product availability) and longer half-life of factor IX (less frequent administration).

25. **Children (see also q 18.)**

I aimed to give cryoprecipitate to small children with haemophilia A seen in the hospital until NHS heat treated concentrate became available in 1985. This policy was very difficult because of a) cryoprecipitate allergy, b) difficulty with venous access, c) cryoprecipitate use was impossible to sustain in home treatment d) serious bleeding unsuitable for cryoprecipitate therapy, e) the need for surgery, f) the development of inhibitors and g) treatment given in other centres.

I can offer no specific examples and many of my children were infected by HIV and HCV but there was at least one case where I know that infection was avoided.

I cannot recall whether or not children with haemophilia B were ever offered fresh frozen plasma rather than a freeze-dried concentrate. I believe that we would have used concentrate because FFP is even more difficult to use than cryoprecipitate and virtually all factor IX was of UK origin.

26. **Rationale for cryoprecipitate for children (see also q 18)**

My reasoning was that cryoprecipitate was probably the safest form of factor VIII concentrate until 1985 and it could be used for children because of the small doses of concentrate required. The problem was that it was difficult to make up and volumes were relatively high, allergy was common and it was really unsuitable for home treatment. Many patients would suffer from serious bleeding, chronically inflamed joints requiring limited prophylaxis or would have difficulty with venepuncture. Then the use of freeze-dried concentrates became inevitable.

27. **Mild or moderately affected patients**

Patients with mild or moderate haemophilia A and von Willebrand disease (VWD) were treated with DDAVP and tranexamic acid, where appropriate (after 1977). This was usually for minor bleeding, such as epistaxis, or for dental extraction. DDAVP was particularly useful for revealed bleeding when there was no risk of haematoma formation. If treatment failed or bleeding was prolonged there was then no risk of an internal haematoma forming and the switch to concentrate use was safe, at least for the control of bleeding. I was never in favour of using DDAVP for concealed bleeding or for surgery (other than dental surgery). DDAVP is not effective in haemophilia B or severe VWD.

Some families with mild or moderate haemophilia A have a genetic predisposition to develop inhibitors to factor VIII, at which point treatment becomes extremely difficult.

28. **Other infections**

I am not aware of any hepatitis A infection at The Royal London Hospital, but I know that it has been recorded elsewhere.

Some of the patients at The Royal London Hospital received concentrate which might have been associated with donations from people who developed nvCJD but I am not aware of any proof that any such infection occurred.

SECTION 4: KNOWLEDGE OF, AND RESPONSE TO, RISK

29. and 33. **Knowledge in 1977 and Knowledge and understanding of hepatitis**

Knowledge about the risk of hepatitis induced jaundice from blood transfusion dates back to the early days of this treatment during the Second World War. The virus which causes hepatitis B

was identified while I was at pre-clinical medical school in the mid-1960s and the incidence of hepatitis B infection then declined sharply because of donor selection. It was hoped that this would bring an end to the problem of transfusion transmitted hepatitis.

The introduction of large pool freeze-dried products for haemophilia care from about 1970 was greeted with enthusiasm by patients and clinicians alike, because of the enormous benefits of avoidance of death, reduction of pain and suffering and limitation of disability offered by effective and easy-to-use treatment. Some patients then developed jaundice due to acute non-A non-B (NANBH) hepatitis from which they recovered clinically. It was thought that the benefits of treatment outweighed the disadvantage of the generally "mild" clinical hepatitis. It soon became apparent that very many patients who had been treated with large pool concentrates developed asymptomatic abnormal liver function tests (LFTs), despite remaining clinically well. Neither the clinicians nor the Haemophilia Society could take effective action because there was no alternative treatment, other than cryoprecipitate, the problem of hepatitis was largely silent, the cause was unknown and the course of the condition and its prognosis were uncharted. (The disadvantages of cryoprecipitate are discussed elsewhere). It was therefore very difficult to issue any useful warning about a treatment to which there was no practical alternative and which appeared to be doing little harm.

The true significance of the information on this "silent" hepatitis did not become apparent until the mid-1980s because of the relatively slow course of the chronic liver damage that was being caused. By this time efforts were being made to inactivate the supposed virus or viruses thought to be causing the laboratory abnormality but these initially failed. By 1985/87 it had become apparent that a mixture of donor selection and viral inactivation was capable of rendering plasma derived concentrates much safer than had been the case in the past.

The hepatitis C virus was finally identified in 1989, just as the true size of the problem began to be appreciated.

My knowledge of NANBH developed through reading the medical literature, discussions with colleagues and the information provided by UKHCDO.

When AIDS was recognised as a risk for people with haemophilia in the early 1980s further efforts were applied to the prevention of what was later recognised as HIV infection and these, also, were not immediately wholly successful. The sources of knowledge were the medical literature and discussions with colleagues within and outside UKHCDO.

The problem of nvCJD in the late 1990s was common knowledge in the population at large and the medical profession and the risk of blood product transmission was also the subject of much discussion between colleagues and within UKHCDO.

30. **Advisory structures**

Discussions took place between colleagues and, in my case, the main source of support was the Haemophilia Centre at the Royal Free Hospital. I tried to align myself with their policies because the Centre at The Royal Free was a "Reference Centre" and I liked and trusted their approach.

There was a Haemophilia Working Party of the North East Thames Regional Association of Haematologists and the Inquiry has provided me with some of the minutes of meetings. Sometimes joint meetings were held with the North West Thames equivalent committee.

UKHCDO provided national coordination of information and advice.

31. **Relative risk**

In 1983 -1985 I became aware that all patients treated with large pool concentrates of any origin would inevitably develop NANBH, whose nature and prognosis was unknown.

It was clear by the end of 1984 that the risk of HIV infection was substantially greater from commercial as opposed to UK sourced plasma concentrate. However, it is now known that, by 1985, HIV had entered the British donor pool and HIV infection did occur as a result of administration of UK sourced products.

At the end of the 1990s it was perceived that the potential risk of nvCJD transmission was far greater from the use of NHS derived products when compared to commercial products. This was because nvCJD was a largely (but not exclusively) British disease. The switch from British to USA sourced plasma was the result but eventually a "recombinant for all" policy was introduced, as recombinant products became available and especially when the recombinant products themselves were produced without the use of human or animal products in their preparation.

32. **Decisions and Actions**

See my answers to questions on product choice.

I also advised patients affected by HIV infection to prevent onward transmission of infection. It is possible that copies of this advice are still available at the Haemophilia Centre.

Hepatitis

33. **Knowledge and understanding of hepatitis**

(See detailed answer to q 29.)

34. **Enquiries and/or investigations**

I undertook two small studies of administration of cryoprecipitate and an early NHS heat-treated product, both of which were published and the results were satisfactory, in that the patients were spared viral infection in both cases. Both studies were performed in the context of everyday clinical practice and patients were given the treatment that was appropriate to their condition. The patients were de-identified in the reports and they (or their next of kin) gave informed consent to their treatment and then consented to follow-up blood testing.

Neither small study made a significant contribution to the literature because:

1) cryoprecipitate was potentially infectious and became redundant when viral inactivation was successful after 1985-88.

2) viral inactivation techniques progressed rapidly after 1985.

The Inquiry has provided copies of these publications. (PRSE0003838 and PRSE0000608).

I was a participant in the UKHCDO study which confirmed the safety of the NHS heat-treated intermediate purity "8Y" product and was published in1988.

35. **Actions**

See previous answers to questions on product choice and efforts to prevent onward transmission of HIV infection.

36. **Understanding**

I believe that the quotes given in the questions addressed to me are a fair representation of my views at the time. It was certainly the case that haemophilia treaters hoped, but were not confident, that NANBH would not represent serious problems for people with haemophilia.

In March 1982 I spoke at a Group Seminar of The Haemophilia Society and the text of my talk was published by the Society in February of 1983. In my talk I referred to the risk of acute hepatitis and also said and wrote: "There is growing evidence that mild inflammation of the liver can continue after clinical recovery and the long-term consequences of this are not yet clear."

Early scientific evidence of the potential for serious consequences of NANBH came from the 1985 study by Dr Charles Hay in Sheffield but it would still be some years before the true severity of the condition became clear, since it often took more than 20 years for chronic liver pathology to be revealed.

37. **Lindsay Tribunal**

My own experience of severe liver disease due to NANBH alone has been modest because I looked after 80 people with HCV infection, of whom 40 were coinfected with HIV. (I cared for one patient with severe haemophilia A and HIV infection who was not HCV positive. He was a refugee who had never been treated with a large pool concentrate and he could have been infected by blood transfusion or through sexual activity in his country of origin).

Most of the liver-related illness I saw before my retirement from clinical practice was indeed combined with HIV infection and there were a number of patients under my care in this category who consumed alcohol, sometimes excessively.

It is widely acknowledged that both HIV infection and alcohol consumption are associated with an accelerated course of HCV related liver disease.

I believe that I saw fewer than 5 patients with significant chronic clinically apparent liver disease who were anti HCV positive and anti-HIV negative.

I retired from clinical practice over 10 years ago and, given what is now known about the natural history of HCV infection, I would expect patients without HIV infection and who had not consumed alcohol, to develop clinical liver disease after an interval of 20 or more years.

HIV and AIDS

38. and 39. **Knowledge and understanding of HIV/AIDS**

I first became aware of cases of groups of men with unexplained, previously unknown, immune suppression in the United States through my reading of the medical literature and, in particular The Lancet, The New England Journal of Medicine and the British Medical Journal, probably by the end of 1982. The condition of Acquired Immunodeficiency Syndrome (AIDS) was then defined. At all times I kept up with the medical literature on the subject and these journals were also the main source of my knowledge concerning blood and blood product viral transmission.

I also received regular briefing from UKHCDO and had discussions with my colleagues, especially with Dr Peter Kernoff and his team at The Royal Free Hospital.

Over time it became apparent that AIDS was probably related to a virus infection and HIV (HTLV III) was discovered during 1983/84.

It is now clear that, by 1984/85 HIV had also entered the British donor pool and we later became aware that some patients became HIV positive and developed AIDS from British sourced products.

Early heat-treated concentrates had failed to prevent HCV infection and it later became apparent that some early heat-treated factor concentrates were capable of transmitting HIV infection, (probably because of heavy contamination and inadequate viral inactivation), until 1986/87. The

first published evidence of the development of a widely available NHS sourced heat-treated concentrate (8Y) was published in The Lancet in 1988.

40. **Enquiries, investigations**

I do not recall any specific enquiries or investigations that were carried out at my Centre in respect of the risks of transmission of HIV or AIDS, other than the tests that were performed for patients and their partners from time to time over the years. I remember that I discussed the limited information available with Dr Peter Kernoff at The Royal Free Hospital in the early days of the risk appreciation.

41. and 42. **Actions and use of concentrates**

I have outlined above the policy of concentrate allocation that I adopted at this time.

The following information is given on the basis of my personal memory and my statements made in the past.

I followed UKHCDO guidance on selection of blood products but neither UKHCDO nor the Haemophilia Society recommended the withdrawal of commercial concentrates in 1984.

During 1984 I aimed to use DDAVP and tranexamic acid, where appropriate. I used cryoprecipitate for very small children, NHS concentrate, (where available) for the home treatment programme and for minor events in selected patients and commercial concentrate for major problems and surgery.

At the end of 1984 evidence began to be presented on the value of viral inactivation by heat treatment of concentrate and the dilemma of what to use became even more difficult to address. The choice of concentrate, where required, then lay between the use of unheated NHS concentrate (in the hope that it was "HIV safe") and heated commercial concentrate. There was already some evidence that heat treatment was not fully effective in the prevention of NANBH and I suspected that this might also apply to the prevention of HIV infection. In the event it became apparent that HIV had already entered the NHS donor pool and that early heat-treated commercial concentrates were capable of transmitting HIV infection, probably because of the viral load and because of inadequate heating. In summary no concentrate was safe from the risk of either NANBH or HIV infection and there was no safe choice to make.

It was not until the evidence provided by the "8Y" study of heat-treated intermediate purity NHS concentrate was published in 1988 that any assurance of safe concentrates could be given. Even this concentrate was later to be regarded as a risk for nvCJD infection, when it was decided to switch to American plasma as a source of prion free donations.

43. **Risk of AIDS during 1983**

I have no recollection of any specific policy decision made by me during 1983, other than those already referred to.

Please see answers to 42 regarding DDAVP.

I have no recollection of any generic information given to patients during this period.

I do recall having discussions with individual patients, particularly before surgery. I believe I would have said that a condition of reduced immunity, causing pneumonia which could be fatal, had been described in the USA and had been called Acquired Immune Deficiency Syndrome (AIDS). I would have said that its cause was uncertain but that some people with haemophilia had been affected. I would have said that the nature and size of the problem was not yet clear but that the national policy (UKHCDO and the Haemophilia Society) was not to cease the use of

commercial concentrates. A record of a discussion may be found in the notes of any patient(s) whose records have not been destroyed.

We continued to use unheated commercial concentrates up to the point when heated commercial concentrates became available, but these were also unsafe until donor selection and the technology of viral inactivation improved.

In 1985 small quantities of heat-treated NHS concentrates became available for special situations and I published a short paper on the use of one of them.

Response to risk

44. **Information and education**

I have no recollection of any generic information given to patients or the public during this period. There were discussions with individual patients in routine clinical consultations and I would have aimed to record these in the clinical notes.

In March 1982 I spoke at a Group Seminar of The Haemophilia Society and the text of my talk was published in by the Society in February of 1983. In my talk I referred to the risk of acute hepatitis and also said and wrote: "There is growing evidence that mild inflammation of the liver can continue after clinical recovery and the long- term consequences of this are not yet clear." This article was written before the risk of AIDS became apparent.

45. **Cryoprecipitate**

I had continued to use cryoprecipitate for small children, where appropriate and possible, throughout this period. Cryoprecipitate use was not appropriate for most patients for reasons explained above (volume of product required, risk of allergy, difficulty with dosage calculation and serious difficulties in preparation).

I do not believe that reversion to cryoprecipitate for all patients in all circumstances was ever a realistic choice and, had it been possible, it would have been associated with a significant NANBH risk because the UK donor prevalence of HCV was probably about 0.3% at that time.

Each case was decided on its own merits but, as explained elsewhere, DDAVP was not an option for most forms of surgery, (because of the uncertain and probably inadequate response, with a declining effect with frequent injections [tachyphylaxis] and the risk of concealed haematoma formation under a closed wound). Cryoprecipitate was attractive for minor bleeds in very small children, simple minor surgery and minor bleeding in people not suitable for DDAVP, especially in mild to moderate haemophilia, where some "intrinsic" factor VIII was present.

The awareness in 1983/1985 of the universality of NANBH infection from large-pool concentrates coincided with AIDS awareness, so that period was especially important in this context, until reliable virally inactivated concentrates became available.

I recall that one of my patients with severe VWD (and therefore not suitable for DDAVP) was taken through five pregnancies and deliveries using cryoprecipitate (and later, perhaps, safe concentrate) without developing HIV or NANBH (HCV) infection. This explains the publication of my small paper on this topic, although by the time of publication, cryoprecipitate use had been superseded by heat treated concentrate (since cryoprecipitate cannot be virally inactivated and is therefore capable of causing NANBH [hepatitis C infection]).

46. **Use of heat-treated concentrates**

I have no recollection of exactly when I began to use heat-treated factor products, but I was in regular contact with Dr Kernoff at The Royal Free Hospital and I received information from UKHCDO.

a) I tried to use the most appropriate concentrate available to me. An early NHS heat-treated concentrate was made available in special circumstances through Dr Smith at Oxford and the subsequent publication illustrates my approach. (PRSE0006059 and PRSE0000608)

b) I have already referred to my concern that early heat-treated commercial concentrates would not be "HIV or NANBH safe" and I was right. I hoped that the UK donor pool would not be affected by HIV, but I was wrong, as demonstrated by my own experience and the experience in Scotland. I have already stated that in the period 1984/5 and really until 1988, there was no demonstrably safe factor concentrate available.

c) Factor IX concentrates were NHS sourced because the UK was self-sufficient in factor IX. It was my view that unheated NHS factor IX concentrate was probably safer than heat-treated commercial factor IX. The reason for this was that I lacked confidence in the viral safety of American sourced, heat-treated concentrate and I understood the concern over the potential increased thrombogenicity of a heated factor IX concentrate that had been potentially denatured by heat. (I believe, however, that I did use some heat-treated factor IX shortly before the virally safe NHS "9A" concentrate was introduced). The end result was that one of my patients with haemophilia B was infected with HIV but I do not know if there is any certainty as to whether this was the result of using NHS unheated factor IX concentrate or a commercial heat-treated concentrate.

47. **Availability of heat-treated concentrates**

I do not have a view on when heat treated concentrates might have been introduced because I have never been an expert in this field.

Any suggestion that "heat-treated concentrate" can be used as a generic term is fundamentally flawed. The safety of a blood product depends on the quality and size of the donor pool, the fractionation process and the methodology of heat treatment or other viral inactivation process.

In the Haemophilia Society talk given in March 1982 and published in February 1983 I wrote "There are plans to produce a low hepatitis risk commercial factor IX concentrate and research on this type of concentrate is also taking place within the NHS". I pointed out that viral inactivation would reduce the "yield" of factor per donation and that "it may also be difficult for manufacturers to substantiate the claim that a given concentrate is free from hepatitis risk". I believe that this statement was entirely correct and I have already referred to the fact that early heat-treated commercial concentrates were capable of transmitting both NANBH and HIV.

48. and 49. **Decisions and Actions**

I profoundly regret that patients under my care were infected with HIV at this time.

My decisions and actions were made in good faith, at a time of great uncertainty, as the effect of two unknown viruses emerged and discussions among experts about how best to tackle the problems took place. I tried to develop and implement an appropriate policy and the result was that some patients were infected by HIV with commercial concentrate and some with NHS concentrate. I am not aware that anyone under my care was infected with a heat-treated concentrate but there were infections from heat-treated concentrates that took place in Birmingham UK and in Canada.

In retrospect it would have been appropriate to defer elective surgery in 1984/5 and beyond, but at the time it was unknown and unknowable when a safe concentrate might become available. I did communicate what I knew of the potential risks and uncertainties to my patients before proceeding with surgery, but, at the time the nature and prognosis of AIDS, especially in the context of haemophilia was still uncertain.

In fact, it was not until the publication of the "8Y" study in 1988 that I believe that there was real evidence of product safety, so that elective surgery could proceed with some confidence. Even then publications, appropriately, spoke of relative rather than absolute safety and that reservation was amply justified by the nvCJD crisis which followed in the late 1990s.

50. **Other clinicians or organisations**

I am not surprised that the government was not able to make the UK self-sufficient in factor VIII concentrate according to the promises made in the mid-1970s. The demand and use of concentrates increased exponentially and it is hard to believe that the UK could ever have caught up. Had self-sufficiency in factor VIII concentrate production been achieved the number of patients infected with NANBH (HCV) would have been unchanged but the incidence of HIV infection would have been reduced.

The fact that hepatitis and HIV infection from infected blood products occurred in the USA and Canada, throughout Western Europe, Australia, New Zealand and Japan shows that this was not a wholly avoidable disaster, as has been suggested, even by our own government.

There has been much discussion concerning the decision of UKHCDO (and The Haemophilia Society) not to recommend the withdrawal of commercial concentrates in 1983. Had the government taken this action, there would have been a profound effect on the quality of haemophilia care and it is possible that some patients would have died or been disabled for lack of treatment. In hindsight, there can be no doubt that the number of patients infected with HIV would have been reduced by withdrawal of commercial products in 1983, but HIV infections would still have occurred from the use of infected NHS concentrates.

It is not my place to criticise decisions made by senior government officials, physicians and patient representatives at a very difficult time and based on very limited information.

51. **Inactivation of blood products prior to 1980 (see q 50)**

I was not involved in developments in and decisions on the processing of blood products before 1980 and am not therefore in a position to comment.

SECTION 5: TREATMENT OF PATIENTS AT THE CENTRE

52. **Information on risk of infection for patients (see qs 18,32,43 and 44)**

The risks of infection in consequence of treatment with blood products prior to such treatment commencing were discussed with patients with bleeding orders in the clinic. I have no recollection of formal or written information provided for patients until HIV infection was identified in 1984/85 when I issued a leaflet to those affected.

I cannot recall the exact contents of the leaflet, but it contained information on home treatment matters, such as waste disposal, personal hygiene and behavioural issues.

For surgical procedures, especially in times of shortage of product in 1983/4, it was necessary to use commercial product in order to maintain the use of NHS product for regularly treated patients, especially those on the home treatment programme.

This meant that some very difficult choices had to be made in discussion with the patient, and I referred to this difficulty in my evidence to the Archer Inquiry.

53. **Alternatives**

Where the use of DDAVP and tranexamic acid was appropriate I would discuss this and advise the patient of my recommended treatment.

In the period before the HIV crisis I do not recall discussing choice of products in a formal way with patients.

I recall discussions with individual patients at the time of elective surgery as the AIDS crisis developed and such conversations may have been recorded in the clinical notes.

At the time of the developing concern over the possibility of nvCJD transmission at the end of 1990s I had many discussions on product choice and availability, especially with parents of children with haemophilia. Very difficult discussions on product choice followed the withdrawal of recombinant concentrate by one manufacturer shortly after the introduction of recombinant concentrate at The Royal London, because some patients had to go back to plasma derived concentrates at that time.

Until the Infected Blood Inquiry, I was not aware of any complaints or dissatisfaction with the content or quality of information given to my patients during the 30 years of my Directorship.

54. **Home treatment**

I wrote a leaflet for home treatment patients, explaining the Centre's policy but at over 40 years distance from start of the home treatment programme I can make no further comment, unless copies of leaflets have been retained at the Centre.

My specialist nurses, working in the hospital and the community, taught and assisted patients and their relatives in venepuncture technique, how to make up the products safely, how to dispose of waste and how to document and communicate details of treatment back to the Centre.

HIV

55. **HIV Discussions**

I have no precise recollection of when I began to discuss the AIDS crisis with patients, but this would have been during 1982/84. I would have passed on the knowledge available at the time and explained to them that some people in the USA had developed a failure of immunity which caused severe pneumonia and could be fatal. I would have pointed out that the condition was associated, at that time, with the homosexual and drug using communities. I would have said that AIDS was probably due to an infection and that there was concern that patients suffering from the condition might have given blood and contributed to the American donor plasma pool.

Once cases of AIDS had begun to occur in people with haemophilia in 1982, I would have explained that there was a perceived risk for patients in the UK treated with these products but that there were many uncertainties.

56. **Knowledge of infection with HIV**

As soon as a laboratory test (anti HTLVIII, later anti-HIV) became available in 1984, I contacted Professor Leslie Collier, consultant virologist, (deceased), and I tried to identify patients who I believed might have been at risk of infection. Many serum samples had been saved in the virology department at The London Hospital. (I believe that this retention was automatic at the time and I was not involved in the decision on retention of samples by that department. The retention policy may have been designed so that a look-back would be possible in general, but especially for

NANBH. I recall that Professor Arie Zuckerman of University College London was also particularly interested in the search for the virus assumed to be the cause of NANBH).

Serum samples of patients under my care were then tested retrospectively in the virology department using a UK prepared method under the supervision of Professor Collier. Early tests were unreliable and I believe that Professor Collier also consulted Dr Richard Tedder at University College.

(As testing became available there was an emerging discussion, which stimulated a considerable divergence of medical and medico legal opinion, as to whether further consent for anti-HIV testing was needed. In the past it had always been assumed that a doctor had implied consent for all diagnostic blood tests when a blood sample had been taken. This was particularly the case for haematologists, who as clinical pathologists, have responsibilities in both the clinic and the laboratory. The initial consent to test a sample of blood is given to investigate what is wrong, rather than to perform a specific set of analyses. The results of initial tests performed as a result of a clinical consultation would, throughout my career, have been used by me to enable further tests to be chosen in order to reach a diagnosis and appropriate treatment, without each specific investigation being formally consented.

The debate, which culminated in the GMC guidance of 1988 [see Penrose Inquiry Report Chapter 32.29] was over whether an HIV test was not a "Standard" blood test, so that the implied consent for more general tests, like a full blood count, did not apply and specific consent was therefore required. The anti-HIV antibody tests on my patients, to identify those infected, were carried out between 1984-1985 and before the GMC guidance of 1988 and therefore, in accordance with usual practice at the time. The GMC guidance of 1988 was specific to HIV infection and was the first time, to my knowledge, that a blood test for a specific infection required specific consent. Following the GMC guidance, the practice changed and specific consent was obtained for any new anti-HIV testing, while the monitoring of identified patients continued.)

57. **Pre-test counselling**

As explained in the answer to question 56 above, testing was undertaken retrospectively on existing serum as soon as laboratory tests became available and without specific consent, as this was considered appropriate at that time and before the GMC guidelines were published. As a result, no pre-test counselling was offered. The priority was to find out what was happening to the patients in order better to care for them in a situation where there were so many unknowns.

58. **Communication**

To the best of my knowledge I personally told each affected patient individually of their HIV status in a personal interview. This was my policy and practice. In many cases a member of the nursing staff would have been present.

I do not believe that telephone communication or written correspondence was used for this purpose.

There was a reluctance to use written communications because of the sensitivity of the information. The comprehensive care that the Centre offered meant that many of my patients never visited their GP. Many patients saw their haemophilia centre as their "first port of call" and did not want their general practitioner (GP) to know about their HIV status. This created some difficulty in communication with the GPs and the lack of patient consent created a dilemma. On the one hand, it might be thought that GPs had a right to know what was happening to their patients, but in the absence of consent from patients, it may well be that some, or indeed many,

GPs were not made aware of patient HIV status. I do not believe that a clear solution was found to this problem or that it was possible to find one.

59. **Whether or not to inform**

As soon as I believed that I had reliable data I personally informed my patients of their status, whether positive or negative. It never occurred to me, or any of my colleagues when I spoke to them, that information should be withheld. Before the Infected Blood Inquiry, I received no complaint, oral or written from any patient concerning the nature or quality of the information I gave them.

60. **A positive test result**

Patients who tested positive were informed about HTLV III (HIV) as we understood it at the time, in a series of interviews with me and my nursing staff. I prepared a leaflet of advice and, I set up an HIV clinic at the end of my routine clinic, which was also attended by my nursing staff and a social worker. When more effective treatment became available this clinic transferred to the Graham Hayton Unit at the hospital, where expertise in the management of HIV infection was provided.

I did not tell any patient to keep their "infection a secret", although they may have chosen to do so.

61. and 62. **Partners (see q 77)**

The matter of the provision of testing for partners or family members who might be at risk was discussed with patients and their partners, although I do not recall what the precise policy was. Many partners were tested over the years and I believe that the subject was covered in the advice leaflet. I do not recall the exact advice given before testing partners, other than that the situation and risks would have been explained and the result communicated personally in some way.

Sadly, I know that the wife of one of my patients was infected with HIV.

I am not aware of any other infection of the partners or family members of patients who were under my care.

63. **Patients at The London Hospital Haemophilia Centre infected with HIV**

As of September 1987 (source personal educational lecture series)

a) Severe haemophilia 31

b) Moderate/mild haemophilia A 9 (the lecture only identifies "mild")

c) Haemophilia B 1

d) Von Willebrand disease 0

e) Children (all haemophilia A)

For the statistics related to moderate and mild haemophilia and for children I would require access to the names, factor VIII levels and dates of birth of all HIV positive patients, together with an Inquiry definition of the criteria for "children".

It is important to appreciate that not all these patients were infected at The London Hospital and in some cases the site of infection cannot be determined. There was significant movement between centres throughout the period covered by the Inquiry and there were many reasons for this.

At least one of the "mild" patients was infected by NHS concentrate and the precise date of infection is known because he suffered the glandular fever like illness associated with acute HIV

infection shortly after treatment. Some moderately or mildly affected patients were infected because of treatment for trauma and/or necessary surgery and/or the presence of factor VIII inhibitors.

64. **Time scale of infection**

The timing of infection was studied using stored serum samples. The result was that it was possible to determine the probable location and even date of infection fairly accurately in a number of patients.

Understandably, patients often wanted to know the site and date of their infection but, given the significant movement between centres throughout the period covered by the Inquiry (see q 63) many of them could have been infected at any centre they had attended. The important thing was that patients be given expert care at whichever Centre they attended at any time.

Hepatitis B

65., 66. and 67. **Information**

Very few patients were infected with hepatitis B during my time at The London, but many showed evidence of previous infection. I do not have and do not think that I could easily obtain an accurate figure. All patients treated with blood products were studied for evidence of active or previous hepatitis B infection. (This approach was partly to assess eligibility for hepatitis B immunisation).

Patients infected with hepatitis B were included in the regular haemophilia follow up programme with referral to a hepatologist, when appropriate.

The majority of patients were informed that they had had hepatitis B infection in the past, presumably due to exposure to blood products. Further discussion was rarely necessary because most patients had cleared their infection. I recall two patients with evidence of continuing infection, both of whom were anti-HIV and anti-HCV positive and their hepatitis B clinical care was included in their overall management.

NANBH /Hepatitis C

68. and 69. **Significance of NANBH infection**

During the period before HCV diagnosis some patients had acute NANBH and all recovered clinically. Many had continuing abnormalities of liver function and were made aware of this fact but no other action was taken because the cause, nature and prognosis of their condition was unknown. I was opposed to the use of hepatic biopsy in these patients, who were clinically well, because of the danger of abnormal and potentially fatal bleeding as a result of the invasive investigation.

70. **Method of communication of HCV infection**

As soon as a diagnostic test for HCV, through the anti-HCV test, became available in 1989/90, stored serum samples were analysed in the virology department. My nursing staff have told me that they recall cases where consent was sought but I have no record of any pre-testing consent process. Patients were informed of their results in person by me, face to face, as soon as reliable results were reported. It is possible that letters on this topic were written but I believe that no infected patient under my care at the time received only written correspondence. HCV PCR testing for viral activity was added, together with more sophisticated measures of assessing liver condition (such as the alpha fetoprotein test), as knowledge developed. Liver biopsy was rarely performed.

71. **Information about HCV infection**

The cause, nature, treatment and prognosis of HCV infection was explained to patients, again as knowledge developed and eventually a clinic was started, within the routine haematology clinic, at which a hepatologist was present. Appropriate warnings were given on the dangers of alcohol consumption, when this knowledge became available.

When interferon became available, its use was explained to patients and I joined Dr Paul Telfer at The Royal Free Hospital in a clinical study of use of the drug and this resulted in a publication. Unfortunately, the result of using interferon was disappointing.

As more effective treatments became available these were used for selected patients, but the regimen was very demanding for patients and results were still not satisfactory, although some patients cleared the virus.

Since my retirement, treatment for HCV infection has improved dramatically and many patients are now believed to have been cured.

72. **Testing for HCV infection (see q.83)**

Testing for anti-HCV began as soon as reliable tests became available in1989/90 and HCV PCR was used to assess viral activity following its development in the mid-1990s. Testing then continued, especially for monitoring the effects of treatment, until my retirement in 2007/2009.

73. **Information sheet**

I do not recall whether the information sheet [BART0002065] quoted in the question was the first that I issued.

74. **Tracing of patients for HCV testing**

I have no recollection of what steps were taken to trace patients who had previously received blood products at the Haemophilia Centre. The Centre itself may have some information on tracing of patients.

75. **Number of patients**

I believe that approximately 84 patients were found to be anti-HCV positive at The London Hospital Haemophilia Centre.

Reference to my lectures shows that I recorded that the distribution of anti HCV patients was as follows.

Haemophilia A	62
Haemophilia B	17
Von Willebrand disease	3
Haemophilia carriers	2

Delay/public health/other information

76. **Delays**

Patients were informed promptly of the results of their blood tests as soon as they were confirmed (see qs 70, 71, 81).

77. **Public Health**

I am not clear what this question means.

All patients treating themselves were given advice on used needle safety precautions and basic hygiene relating to injection technique and material disposal.

The possibility of sexual transmission of HIV infection was certainly emphasised as was the need for anti-HIV positive patients to take care with social hygiene (for example having separate towels and toothbrushes).

In the case of HCV infection, it was perceived that the likelihood of onward transmission was low. The advice sheet I prepared in March 1995 [BART0002065] stated "Dr Colvin will have mentioned the low risk of sexual transmission of the virus to any partner. He will have reassured you that ordinary everyday household contact will not transmit the virus so your family do not need to worry".

78. **Other infections**

Patients with HIV infection were made aware of the risk of "other" infections, such as pneumocystis pneumonia and oral candidiasis, which formed a part of the AIDS complex, and were checked for such conditions as cytomegalovirus infection.

79. **Infecting others**

See answer to question 77.

A single tragic case of HIV infection occurred in the wife of a patient with HIV infection before 1987.

To the best of my knowledge and belief no other onward infection of any transmissible agent occurred in my patients during my time as Director of the Haemophilia Centre.

Consent

80. **Sampling**

Samples were taken for routine haematology and liver function tests at most clinic attendances, mostly at three to six-month intervals, but sometimes more frequently. Further tests relating to the monitoring of HIV and HCV infection were taken, as indicated.

Patients were told, and I believe understood, the reasons for testing. Further and more specific explanations were given if patients had queries or if more information was needed clinically.

No explicit consent was given to the storing of samples, which I believe was automatic in the case of the Department of Virology.

81. **Consent to treatment (see also qs 70 and 71)**

All patients attending hospital were given a clear explanation of their condition (haemophilia A or B or vWD) and the treatment available (with factor concentrates or other blood products) and necessary to correct the factor VIII or IX which was missing in their blood. Patients would therefore have been clear as to and consented to the treatment they were receiving. Patients were also given the opportunity to question me or my senior colleagues, either in the clinic or at the time of treatment. As I was on call all the time, it was always possible for any questions to be referred to me. In all the circumstances, no written consent form was used or thought necessary at the time.

When patients attended needing treatment for a bleed, which could be day or night, they were given the specified treatment which they were used to. Nursing staff and/or junior medical staff knew from experience or from the "red envelope" system, which treatment a particular patient was used to receiving. Staff were instructed to remember the importance of using the correct

treatment, including the value of using a single batch number of a product for a particular episode, where this was possible, but it cannot be certain that every patient was always given the treatment of choice on each occasion.

Patients or relatives who administered the treatment themselves on the home treatment programme were using treatment that was familiar to them.

"Express" consent was, of course, taken before surgery.

I believe that my policy of providing and administering treatment was the same as that provided by other haemophilia centres.

82. **Consent in 1996 [BART0000555 001-5]**

The correspondence referenced concerned work which I started as Chairman of UKHCDO with Dr Marcela Contreras, Chairman Transfusion Medicine Sub-Committee and concerned National and not Local policy.

In making any change to the policy on consent for blood product administration in the context of haemophilia practice, it was necessary for the authorities responsible for all blood transfusion nationally to be involved, because written consent had never been required for the administration of blood or blood products in the UK. The correspondence demonstrates how difficult it was to reach agreement on a national policy in haemophilia practice, which was also compatible with the policy for blood transfusion as a whole.

The result of these discussions was inconclusive, but my personal view is recorded in a letter to Dr Elizabeth Mayne, dated 4th March 1996, stating that "written consent is appropriate, at least for first use of blood products or for change of a type of blood product".

I left office as Chairman of UKHCDO in 1996 and do not remember what then happened to the proposals, (which had met with widespread national opposition at UKHCDO's Annual General Meeting, probably in September 1995).

I do not recall if and/or when any formal consent process for treatment was introduced at The Royal London Hospital. This might be recorded at the Haemophilia Centre.

83. **Testing for HIV and hepatitis (qs 70 and 71)**

As explained above (question 56-60), patients under my care were tested for anti HIV and anti HCV antibodies from stored samples as reliable tests became available. Patients had consented to samples being taken for monitoring purposes at each clinic visit, often at three monthly intervals.

Anti HTLVIII (anti-HIV) testing would have been completed on existing patients by the middle of 1985 and results would have been given and explained to them. There were no further seroconversions after 1985, although testing was performed if requested by patients, with their specific consent. Some patients were referred to me with their known results and monitoring would then continue.

As referred to above, it was only in 1988 that clear advice on anti-HIV testing consent was issued by the GMC. (See Penrose Inquiry Report Chapter 32.29).

After 1985, clinical progress was monitored by tests of CD4 lymphocyte counts and HIV viral load as they became available. The results of these tests were an essential part of consented care and were discussed extensively with patients, especially as specific treatment with drugs such as zidovudine (AZT) was introduced.

Hepatitis C was identified and anti-HCV antibody testing became available in 1989/90, at a time when awareness of chronic abnormality of liver function tests in people with haemophilia was already well established. I had already explained the problem of NANBH to patients, but information was still limited. The availability of a specific test for a newly identified virus was an extension of existing knowledge. I do not believe that it was perceived by haemophilia treaters that new express consent was required to gain further insight into an established but poorly understood condition. When HCV PCR virus testing became available in the mid-1990s, this test was used to clarify which patients (about 10%) had fully recovered from infection and eventually to monitor progress as drugs became available. This monitoring was also undertaken with patient consent.

I believe that initial HIV and HCV antibody testing to identify those infected and subsequent monitoring were standard practice in the haemophilia treating community at the time, as we strove to understand and react to the unfolding information on the evolving problem of blood borne infection. As soon as reliable results were available, I explained to patients what I thought the answers meant and we planned a way forward together. At the time no patient questioned the propriety of what had been done or implied that additional consent to the original consent to blood testing should have been obtained.

PUPS

84. **Meaning and decisions and actions related to "PUPS"**

I was involved in treating some patients who had previously not been given blood products (or, in some circumstances, who had been given very little previous blood product treatment), as part of the common effort to evaluate new and safer products. Studies of this kind are essential to confirm product safety and are very much in the interests of the haemophilia community.

The Inquiry has asked me about PRSE 0003838 (cryoprecipitate) and PRSE 0000608 (early heat-treated factor VIII) but these were not "PUP" studies. On the contrary they were my attempt to provide published clinical data as I strove to provide my patients with what I saw as the most appropriate and safest treatment available for them.

The only study of untreated patients in which I was involved was the 8Y study and even here some patients had received small amounts of treatment in the past.

85. **Use of term PUP (see also q 84)**

It is extremely common for doctors, healthcare professionals (and the media) to use this type of abbreviation and examples are "COPD" for "Chronic Obstructive Pulmonary Disease" or "SOB" for "Shortness Of Breath" The term "PWH" to signify "Person (or People) With Haemophilia" has been widely used (by the Haemophilia Society and by myself) to avoid the less satisfactory term "Haemophiliac". The point of this is to avoid the "depersonalisation" of people with haemophilia. It should also be pointed out that the abbreviation "PUP" replaced an earlier commonly used term, "virgin patient", which was thought to be inappropriate.

I may well have used the term "PUP" because it is an abbreviation for a scientific category. Like my professional colleagues, I would have used it mainly in professional discussion and correspondence.

I have not heard the term criticised or challenged before the Infected Blood Inquiry began its work.

86. **Use of NHS "8Y" factor VIII concentrate**

By 1987 it had become clear to the investigators that 8Y was as safe a product as was available anywhere, although publication was in 1988. 8Y was an intermediate purity heat-treated factor VIII concentrate but it was produced by the NHS and it may even be the case that it was less likely than high purity products to induce inhibitor development. 8Y was the best NHS product available at the time. I believe that I used it for my new patients, but I do not recall if 8Y was used for **all** new patients.

8Y was eventually superseded by high purity products produced within the NHS and commercially and then by commercial recombinant products, first those which contained human albumen and then those made without the presence of human or animal proteins.

Research

87. **Research studies**

See the attached curriculum vitae for the list of my publications. I have italicised below those papers which might be considered to be research orientated towards haemophilia and allied disorders with explanatory comments as requested. I cannot estimate the number of patients involved.

For each publication there is a brief commentary which covers the purpose of the work and any involvement of other bodies. I am not aware of any external funding for any of these papers, (other than the work undertaken for BPL on behalf of the NHS) and I do not believe that anyone in the Haemophilia Centre at The London Hospital benefited in any way personally from any research project. I did not consider obtaining consent from patients for the publication of de-identified case reports.

PEER REVIEWED AND INVITED PAPERS

1. Colvin, Brian (1968). Criminal Liability in Mental Disorder London Hospital Gazette, LXXI No. 2, 16-20.

2. Colvin, B.T., Rogers, M. and Layton, C. (1974). Benzylpenicillin induced leucopenia. Complication of treatment of bacterial endocarditis. British Heart Journal, 36, 216-219.

3. Colvin, B.T., Lancaster-Smith, M.J., Suggett, A.J. and Fisher, D.J.H. (1975). Leukaemoid reactions associated with fulminating ulcerative colitis. Postgraduate Medical Journal, 51, 178-180.

4. Ibbotson, R.M., Colvin, B.T., and Colvin, M.P. (1975). Folic acid deficiency during Intensive Therapy. British Medical Journal, 4, 145-147 and 522 (letter).

5. Colvin, B.T., and Lloyd, M.J. (1977). Severe coagulation defect due to a dietary deficiency of vitamin K. Journal of Clinical Pathology, 30, 1147-1148.

6. *Colvin, B.T., Aston, C., Davis, G., Jenkins, G.C. and Dormandy, K.M. (1977). A regional co-ordinator for haemophilia in domiciliary practice. British Medical Journal, 2, 814-815.*

   This was a paper describing the appointment of a domiciliary nurse to the old North East Metropolitan Region (really the catchment area covered by the Royal Free and The London hospitals)

7. *Marshall, W.G. and Colvin, B.T. (1977-1978). Maxillofacial injury in severe haemophilia. British Journal of Oral Surgery, 15, 57-63.*

This was a case report of a very serious road traffic injury in a patient with severe haemophilia A.

8. *Newland A.C., Walter, P.H., Wylie, I.G. and Colvin, B.T. (1979). The diagnosis of intracranial haemorrhage in haemophilia by computerised axial tomography. Clinical and Laboratory Haematology, 1, 139-145.*

   This was a case report of an early CT scan to investigate a head injury in a patient with haemophilia.

9. Colvin, B.T., Revell, P.A., Ibbotson, R.M. and Turnbull, A.L. (1980). Necrosis of bone marrow and bone in malignant disease. Clinical Oncology, 6, 265-272.

10. Colvin, B.T. (1980). How to biopsy the marrow. British Journal of Hospital Medicine, 24, 176-178.

11. Colvin, B.T. (1980). Treatment of stroke: the role of anticoagulants. Geriatric Medicine, 10, 60-64.

12. Colvin, B.T. (1980). Systemic fibrinolytic therapy. Pharmacy Bulletin of the North East Thames Region, 8, 1-7.

13. *Slocombe, G.W., Newland, A.C., Colvin, M.P., and Colvin, B.T. (1981). The role of intensive plasma exchange in the prevention and management of haemorrhage in patients with inhibitors to factor VIII. British Journal of Haematology, 47, 577-585.*

    This was a case report in a patient with severe haemophilia A who had an appendicectomy without factor VIII cover at another hospital. He was critically ill and then developed an inhibitor to factor VIII. Plasma exchange was an unusual approach which was felt to be lifesaving in his case.

14. Shinton, N.K., Bloom, A.L., Colvin, B.T., Flute, P.T., Preston, F.E. and Kennedy, D.A. (1981). Tentative protocol for the evaluation of coagulometers based on one-stage prothrombin time. Clinical and Laboratory Haematology, 3, 71-76.

15. Norris, R.W., Colvin, B.T., Kenwright, M.G., Flynn, J.T. and Blandy, J.P. (1981). In vitro studies on optimum preparation of coagulum for surgery of renal calculi. British Journal of Urology, 53, 516-519.

16. Fitzcharles, M.A., Kirwan, J.R., Colvin, B.T., and Currey, H.L.F. (1982). Sideroblastic anaemia with iron overload presenting as an arthropathy. Annals of the Rheumatic Diseases, 41, 97-99.

17. *Colvin, B.T., Ainsworth, M., and Buckley, C. (1983). Experience with highly purified porcine factor VIII in a patient with haemophilia A and a factor VIII inhibitor. Clinical and Laboratory Haematology, 5, 55-59.*

    This was a case report of a patient with a moderate factor VIII inhibitor who responded to treatment with porcine factor VIII.

18. *Colvin, B.T. (1983). Role of plasma exchange in the management of patients with factor VIII inhibitors. La Ricerca in Clinica e in Laboratorio, XIII, 85-93.*

    This was an invited review by an Italian journal as a result of paper 13. (above).

19. *Penny, W., Colvin, B.T. and Brooks, N. (1985). Myocardial infarction with normal coronary arteries and factor XII deficiency. British Heart Journal, 53, 230-234.*

This was a case report concerning a young patient with factor XII deficiency who, very unusually for a person of her age, suffered a myocardial infarction.

20. *Colvin, B.T., Ainsworth, M., Machin, S.J., Mackie, I.J.,Smith, J.K., Winkelman, L. and Haddon, M.E. (1986). Heat treated NHS factor VIII concentrate in the United Kingdom - a preliminary study. Clinical and Laboratory Haematology, 8, 85-92.*

    This was a small clinical study which is discussed in detail at 89.b) (PRSE0000608)

21. *Colvin, B.T., Collier, L.H. and Craske, J. (1987). A prospective study of cryoprecipitate administration: absence of evidence of virus infection. Clinical and Laboratory Haematology, 9, 13-15.*

    This was a small clinical study which is discussed in detail at 89.c) (PRSE0003838)

22. *Roy, V., Tillyer, M.L., and Colvin, B.T. (1988). Acute abdominal pain due to an acquired disorder of coagulation (Lesson of the Week). British Medical Journal, 296, 1460.*

    This was a case report/review of a patient who presented with abdominal pain but was then diagnosed with an acquired deficiency of factor VIII (acquired haemophilia). The Lesson of the Week series was a way of informing the wider medical community of rare conditions requiring specialist care.

23. *Study group of the UK Haemophilia Centre Directors on surveillance of virus transmission by concentrates (1988). Effect of dry-heating for 72 hours on transmission of non-A non-B hepatitis. Lancet, ii, 814-816.*

    This was the paper which defined NHS 8Y intermediate heat-treated factor VIII as a safe product. There was no named authorship, but my patients contributed to the study, which was coordinated in Oxford. It is discussed in detail at 89.d) (BART0002340)

24. *Newland, A.C., Macey, M.G., Moffat, E.H., Ainsworth, M., and Colvin, B.T. (1988). Effect of intravenous immunoglobulin on a spontaneous inhibitor to factor VIII. Clinical and Laboratory Haematology, 10, 435-442.*

    This was a case report on a patient with acquired haemophilia who was treated with intravenous immunoglobulin.

25. *Dalrymple-Hay, M., Aitchison, R., Collins, P., Sekar, M. and Colvin, B. (1992). Hydroxyethyl starch induced acquired von Willebrand's Disease. Clinical and Laboratory Haematology, 14, 209-211.*

    This was a case report on the very rare condition, known as acquired von Willebrand disease. The phenomenon was directly due to the use of hydroxyethyl starch to treat an ENT patient.

26. *Muckenthaler, M., Gunkel, N., Levantis, P., Broadhurst, K., Goh, B., Colvin, B., Forster, G., Jackson, G.G. and Oxford, J.S. (1992). Sequence analysis of an HIV-1 isolate which displays unusually high-level AZT resistance in vitro. Journal of Medical Virology, 36, 79-83.*

    Papers 26, 27, 29, 30 and 36 were the result of cooperation between the haemophilia centre, the HIV service and the Department of Immunology at The Royal London Hospital. The work involved the analysis of saved serum samples to study the nature and course of the immunological response to HIV infection in people with haemophilia. My personal involvement was limited, and I have no memory of the details of the study work or the

process of Research Ethics Committee approval. I have no knowledge of how external funding, if any, was sought or achieved.

27. *O'Toole, C.M., Graham, S., Lowdell, M.W., Chargelegue, D., Marsden, H. and Colvin, B.T. (1992). Decline in CTL and antibody responses to HIV-1 p17 and p24 antigens in HIV-1-infected haemophiliacs irrespective of disease progression. A 5 year follow up study. AIDS Research and Human Retroviruses, 8, 1361-1368.*

    See 26.

28. Colvin, B.T., and Barrowcliffe, T.W. (1993). The British Society for Haematology Guidelines on the use and monitoring of heparin. 1992 Second Revision. Journal of Clinical Pathology, 46, 97-103.

29. *Chargelegue, D., O'Toole, C.M. and Colvin, B.T. (1993). A longitudinal study of the IgG antibody response to HIV-1 p17 gag protein in HIV-1+ patients with haemophilia: titre and avidity. Clinical and Experimental Immunology, 93, 331-336.*

    See 26.

30. *Chargelegue, D., Colvin, B.T. and O'Toole, C.M. (1993). A seven year analysis of anti-Gag (p27 and p24) antibodies in HIV-1-seropositive patients with haemophilia: immunoglobulin G titre and avidity are early predictors of clinical course. AIDS, 7, (suppl 2): S87-90.*

    See 26.

31. *Castenskiold, E.C., Colvin, B.T. and Kelsey, S.M. (1994). Acquired factor VIII inhibitor associated with chronic interferon-alpha therapy in a patient with haemophilia A. British Journal of Haematology, 87, 434-436.*

    This was a case report on a patient with acquired haemophilia who was treated with interferon-alpha.

32. *Cartwright, I.J., Hampton, K.K., Macneil, S., Colvin, B.T. and Preston, F.E. (1994). A haemorrhagic platelet disorder associated with stimulus-response coupling and abnormal membrane phospholipid composition. British Journal of Haematology, 88, 129-136.*

    This was a joint paper with colleagues in Sheffield concerning a rare platelet disorder but I have no recollection of the detail.

33. *Thomas, D.P., Lee, C.A., Colvin, B.T., Dasani, H., Dolan, G., Giangrande, P.L.F., Jones, P., Lucas, G., Cantwell, O., and Harman, C.T. (1994). Clinical experience with a highly purified factor IX concentrate in patients undergoing surgical operations. Haemophilia, 1, 17-23.*

    This was a clinical trial of a highly purified factor IX concentrate in surgery, conducted by the NHS through BPL. It would have been organised and documented with appropriate information and consent by BPL and I believe that it was fully compliant with contemporary standards.

34. *Telfer, P., Devereux, H., Colvin, B., Hayden, S., Dusheiko, G., and Lee, C., (1994). Alpha interferon for hepatitis C virus infection in haemophilic patients. Haemophilia, 1, 54-58.*

    This was a study of the use of alpha interferon in the treatment of hepatitis C infection in people with haemophilia and was organised and coordinated by Dr Paul Telfer at the Royal Free Hospital. It would have been organised and documented with appropriate information

and consent by Dr Telfer and his colleagues, including myself, and I believe that it was compliant with contemporary standards.

35. Colvin, B.T., (1995). Originating author of Management of Patients with Thrombophilia Drug and Therapeutics Bulletin, 33, 6-8.

36. *Chargelegue, D., Stanley, C.M., O'Toole, C.M., Colvin, B.T. and Steward, M.W. (1995). The Affinity of IgG antibodies to gag p24 and p17 in HIV-1 infected patients correlates with disease progression. Clinical and Experimental Immunology, 99, 175-181.*

    See 26.

37. *Colvin, B.T., Hay, C.R.M., Hill, F.G. and Preston, F.E. (1995). The incidence of factor VIII inhibitors in the United Kingdom 1990-1993). British Journal of Haematology, 89, 908-910.*

    I was first author on this review paper, which must have been based on information available to UKHCDO through the National Database. UKHCDO will have information on the source material and its regulation.

38. Colvin, B.T. (1995). Haemophilia in the UK: past, present and future, Haemophilia, 1, (suppl 2), 4-5.

39. *Cahill, M.R., Woosey, C.P., Hayden, S.M., MacLean, M. and Colvin, B.T. (1995). Implementation of a nurse practitioner policy for the requisition and administration of drugs in a haemophilia comprehensive care centre. Haemophilia, 1, 172-174.*

    In the mid-1990s I was involved with the expansion of the role of the haemophilia nurse specialist at The Royal London Hospital. This had national significance for the organisation and delivery of haemophilia care in the United Kingdom

40. *Lee, C.A., Colvin, B.T., Jones, P. and Dolan, G. (1995). Clinical experience with a purified factor IX concentrate (Replenine) Haemophilia, 1, (Suppl 3) 28-31.*

    This was a clinical trial of "Replenine" factor IX concentrate, conducted by the NHS through BPL. It would have been organised and documented with appropriate information and consent by BPL and I believe that it was fully compliant with contemporary standards.

41. Cavenagh, J.D., and Colvin, B.T. (1995). Guidelines for the management of thrombophilia. Postgraduate Medical Journal. 72, 87-94.

42. Perry, D.J., Daly, M.E., Colvin, B.T., Brown, K. and Carrell, R.W. (1995). Two antithrombin mutations in a compound heterozygote: MET20Thr and Tyr166Cys. American Journal of Haematology, 50, 215-216.

43. Hay, C.R.M., Colvin, B.T., Ludlam, C.A., Hill, F.G.H. and Preston, F.E. (1996). Recommendations for the treatment of factor VIII inhibitors: from the UK Haemophilia Centre Directors Organisation Inhibitor Working Party. Blood Coagulation and Fibrinolysis, 7, 134-138.

44. Colvin B.T. (1996). So you want to train in haematology. British Journal of Hospital Medicine, 56, 283-284.

45. *Hay, C.R.M., Ollier, W., Pepper L., Cumming, A., Keeney, S., Goodeve, A.C., Colvin, B.T., Hill, F.G.H., Preston, F.E., and Peake, I.R., (1997). H.L.A. Class II profile: A weak determinant of factor VIII inhibitor development in severe haemophilia A. Thrombosis and Haemostasis, 77 (2), 234-237.*

This study was designed and published by Dr Charles Hay. My memory is that it was achieved through analysis of the UKHCDO database. I contributed information about one or more of my patients. Dr Hay will know whether any consent or information process was undertaken.

46. Cahill, M.R., and Colvin, B.T. (1997). Classic diseases revisited. Haemophilia. Postgraduate Medical Journal, 73, 201-206.

47. *Tagliavacca, L., Rowley, G., Green, P.M., Hayden, S., Woosey, C., Colvin, B., and Giannelli, F. (1997). Analysis of the haemophilia A mutation in sporadic patients registered at The Royal London Hospital and their families. Haemophilia, 3, 177-182.*

    This study was organised by Dr Francesco Giannelli at Guy's Hospital on data provided by my patients and their relatives at The Royal London Hospital. I am certain that the participants were fully informed of the nature and results of the work, which provided important information about the probable origin of sporadic heritable haemophilia A. I know that a proper consent process was undertaken and the families of my patients were informed of the results.

48. Cahill, M.R., and Colvin, B.T. (1997). Current practice in the treatment of haemophilia. Hematology, 2, 351-358.

49. Colvin, B.T. (1998). Management of disseminated intravascular coagulation.

    British Journal of Haematology, 101, Supplement 1. 15-17.

50. *Hay, C.R.M., Ludlam, C.A., Colvin, B.T., Hill, F.G.H., Preston, F.E. et al (1998). Factor VIII inhibitors in mild and moderate-severity haemophilia A. Thrombosis and Haemostasis, 79, 762-766.*

    This study was designed and published by Dr Charles Hay and my memory is that it was achieved through analysis of the UKHCDO database. I contributed information about one or more of my patients. Dr Hay will know whether any consent or information process was undertaken.

51. *Gale, R.F., Hird, M.F. and Colvin, B.T. (1998). Management of a premature infant with moderate haemophilia A using recombinant factor VIII. Haemophilia, 4, 850-853.*

    This case report described the management of a child with moderate haemophilia A who was born at 28 weeks gestation. A discussion concerning the optimal management of such a rare event was important for the treating community.

52. *Bagnall, R.D.,Waseem, N.H., Green,P.M., Colvin,B., Lee,C.A. and Giannelli, F. (1999). Creation of a novel donor splice site in intron 1 of the factor VIII gene leads to activation of a 191 bp cryptic exon in two haemophilia A patients. British Journal of Haematology 107, 766-771*

    I do not recall the reason for the publication of this academic work in collaboration with Professor Giannelli at Guy's Hospital. It may well have arisen from the investigation referred to in 47. (above).

53. *Parameswaran, R., Dickinson, J.P., De Lord, S., Keeling, D.M. and Colvin, B.T. (2000). Spontaneous intracranial bleeding in two patients with congenital afibrinogenaemia and the role of replacement therapy. Haemophilia, 6, 705-708.*

These case reports from The Royal London Hospital and Churchill Hospital Oxford, highlighted the dilemma of how to manage patients with the very rare condition of hypofibrinogenaemia.

54. Doyal, L and Colvin, B. (2002). The Clinical Ethics Committee at Barts and The London NHS Trust: Rationale, Achievements and Difficulties. Health Care Ethics Committee (HEC) Forum, 14, 26-36.

55. Sayer, M.M., Colvin, B.T. and Wood, D. (2002). The Pastoral Pool: an evaluation of a new system of pastoral care provision. Medical Education, 36, 1-8.

56. *Makris, M., Colvin, B., Gupta, V., Shields, M.L. and Smith, M.P. (2002). Venous thrombosis following the use of intermediate purity factor VIII concentrate to treat patients with von Willebrand's disease. Thrombosis and Haemostasis, 88, 387-388.*

This was a case report series, written from Sheffield, highlighting the potential danger of venous thrombosis in patients with von Willebrand disease following treatment with intermediate purity factor VIII concentrates. I recall contributing my experience with one patient's care.

57 Colvin,B.T. (2003). Why we do not need a Hippocratic Oath. Medical Education, 37, 1125-1127.

58 Colvin,B.T. (2004). Physiology of Haemostasis. Vox Sanguinis, 87(Suppl.1), S43-46

59 Colvin B.T., Astermark J., Fischer K., Gringeri A., Lassila R., Schramm W., Thomas A. and Ingerslev. J. for the Interdisciplinary Working Group (2008). European principles of haemophilia care. Haemophilia, 14, 361-374.

60 Colvin Brian, Dolan Gerry, Martinoli Carlo and O'Mahony Brian (2013) Understanding health outcomes: focus on haemophilia. European Journal of Haematology, 90, Suppl. 73 (1-9)

Unpublished work

In the late 1970s I collaborated in a clinical project with The Royal Free Hospital and The Hospital for Sick Children Great Ormond Street. We collected samples from consenting obligate haemophilia A carriers and normal female subjects to create a database of factor VIII and von Willebrand antigen values for each group. Mathematical analysis of the results enabled the writing of a formula which could be used to distinguish the two groups and provide a numerical probability for consultants who wished to know their likelihood of being a haemophilia A carrier. This work reproduced established methodology and was clinically useful, until superseded by genetic analysis in the 1980s. A paper was submitted but the work was not accepted for publication and indeed was related to clinical practice rather than original research.

In the early 1980s I collaborated with the Royal Free Hospital Haemophilia Centre in an attempt to classify von Willebrand Disease (vWD) patients under our care in the North East Thames Region. I recall that I presented preliminary results at a meeting of the World Federation of Haemophilia. The project was initiated and managed from The Royal Free and I have no other details of the protocol used or the results of the work. I do not think that a publication resulted.

About 20 years ago Dr Peter White, consultant psychiatrist at Barts and The London (and a junior colleague in the Psychiatry Department) undertook a questionnaire-based survey on fatigue in people with haemophilia and HCV infection. I believe they asked a group of anti HCV negative patients to act as a control group. The study was fully regulated and consented and results were

obtained but no publication resulted, to the best of my knowledge. Only Dr White can explain the reason for non-publication.

Other research

It is possible that I contributed to a study of the use of an early heat-treated commercial product manufactured by Alpha and named Profilate. I know that Dr Kernoff at The Royal Free Hospital contributed to the study and that we discussed it together, but I have no memory of my direct participation or of any publication.

Research reference 40 is an example of my collaboration with BPL in the development of high purity factor concentrates within the NHS. In this case a factor IX concentrate (Replenine) was the subject of study but I believe that I was also involved in some way with BPL's work to develop their high purity factor VIII (Replenate).

I contributed patients to one or more formal studies of the clinical use of the first recombinant factor IX concentrate (BeneFIX). At the time the product was marketed by Baxter and there is evidence of the Haemophilia Centre's involvement in:

Lambert T. et al (2007) Reformulated BeneFix: efficacy and safety in previously treated patients with moderately severe to severe haemophilia B. Haemophilia, 13, 233–243.

Professor Pasi, who is now Director of the Haemophilia Centre, is shown as a contributor from The Royal London Hospital, (since I had retired by the date of publication).

88. **Epidemiological research**

I do not believe that I was involved in any epidemiological research other than the studies already listed.

89. and 90. **Clinical research**

a) Prothrombin Complex Concentrates. (OXUH0001005)

I have no recollection of this Medical Research Council (MRC) study which does not appear on my personal list of publications, although I clearly contributed to it. I can make no further comment.

b) Heat treated NHS Factor VIII concentrate in the United Kingdom (PRSE0000608)

This study was clinical observation rather than research, as I believed that the concentrate I used was the safest and most appropriate available treatment in the circumstances. I believe that its use saved two of my patients from HCV infection. I would have obtained patient consent before treatment, although I recall that one patient, who was also pregnant, may have been very sick at the time and consent would have been obtained from her husband, who I remember well. It was necessary to take regular samples of blood after treatment to confirm the absence of infection and these were also obtained with patient consent. The very sick patient remained deeply grateful because she perceived that I had protected her from infection at a critical time.

c) A Prospective Study of Cryoprecipitate Administration (PRSE0003838)

This study was clinical observation rather than research, as I believed that the cryoprecipitate I used was the safest and most appropriate available treatment in the circumstances. I believe that its use saved six of my patients from HCV infection. I would have obtained their consent before treatment. It was necessary to take regular samples of blood after treatment to confirm the absence of infection and these were obtained with the patient consent.

d) 8Y Study (BART0002340)

This was the definitive study that demonstrated the safety of the intermediate purity heat treated factor VIII concentrate. The product became the standard safe treatment for people with haemophilia and some cases of von Willebrand Disease for many years until the adoption of high purity concentrates by some centres and then the advent of recombinant concentrates. My patients and/or their parents would have been aware of their participation in a national study, according to protocol but I have no precise recollection of how the information was given or consent obtained. The details should be available at the Oxford Haemophilia Centre, where the study was designed, approved and coordinated.

I can confirm that all patients and/or parents and/or next of kin gave their consent to participate in b) c) and d). I believe that study d) had a formal protocol, with which I complied.

I have no recollection of what or how patient data was shared with any party in these clinical studies but I believe that the patients fully understood the nature and purpose of the work, that it was a valid extension of their clinical care and that the knowledge gained was very much in their best interests and that of the haemophilia community.

91. **Ethics**

The main ethical principle guiding medical research is that it should advance scientific knowledge in order to assist in maintaining health and preventing and treating illness. It should also concentrate on the avoidance of doing harm.

Not all of the studies listed above were under my direct control but, in as much as they were, the above principles were followed. I would not have taken part in any studies which I believed to be contrary to the interests of my patients.

In practice, during my time in medical practice from the 1970s onwards, permission to undertake research has been governed by Research Ethics Committees. My understanding is that, with certain exceptions, express patient consent is required for research to be undertaken, and it is now obligatory to seek Research Ethics Committee approval for research work to be undertaken.

92. **Research studies**

In my training and subsequent experience there was never a suggestion that it was necessary to seek patient consent for the publication of anonymised case reports.

I believe that it is acceptable, with patient consent, to follow the clinical course of a particular treatment in the patient's best interests, without seeking Research Ethics Committee approval.

I believe that it is ethical to undertake research on anonymised laboratory samples with Research Ethics Committee approval.

I do not believe that patients were involved in research studies without their express consent, save that

1. I have no information or recollection of the Prothrombin Complex Concentrates. (OXUH0001005) referred to above at 89 and 90 a).
2. I have no information or recollection of the Research Ethics Committee details of the papers listed as 26, 27, 29, 30 and 36.

93. **Patient data**

See my answer to questions 142 and 143. I am confident that the Baxter rIX study was fully compliant with all regulations and with express consent.

I have no information on how any data was provided to Speywood, Alpha or Novo Nordisk.

94. and 95. **UKHCDO, Oxford and Manchester**

Patient data was shared with third parties such as UKHCDO, the Oxford Haemophilia Centre, BPL and Dr Craske of the Public Health Laboratory in Manchester, and also within different departments of The London Hospital and with shared-care hospitals in the North East Region. I regarded all these bodies as part of the overall NHS effort to care for my patients in an optimal way. This was the view among my colleagues in the haemophilia community.

Data collected from the 1960s for UKHCDO and the resultant research, have been overwhelmingly in the best interests of the haemophilia community. The issue of consent for this to be collected did not arise until my tenure as Chairman of UKHCDO from 1993-1996, when the matter was debated at UKHCDO meetings, without agreement on the idea of taking explicit consent for treatment and/or data handling.

In recent years, much greater emphasis has been placed on ensuring that permission is given for undertaking work which has also led to valuable research publications.

96. **Management of the UKHCDO Database [BART0000899]**

While I was Chairman of UKHCDO from 1993 to1996, the subject of obtaining explicit consent from the haemophilia community to permit their data to be passed on to the UKHCDO database was raised, to my knowledge, for the first time. The database contained very detailed information, including patient names, and there was concern that an anonymised national database would lack the accuracy and completeness that had been achieved up to that time. It was decided that an information sheet should be sent to all patients informing them of the database in writing and inviting them to request the removal of their names and data should they wish it. I believe that this was done and, although I received at least one call from a patient asking for clarification, there were no instructions to remove anyone's name from the database. After I retired as Chairman in 1996, I believe that this policy of "implied" consent continued to be used but I understand that it has now been replaced by a policy of explicit consent.

My letter of 14th May 2002 confirms my understanding of the policy as it was at that time. It is not accompanied by the letter from the Department of Health to the Chairman of UKHCDO to which it refers, but this correspondence must still be available, either from the Department itself or from the archives of UKHCDO. Without the text of Department of Health letter, I can make no further comment.

I believe that the UKHCDO database has played a vital role in the management of haemophilia in the UK for over 50 years, placing our country in the forefront of international knowledge of the condition. Similar databases have been important for cancer care and their management has raised comparable ethical issues.

97. **The Inquiry's Terms of Reference**

I submit below a list of my Books and Chapters in which articles relating to haemophilia care are listed in italics.

BOOKS AND CHAPTERS

1. Contribution to Hutchison's Clinical Methods. Mason, S. and Swash, M. (1980). 17th Edition. Bailliere Tindall. Swash, M. and Mason, S. (1984). 18th Edition. Bailliere Tindall. Swash, M. (1989). 19th Edition.

   Bailliere Tindall. Swash, M. (1995). 20th Edition. W.B. Saunders Co.

2. Chapter on Problems of Haemostasis in - Preparation for Anaesthesia, (1980). Ed. A.J. Stevens. Pitman Medical, p. 142-164.

   Republished with revisions in 1986 in Clinics in Anaesthesiology, 4, 667-686. W.B. Saunders Co.

3. *Section on Haemophilia in - Reports on Rheumatic Diseases (1983). (with C.G. Barnes). Ed. C. Hawkins and H.L.F. Currey. Arthritis and Rheumatism Council.*

4. Chapter on Haematological Disorders in Pregnancy: Thrombocytopenia (1985). Ed. E. Letsky. Clinics in Haematology, 14, 661-681. W.B. Saunders Co.

5. Chapter on Blood Disorders in - Hazards and Complications of Anaesthesia (1987). (with G.C. Jenkins and A.C. Newland). Ed. T. Taylor. Churchill Livingstone.

6. Haematology Pocket Consultant (with A.C. Newland). (1988). Blackwell Scientific Publications, Oxford.

7. Contributions to (Guidelines documents in haemostasis and thrombosis) in Standard Haematology Practice. Volume 1 Roberts, B. Ed. (1991). and Volume 2 Wood, J.K. (1994). Blackwell Scientific Publications, Oxford.

8. Colvin, B.T., Colvin, M.P. and Mibashan, R.S. (1991). Disorders of haemostasis. Chapter in Introduction to Intensive Care. Potter, D. Ed. Farrand Press, London.

9. *Colvin, B.T. (1994). Human Immuno Deficiency Virus (HIV) and Haemophilia. Chapter in Haematology and Infection. Jenkins, G.C. and Williams, J.D. Eds. Butterworth. Heinemann, Oxford.*

10. Cavenagh, J.D., and Colvin, B.T. (1996). Haemostasis and its assessment in Textbook of Intensive Care. Goldhill, D. and Withington, S. Chapman and Hall.

11. Kelsey, S.M. and Colvin, B.T. (1996). Bleeding and Clotting Disorders in Textbook of Intensive Care. Goldhill, D. and Withington, S. Chapman and Hall.

12. *Cohen, H., Kernoff, P.B.A. and Colvin, B.T. (1998). Plasma, plasma products and indications for their use.*

    In: ABC of Transfusion. Third Edition. M. Contreras, Ed. BMA Publishing Group.

13. Colvin B.T. (2004). Disorders of Haemostasis Medicine, 32:5, 27-33.

14. *Colvin B.T. (2005) Contribution on haemostasis in Clinical Medicine: Kumar and Clark Eds. 6th Edition (and previous editions). Chapter 8 Haematological Disease. Elsevier. Oxford.*

One contribution to haemophilia care, perhaps within the Inquiry's Terms of Reference, has been paper 59 of the list of peer-reviewed and invited papers. This is the article entitled "European principles of haemophilia care" which makes recommendations for haemophilia care in Europe. The publication dates from 2008, just as I retired from the NHS. It is mostly prospective, but it inevitably relies on the experiences of the past.

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

98. and 99. **Care and treatment of patients with HIV/AIDS**

The first steps were to identify those affected by HIV and for this I relied on the expertise of Professor Leslie Collier, then consultant virologist at The London Hospital (see q 81). Initial testing for anti HTL VIII antibodies (as HIV was then called) was neither fully sensitive nor

specific and I recall that both false positive and false negative test results were obtained. As soon as I had received reliable results, I informed each of approximately 40 patients in a personal interview (see qs 70, 71, 81.) I believe that, had I attempted to gain prior consent to testing, serious emotional and logistic problems would have arisen, both for false positives and false negatives.

No patient ever said to me, in person or in writing, during my career at The London Hospital, that they were dissatisfied with the way the information was managed.

Once the position was established, I set up a dedicated out-patient clinic, at the end of my usual clinic, for my patients and any relatives who wished to attend, together with a specialist nurse and a social worker with HIV related skills. We followed patients using lymphocyte CD4/8 values and ratios and then HIV viral load, as testing became available. Treatment with antiviral agents was introduced as drugs were developed and licensed.

I often saw patients in my office in the hospital, away from the clinic, when one of my nurses was normally present.

An information sheet was provided giving advice, for example on home treatment methods, personal hygiene and behavioural issues. I do not have a copy of this.

As soon as zidovudine (AZT) became available, I prescribed it to patients, as appropriate. The advent of triple therapy in the mid-1990s required a different approach and I transferred the clinic to the Graham Hayton Unit where each patient saw the same team plus an HIV specialist, initially Dr Guy Baily and then Dr Celia Skinner, who both had the skill to prescribe appropriate triple therapy and other management. The risks and benefits were initially explained by me but when the clinic transferred, they were explained by the HIV specialist. I attended all these clinics myself with my nursing staff and my patients very generously agreed to go to the Unit for their care, even though the Unit was mainly associated with sexually transmitted disease.

Many anti-HIV positive patients also eventually developed liver disease due to hepatitis C infection and I also established a clinic attended by a hepatologist, initially Dr Paul Swain and then Dr Graham Foster. Some patients also agreed to be seen at The Royal Free Hospital, partly because of that hospital's expertise and partly because of the trial of interferon therapy being undertaken by Dr Paul Telfer.

Psychiatric illness often required in-patient care.

Some patients required admission to intensive care in an infectious diseases ward, where it was also possible to deliver psychiatric care.

Surgical care was delivered in surgical wards.

I believe that virtually all clinical consultations, other than routine dentistry, were attended by me personally and my patients did not attend clinics without my presence, if at all possible.

Psychiatric support for my clinical colleagues was provided through regular group meetings for the hospital HIV service, offered by Dr Colin Murray Parkes, consultant psychiatrist and I tried to attend these myself, when possible.

My name was on the list of physicians who were willing to counsel Trust staff who had suffered needle stick injuries.

100. and 101. **Care and treatment of hepatitis B**

There were very few patients with active hepatitis B under my care, at least two were also anti-HIV positive and all were later shown to be anti-HCV positive, so their care was linked to the

HIV and hepatitis services offered. Any advice on investigation, treatment and prognosis would have been explained by the hepatologist, but I was also personally involved and would have discussed any particular issues that were relevant to haemophilia and its care. A good example of this is the indication and consent for, and the method of performing, a liver biopsy, which require the closest cooperation between patient, hepatologist and haemophilia consultant.

102. **Non-A non-B hepatitis (NANBH)**

Some patients developed clinical NANBH, usually following first treatment with a large pool concentrate in the 1970s and early 1980s, but many did not. There was no specific treatment for an acute attack and all resolved without serious illness. Some were later found to have chronically abnormal liver function tests and there was regular follow up for some patients, but none complained of clinical symptoms. HCV related fatigue, which was particularly noted after HCV was identified in 1989, was not an issue in the 1970s and 1980s and the condition was simply observed. No treatment was available or was sought. It was not appreciated until the mid-1980s that NANBH should be discussed and, by then, HIV infection had become the most important issue in haemophilia care.

Some haemophilia centres began to offer liver biopsy to their patients by the mid-1980s, but The London Hospital did not, mainly because of the risks involved. As previously mentioned, my decision was to try to align my policies to the Royal Free Hospital. The haemophilia centre there became opposed to liver biopsy, after one of their patients suffered a post-biopsy death due to haemorrhage.

The answer to the question 102 is therefore that, for NANBH, no treatment was available and little, if any information or advice could be offered.

103.,104. and 105. **Hepatitis C (HCV) Care**

Hepatitis C infection became diagnosable in 1989 but it would be 1990 before it was possible to take confident action. The first task was to identify those affected by HCV and for this I relied on the expertise of Professor Leslie Collier, consultant virologist. Initial testing for anti HCV antibodies was neither fully sensitive nor specific, although increasingly reliable results were obtained. All relevant patient samples were tested, and as soon as I had received validated results, I believe that I told all the approximately 80 affected patients personally. It was my policy to inform patients in personal interviews with a member of the nursing staff present but it is possible that a small number of patients may have been informed by post before I had the opportunity to speak to them. Had I attempted to gain prior consent to testing, then serious emotional and logistic problems would have arisen for the patients and I still believe that this course was in the best interests of the patients.

I have since become aware that some patients infected by HCV under my care may not have been informed of their status and I believe that these would mainly be occasional patients or registered patents who had been lost to follow up. I am very sorry if these patients were not told in a timely manner.

An information sheet was provided giving advice and a copy has been provided by the Inquiry at BART0002065.

I then established a liver disease clinic attended by a hepatologist, initially Dr Paul Swain and then Dr Graham Foster. Some patients were also seen at The Royal Free Hospital, partly because of that hospital's expertise and partly because of the trial of interferon therapy being undertaken by Dr Paul Telfer there. I contributed patients to this study and I believe that they were fully

informed, according to contemporary standards and with all necessary approvals. The course of treatment was very challenging for the patients and the results were disappointing, but this was, I believe, the first clinical study of potentially effective treatment for haemophilia related HCV infection in the UK.

I do not believe that every patient with HCV infection was seen in the liver clinic and I know that some declined to attend. In addition, some patients had fully cleared their infection spontaneously (HCV PCR negative) and only needed follow-up in the haemophilia clinic. Only referral to the individual patient notes could establish who did or did not attend and why.

As patients began to suffer clinical illness after up to 25-30 years of infection, treatment also began to improve, although the courses of treatment were very difficult for the patients to endure. I continued to liaise with Dr Foster at The London and Dr Dusheiko at The Royal Free to provide advice and care for patients.

Apart from the patients who entered Dr Telfer's Royal Free study, many patients with haemophilia were offered and received antiviral therapy for HCV infection at The London. The treatment was initially single agent, but more agents were added or substituted as treatment developed and improved. Unfortunately, the treatments were very challenging for the patients, because of side effects and duration of treatment, but I believe that all the potential difficulties were explained and managed, usually with the help of the hepatologist, and the nursing staff played a major role in supervising the very difficult treatment programmes.

I retired from clinical practice before very effective treatment became available.

106. **Children with HIV and hepatitis**

I do not recall making special arrangements for children with HIV and hepatitis.

I recall seeing one adolescent with a hepatologist and, by the time chronic liver disease became diagnosable and treatable, the children with HCV infection would also have reached the age where they could attend an adult clinic.

The children's clinic was run by me in collaboration with a consultant paediatrician and a children's dentist. I can recall difficult and painful discussions in my office in the presence of my nursing staff and I am still in touch with the parents of one of my anti-HIV positive children who sadly died as a result of an injury unrelated to HCV or HIV infection.

107. **Counselling, psychological, social and other support**

Trained counselling was provided by a Social Worker, Mr Nigel Harvey, especially for anti-HIV positive patients, and my nursing colleagues provided much support of all kinds, including in the community, especially for home treatment patients. Junior medical staff also played a part. A number of patients needed formal psychiatric referral and in-patient care.

During the delivery of care for very psychologically disturbed anti-HIV positive patients, I was personally assaulted or threatened with assault by more than one patient, but no injuries resulted.

I have already stated that Dr Colin Murray Parkes, consultant psychiatrist, offered counselling sessions for health care professionals working in the field of HIV infection and I and my colleagues took advantage of this service.

108 and 109. **Allocation of support**

I do not recall any specific funding from any source being allocated to the haemophilia centre to help with the counselling of patients infected with HIV but I remember that Mr Harvey's assistance was specifically offered by the Trust, I think from within its existing resources.

Mr Harvey was the key to the provision of trained counselling, but I have already explained that the burden of support fell on all members of the haemophilia team, especially the nursing staff.

110. **Funding for HIV and hepatitis C care [BART0000581]**

I was never aware of any attempt to deny my patients appropriate treatment for their HCV or HIV infection, as therapy became more complex and effective. I know that this topic was much discussed, as evidenced by the minute to which my attention has been drawn, but the Trust never denied me access to treatment which I regarded as appropriate and essential for the care of my patients. The cost of treatment for inhibitor patients, in particular, could be enormous and unpredictable but product choice was always left to the discretion of the Haemophilia Centre Director.

Securing adequate funding for the care of the haemophilia community was a challenge throughout my career but it was not always clear that the newest and most expensive treatments were either the best or the safest. In my experience it was the lack of self-sufficiency in concentrate provision by the NHS which mainly affected the cost of care, as commercial factor concentrates had to be purchased to keep up with demand.

Nursing services expanded greatly during my time as Director of the Haemophilia Centre and data management services also increased and funding was made available.

Records

111. **HIV and hepatitis recording**

My policy and practice was to make full and accurate records of the condition of my patients, but also to protect information resulting from confidential conversations, if that information could be regarded as sensitive and was not essential for their care.

a) The Inquest of December 2016

The Inquiry has specifically asked me to comment on my report to the Coroner in the case of GRO-A in December 2016.

In my report I wrote that "It is interesting to note that I did not actually write down the result and I think that this was probably related to my reluctance to write information about HIV in the notes at this time, for reasons of confidentiality and possible stigma". I believe that I was trying to protect my patient's interests because we knew that stigma was a real issue for some patients at this very difficult time. On the other hand, I had the responsibility of protecting carers from the risks of onward transmission.

Shared care

It was also difficult to know what to say to general practitioners, many of whom had never seen my patients despite technically sharing patient care with the Centre. The comprehensive care that I offered meant that many of my patients never visited their GP. Some patients were reluctant to allow their condition to be revealed and yet I knew that there could be occasions when knowledge might be vital, both for the safety of the patient and for that of the health care professionals in the community. I do not believe that a clear solution was found to this problem or that it was possible to find one.

b) BART0000509

I have no recollection of the letter [BART0000509] but I note that the minutes of the North East Thames Haemophilia Working Party 22nd May 1985 Note 85/1 (iv) (BART0000675) state:

Concern was expressed about the confidentiality of personal details of HTLV III Ab positive patients. No lists are circulated to avoid the risk of misuse by unauthorised people. All patients will be informed of the result of their HTLV III antibody test on request and counselled on the implications of a positive result to themselves and their families. It was agreed that doctors and dentists responsible for the care of 'positive' patients should be informed of positive tests so that they and their staff may take appropriate measures. Hospital notes should be marked with 'High Risk/Danger of Infection' labels.

[BART0000509] was probably personally directed to the individual Director of each local Haemophilia Centre in The London Hospital's catchment area to confirm the status of shared patients thought to be at risk, in order to ensure the safety of patients and staff. I note that there are no addressees, the letter is marked "enc." and each haemophilia centre's patients are listed on a separate sheet of paper. The letter, together with the individual relevant sheet, would therefore have been sent in confidence, individually, to each Director.

112. **Death certificates**

I believe that I completed death certificates accurately. I have a very distant recollection of a relative asking me not to mention HIV infection on a death certificate and my memory is that I insisted on a full and accurate description, which I believe was my legal responsibility.

113. **Retention policies**

The clinical notes of the most frequently seen adult patients were kept in the department to ensure their availability both for emergencies and for routine clinics. Other notes were kept in the hospital's Medical Records Department and were sourced as required. If notes were required for consultations in other departments, they were sent around the hospital in the normal way. In-patient notes were kept on the wards in the normal way. The effort required to make sure that the hospital notes were available for all consultations was considerable.

Children's notes were kept in the Children's Department and all correspondence was managed from there.

I am not aware of any retention policy being in existence while I was at the hospital and I believe that there was no policy of notes destruction during my career. I was aware of an effort, made by the hospital Records Department, to microfilm very old notes but I had no involvement in this. If there was a policy to destroy any notes after my retirement, I was not aware of it and I played no part in it. Professor Pasi, as current Director of the Haemophilia Centre or the Medical Records Department at Barts Health NHS Trust, might be able to comment further.

114. **Other files**

Before I became Director of the Haemophilia Centre a "brown envelope", (later renamed "red envelope") system had been set up and these envelopes were kept in the department. The purpose of this set of records was to make sure that, even if the main notes had been taken from the department, there was always enough information to allow junior staff on duty to understand the patient's profile and needs and to select appropriate treatment by day or night. There was nothing in these files which were not present in the main notes.

They gave basic duplicate information about patients and initially contained a running clinical record summary of consultations, together with details of results such as factor VIII level, inhibitor status, blood group, an indication of the appropriate concentrate to administer and copies of correspondence.

When HIV and then HCV laboratory data became available after 1984, I kept a card index file, hand-written by me, which contained essential information I had on HIV and HCV status. I kept another similar file, which contained the results of lymphocyte marker tests for HIV positive patients and this was particularly useful in the management of anti-retroviral therapy.

When I retired, I left the brown/red envelope system in the care of the data manager and gave the card index files to the new Director. I believe that these records have been retained but have no knowledge of what has happened since 2007.

115. **Records or information outside the centre**

Frequently required medical records were kept in the Haematology Department and the rest were stored in the Medical Records Department. The notes were moved around the hospital as needed for the care of patients, for example out-patients (see q 113) or in-patients. The Haemophilia Centre was run from the administrative offices and the laboratory space of the Haematology Department, where there was a small clinical area available. Eventually a Day Ward was provided for the Haematology Department, where people with haemophilia were seen and where concentrates were kept.

Adult out-patients were seen in medical out-patients (and the Graham Hayton Unit) and children were seen on the children's ward and in the Paediatric Department.

Patients might be admitted to Mile End Hospital and, later to The London Chest Hospital and St. Bartholomew's Hospital, as the administration of the NHS changed and developed.

When I retired in 2007, I handed all relevant files, including any research material, over to the Haemophilia Centre. I have no knowledge about the storage of any records since my retirement.

I did not keep records or information about any of my patients at my home, until I was required by the Coroner to study the records of the patient whose inquest was held in 2016/17. As soon as the inquest was over, I promptly returned all the records to the Coroner's Milton Keynes offices by driving there myself and handing them over personally.

116. **Retention of information**

I do not hold any records or information about any of my patients.

I have retained electronic copies of about 60 professional lectures that I delivered over the years, covering the whole of my professional and educational career. Some of these include slides relating to past cases but they are anonymous and patients are not identifiable. (see answer to question 119).

SECTION 6: SELF-SUFFICIENCY

117. **December 1974 announcement**

a) I would have known about the announcement before my appointment as an honorary consultant in 1977.

(I was not appointed as Director of the Haemophilia Centre in 1977 and indeed I am not aware that such an appointment was ever made officially, not least because the Haemophilia Centre did

not really exist in the 1970s. Its function and scope grew over the years and was finally recognised when I was appointed as Chairman of UKHCDO in 1993).

b) I do not know that the concept of self-sufficiency was ever defined. Self-sufficiency can only ever have meant the provision of sufficient NHS plasma sourced factor VIII (and IX) concentrate to meet clinical demand. It was clinical demand that increased exponentially, not the meaning of the term.

During the 1970s elective surgery was being undertaken, so the term cannot have been limited to bleeding episodes. My own experience of the late 1970s was that we tried to locate and register patients with haemophilia and allied disorders in our catchment area, attempted to assess their immediate needs and began a home treatment programme with the very limited resources available to us. Prophylaxis was not an option.

c) No.

d) I do not have a view.

e) I played no role.

118. **Estimation of need**

a) I believe that the Reference Centre Directors group would have fulfilled this role. In practice and for historical reasons, the Oxford Haemophilia Centre was dominant in making decisions and recommendations.

b) Only UKHCDO can answer this question. By the time I joined the Executive Committee as Chairman in 1993, it was generally thought that the goal of self-sufficiency had become an unachievable objective.

c) I doubt whether anyone, at any level, really understood how demand would develop.

d, e and f) I have no knowledge.

119. **Demand in 1988 [NHBT0009593]**

I have no recollection of the claim made by Dr Harrison in her letter to Dr Gunson.

I do however recollect that a world shortage of factor VIII was recorded in 1988. I remember that I discussed the issue with the late Dr Peter Kernoff, but I do not have the original research article or reference from which the data was taken. I used to teach that, in 1988, European annual demand was 600 million units, USA demand was 600 million units, Japanese demand was 100 million units, while in the Rest of the World (RoW) demand was 100 million, giving a total of 1400 million units. World supply at the time was 1000 million units, giving a shortfall of 400 million units (and, of course most of the RoW received no treatment at all).

This shortfall was partly related to the loss of yield caused by the heat-treatment viral inactivation process but production in the UK never remotely caught up with demand.

Plasma derived factor concentrates could not be regarded as "probably safe" until the publication of the 8Y study in 1988 (BART0002340). Even then safety was "not proven" because it is not possible to confirm a negative (i.e. that administration of concentrate does not lead to infection). Indeed, it was only 10 years or so until the nvCJD crisis arose, when suddenly USA derived plasma became preferable to UK sourced plasma because of the absence of nvCJD in the United States.

120. **Annual factor VIII usage**

Every dose of blood product, including factor VIII, was recorded by the medical and nursing staff in the hospital and we tried to ensure that every dose given at home was recorded by the patient or carer. Completed record sheets were returned to my secretary from home, by post, at the end of the month and she chased up unreturned records.

The record consisted of name, diagnosis, product used, reason for administration, dosage and batch number. My secretary, and in later years the data administrator, collated all the information which was sent annually to UKHCDO Headquarters in Oxford.

a) It was the director's responsibility to ensure that the records were completed and to sign off the annual return before it was sent to Oxford.

b, c, d, e and f) The Oxford Centre processed all the data, (which I believe were computerised as early as the late 1970s) on behalf of UKHCDO and the results were returned to individual centres and analysed for national understanding and planning. I was not involved in this process until I was appointed Chairman of UKHCDO in 1993.

The main developments during my term of office were to use the data to formalise the recognition of Comprehensive Care Centres [CCCs] and of Haemophilia Care Centres [HCCs], using World Federation of Haemophilia criteria, and to begin a process of regular Audit in order to recognise confirm, ensure and improve the quality of care given nationally. At the same time, we began to address the issue of patient consent to allow their data to be included in the national data base, beginning with the concept of "implied" consent referred to elsewhere in this document (91).

Exact details of how the database was and is managed must be available from UKHCDO.

Further developments have taken place over the years and the Manchester Centre now looks after the database.

121. **Significant differences**

It has always been difficult to ensure that every dose of factor concentrate administration was recorded, partly because many doses were given out of hours by relatively inexperienced staff, but mainly because of the difficulty of ensuring the completeness of home treatment data.

It has been particularly difficult to reconcile predicted usage with actual usage because:

1) serious accidents, major bleeding episodes and emergency surgery

2) development of inhibitors to factor VIII

3) referral of patients with auto-immune acquired haemophilia

4) unexpected transfer of patients between centres

are not predictable.

It has always been very difficult to reconcile stock with usage, although I believe that modern computer technology will have made this more possible.

In my view, the data that has been collected and analysed by UKHCDO for 50 years is of very high quality.

122. **Achievement of self sufficiency**

In my view self-sufficiency was never achievable and has not been achieved.

Demand was always going to exceed supply because of the exponential increase in demand. My own use of commercial products was mainly due to the fact that insufficient NHS concentrates

were being made available up to 1984. NHS concentrates were less expensive for the NHS and were generally fit for purpose.

The purchase of commercial concentrates was unavoidable, for the management of inhibitors, partly because of the huge volumes of factor VIII that would have been required for treatment of bleeding episodes or tolerance induction. Most of any factor VIII used would have been ineffective, because of the inhibitory activity and tolerance induction was thought to be both unsuccessful and unaffordable. (It later became apparent that tolerance induction, although very expensive in the short term, could be successful and might be financially viable, using a long-term view.)

FEIBA was an activated form of plasma derived factor IX and was available from the 1970s. It was at least partly effective in the management of inhibitors and was only available commercially. The commercial recombinant factor VIIa which was first described in 1988, was a major advance in inhibitor management but did not always reliably treat or prevent bleeding in people with haemophilia and inhibitors (and was extremely expensive).

There were other pressures to use commercial concentrates because they were often "technically" superior to NHS concentrates and during the HIV crisis from 1984 onwards, there were those who believed that "high-purity" commercial products were "better for patients" than intermediate purity products. (See BART0000581). This was almost certainly incorrect.

As it happened the NHS intermediate purity heat-treated 8Y concentrate, although technically less sophisticated than many commercial products, proved to be remarkably safe and effective and was my product of choice from its introduction until the advent of high purity NHS factor and commercial recombinant concentrates in the mid-1990s and beyond.

Recombinant products were at first very expensive and contained human albumen, so that their advantage was difficult to confirm but by the time nvCJD was reported in the late 1990s, methods of production were improving and it was not long before recombinant products became available without human or animal protein in their preparation. Recombinant factors were then adopted for children and then for all people with haemophilia, rendering plasma derived products largely obsolete in the care of haemophilia. Unfortunately, one of the American companies producing an early recombinant factor VIII had to interrupt production, just as the UK was trying to switch to a recombinant treatment policy because of the nvCJD threat. Many patients had to switch back to plasma derived products, creating serious problems of supply, communication and anxiety, particularly for children (and their parents) although children were given high priority during that crisis.

It should not be forgotten that the UK was self-sufficient in factor IX for the treatment of factor IX deficiency (Christmas Disease) from the beginning, because of the relative rarity of the condition and the longer half-life of factor IX. Some commercial virally inactivated commercial factor IX was used during the AIDS crisis but there were doubts about the prothrombotic risk of heat-treated factor IX, quite apart from the lack of evidence of viral safety of early heat-treated commercial IX. The result was that relatively few British patients with factor IX deficiency were infected with HIV from factor IX concentrates, (but virtually all patients treated before 1985 were infected with HCV from UK sourced NHS products).

Recombinant factor IX was available from the mid-1990s, without any human or animal protein being used in its preparation methodology, and it eventually replaced plasma derived factor IX concentrate in the UK.

In summary, my opinion is that NHS self-sufficiency in factor VIII production was desirable in the period from 1970 to 1988 and also from then until the advent of advanced recombinant products. I do not believe that self-sufficiency in factor VIII production was ever achievable in the NHS.

123. **Possible failure by UK clinicians to provide timely and accurate estimates of future demand for factor VIII blood products**

The system in use did not provide requests for estimates for future use. Rather, Centres were required to submit data on the amount used in the previous year. I was never in a position to influence the production of factor VIII concentrates in the UK. See my answer to Section 6 above.

124. **Potential effects of self-sufficiency**

(i) hepatitis B – almost no effect.

Hepatitis B was rare in haemophilia in my experience and I cannot recall more than one or two patients who were affected by it. My recollection is that they were infected in the early 1970s.

(ii) hepatitis C – almost no effect.

It became apparent in the mid-1980s that virtually everyone treated with a large pool concentrate (either factor VIII or factor IX) of British NHS or American origin developed NANBH and this was confirmed when HCV testing became available in 1990. Infection was due to the prevalence of HCV in the British donor community which was not then known but was probably about 0.3%. A concentrate pool size of many thousands of donations made infection inevitable.

It might be argued that the sub-types of HCV present in American plasma were different from those in British plasma and that the pathology of infection might carry a different prognosis. I am not an expert in HCV infection and did not become aware of scientific evidence to support this concept before my retirement over 10 years ago.

(iii) HIV – My answer is that "self-sufficiency would have needed to be achieved" by 1980.

In that case the incidence of HIV infection in the UK haemophilia population would have been very much reduced, but not eliminated.

Causes of HIV infection, despite UK self-sufficiency, would have been i) the use of FEIBA (before it was virally inactivated) to control bleeding in inhibitor patients and ii) infection in the general haemophilia population caused by donation of HIV positive blood by British donors. We now know that this had occurred before heat-treatment was introduced in 1985. I believe that two of my patients were infected in this way.

We also know that early heat treatment methods were not fully effective.

125. **Factor IX self-sufficiency**

See my answer to 122.

The UK was indeed self-sufficient in factor IX for the treatment of factor IX deficiency (Christmas Disease) from the beginning, because of the relative rarity of the condition and the longer half-life of factor IX. Some virally inactivated commercial factor IX was used during the AIDS crisis but there were doubts about the prothrombotic risk of heat-treated factor IX, quite apart from the lack of evidence of viral safety of early heat-treated commercial IX. The result was that relatively few British patients with factor IX deficiency were infected with HIV from factor IX concentrates, (but virtually all patients treated before 1985 were infected with HCV from UK sourced NHS products).

Recombinant factor IX was available in the mid-1990s, without any human or animal protein being used in its preparation methodology, and eventually replaced plasma derived factor IX concentrate in the UK.

The very rare patients with factor IX deficiency who also had an inhibitor to factor IX would probably have been treated with FEIBA and would have been at risk of HIV infection from a commercial product. (Recombinant factor VIIa (rVIIa) was introduced after the infection risk period was over).

126. **Preference for NHS factor IX concentrates**

I used almost exclusively NHS factor IX concentrate to treat haemophilia B. I believe that I reluctantly used very small quantities of commercial heat-treated factor IX just before heat-treated NHS factor 9A was introduced. I cannot now recall the exact circumstances. The difficulty was that it was thought that the British donor pool was not infected with HIV (which was not case).

Initially there was doubt about what level of heat and other methodology was appropriate to administer to the concentrate to render it safe or safer.

There was also anxiety that a heat-treated factor IX concentrate might be thrombogenic because of protein denaturation during the viral inactivation procedure. This was a real concern because it was well known that the intermediate purity NHS factor IX concentrate was capable of causing thrombosis, including pulmonary embolism, especially following orthopaedic surgery.

SECTION 7: BLOOD SERVICES AND BPL

127. **Relationship with Blood services BPL**

I had a very strong and close relationship with BPL throughout my career. I regarded the Blood services and BPL as an integral part of the NHS and their concentrates were generally my products of choice (save for the management of inhibitors – see above in "self-sufficiency"). I worked with them at various times to evaluate their products, either directly or through UKHCDO and the Oxford Haemophilia Centre.

128. **Interactions**

I trained in Blood Transfusion at the Brentwood Blood Transfusion Centre under Dr John Jenkins and knew the staff there very well. I also worked closely with Dr Jean Harrison when she was appointed Director there.

I visited the Lister Institute laboratories at Elstree and met Dr W. D'Arcy Maycock,

Dr Richard Lane and Dr Terry Snape during and after training.

I knew Dr Ethel Bidwell and Dr Jim Smith, who were based at Oxford.

I worked with Dr Clive Dash during his time as Medical Director of BPL.

My commitment was to the NHS, despite the fact that NHS products were in short supply and not as "technically advanced" as commercial products.

My centre was politically unimportant and relatively small, compared to the mostly larger Reference Centres and I relied on my contacts with Dr Peter Kernoff at The Royal Free Hospital and Dr Charles Rizza at Oxford for support in decision making and centre development. I developed a patient register that resulted in the identification of an increasing number of patients and I was involved in some clinical trials and the evaluation of concentrates over the years.

129. **Risk reduction**

I have no knowledge of efforts to reduce risk at any level, perhaps because I was not a member of the Reference Centre Directors Committee. When I heard of the availability of small quantities of a small pool and "virally reduced" concentrate in Oxford in 1984/5 I requested a small supply to treat two patients and my experience was published. (PRSE000608).

130 and 131. **Meetings or interactions**

I attended virtually all open meetings of UKHCDO. I also attended meetings of the North East Thames Regional Haemophilia Working Party and the Inquiry has sent me copies of the minutes. Both discussed the risk of infection.

I cannot recall having any discussions with the Blood service or BPL which affected policy on the risk of infection of blood or blood products with hepatitis or HIV/AIDS and was not involved in any decisions or actions on the issue.

132. **Record keeping for blood and blood products**

Record keeping for blood transfusion in the hospital was identical to that of any person transfused at The London Hospital. Blood was obtained for blood grouping and antibody screening in the usual way. If blood was requested it was cross-matched and issued, a record being kept of its administration and any side-effects.

Every dose of blood product, including cryoprecipitate, factor VIII and factor IX, was recorded by the medical and nursing staff in the hospital and we tried to ensure that every dose given at home was recorded by the patient or carer. Completed record sheets were returned to my secretary from home, by post, at the end of the month and she chased up unreturned records.

The record consisted of name, diagnosis, product used, reason for administration, dosage and batch number. My secretary, and in later years the data administrator, collated all the information which was sent annually to UKHCDO Headquarters in Oxford. I do not know how much or how many of these records have been retained or discarded at The Royal London Hospital, at Oxford or at the current database in Manchester.

SECTION 8: UKHCDO

133. **Personal involvement**

From the early 1970s I was a member of UKHCDO as Centre Director (or to begin with a *de facto* Director) of the haemophilia service at The London Hospital. I attended open meetings, especially the AGM and I returned our annual statistics and regular adverse events reports to the Oxford Haemophilia Centre, where UKHCDO was based. From 1977 to 1993 I was therefore a member and observer within the Organisation but had no executive role. I also contributed to some UKHCDO led clinical studies according to the regulations in place at the time

I was unexpectedly invited to chair the organisation from 1993 to 1996 and after that acted as immediate Past Chairman during the chairmanship of Professor Christopher Ludlam from 1996-1999. During those six years I believe that the following actions were important.

Reorganisation of UKHCDO

UKHCDO was set up as the United Kingdom Haemophilia Centre Directors Organisation (UKHCDO). Its Executive Committee was based on "Reference Centres" which had been self-nominated from the 1960s onwards and reflected the interest of various physicians and pathologists across the UK at that time. Some were general physicians, some were clinical haematologists, some were mainly laboratory-based haematologists and some were

paediatricians. The ability and commitment to collect data and to understand and organise haemophilia care in the UK was, in my opinion, an outstanding achievement and gave a secure basis to the management of the condition in dialogue with the Haemophilia Society and the Department of Health (DoH). At that time no one considered that any kind of patient consent was required or desirable to undertake UKHCDO's mission, which was regarded as being very much in the patients' best interests.

By the mid-1990s the DoH and the World Federation of Haemophilia (WFH) had begun to publish haemophilia care standards and one of my first duties as chairman was to define and, where appropriate regulate, the recognition of "Comprehensive Care Centres" (CCC) and "Haemophilia Treatment Centres" (HTC). This was done by a series of visits to centres and membership of the Executive Committee was altered to include the CCCs' Directors. This provided a more "democratic" and transparent governance system for the organisation. We also undertook a full review of the whole organisation and eventually changed our name to the "United Kingdom Haemophilia Centre Doctors Organisation".

Constitution

I recall that I assisted Professor Ludlam in the drafting of a revised UKHCDO constitution.

Audit

At the same time, it was decided to undertake Triennial Audits of CCCs to attempt to create quality assurance within the organisation. This process was originally performed by directors from other centres but also included anonymous patient feedback. The audit process gave directors a partially independent view of the quality of the service they offered and, for the first time, a 360 degrees assessment with a voice for patients. It also gave directors help in going to their own Trusts with sensible requests for changes to, or expansion of, their services.

Guidelines

During my chairmanship guidelines for the care of people with haemophilia and allied disorders were written and published.

Data protection

I was also responsible for attempting to coordinate UKHCDO's first responses to the various Data Protection Acts. In the mid-1990s UKHCDO believed that its database was an essential part of haemophilia care in the UK and that a named database was essential to avoid confusion and duplication of information relating to people with haemophilia and allied disorders. It was appreciated that patient consent to be included in the database was an important issue, but it was also thought that some kind of "implied" consent with an "opt-out" would suffice. I was involved with trying to create an information system that would facilitate introduction of this policy.

Patient consent

There was also some discussion within UKHCDO about taking patient consent for administration of blood products, but this had to be coordinated with consent to blood transfusion in general. I have been provided with some correspondence on this subject by the Inquiry and see that, in principle, I was in favour of explicit consent for first treatment and changes of treatment but I have no recollection of exactly what was done then or what has been done since.

Recombinant factors and nvCJD

Recombinant factors became available in the mid-1990s but the first factor VIII concentrates contained human albumen and it was difficult to appreciate any advantage that they might have,

bearing in mind their very high cost. The first recombinant factor IX was entirely free of human and animal protein but for many directors and also for UKHCDO its cost was felt to be prohibitive, especially as the UK had always been self-sufficient in factor IX and high purity plasma products were regarded as "safe". Nevertheless, some directors were keen to use recombinant products and this created some controversy within the organisation. During Professor Ludlam's chairmanship, UKHCDO was faced with the threat of new variant CJD (nvCJD) and I was involved in, but not directly responsible for, the decision to abandon the use of UK sourced plasma in favour of USA sourced plasma, since nvCJD was not present in North America. The pressure to switch to recombinant factor concentrates became overwhelming in the following years as it became apparent that prion disease could be transmitted by blood and blood products and as recombinant manufacture began to exclude the use of human and animal protein. Unfortunately, recombinant production was severely curtailed for a period around the turn of the millennium, creating major problems for the haemophilia community, as some patients who had been transferred to recombinant factors had to be switched back to plasma derived products. During this time, I was consulted, but not directly responsible for advice given by UKHCDO.

Information Technology (IT) Working Party

I chaired the IT Working Party for a few years from 1996-1999 but the IT service was soon taken over by Professor Charles Hay in Manchester.

Records of UKHCDO meetings, advice and practice may be available from the Organisation itself and will form an objective record of its activities and my contributions.

134. **UKHCDO outline**

I cannot give a comprehensive view of UKHCDO's structure and function, which is a matter of record.

a) I believe that its purpose has always been to identify and register people with haemophilia and allied disorders within the United Kingdom, in order to understand their needs and facilitate and improve their treatment and overall management. UKHCDO has provided a unified voice for discussion and negotiation with the Haemophilia Society and the DoH in order to ensure that people with haemophilia are offered appropriate care within the NHS.

b) UKHCDO's structure has been discussed above but, in summary:

1. The headquarters were in Oxford for many years but was later transferred to Manchester.

2. There was a database of all patients in the UK, with details of clinical condition, product use, adverse events and outcome.

3. There was an Executive Committee of Reference Centre Directors which was replaced in the mid-1990s by CCC Directors.

4. UKHCDO was responsible for many publications associated with the database results and interpretation.

5. There were a number of sub-committees, whose membership was nominated from within the organisation, and they were charged with addressing specific issues. The working parties reported back to the Executive who would approve reports and authorise publications, especially guidelines documents.

c) Any specific relationship with the pharmaceutical companies will be a matter of record at UKHCDO headquarters.

d) My own perception is that all important decisions were taken with the authority of the Executive Committee and with the consent of the overall membership.

e) The secretariat at Oxford Haemophilia Centre collected and disseminated information and advice by post and by publication in scientific journals, at least until the advances in information technology created the opportunity for electronic communication.

f) i to iii) I am not aware of any policies, guidance, actions or decisions in which I was involved which related to the importation or purchase of blood products or the manufacture of blood products, or self-sufficiency, save insofar as I was involved in the publication of guidelines documents by UKHCDO.

iv) I recall co-signing a letter as Chairman of UKHCDO (and probably addressed to the DoH), which I think was originally written by Professor Christine Lee of the Royal Free Hospital and which supported the use of recombinant products. I believe that this may be the letter referred to in BART0000581. (The meeting was of the combined North Thames Haemophilia Centre Directors which took place at The Royal Free Hospital on 16th February 1995.)

6/95 Recombinant Factor VIII

Dr Lee reported that she had written to Kenneth Calman expressing the opinion that experience had shown that plasma derived products could never be guaranteed to be completely safe and pointing out that the availability of a recombinant product could overcome doubts about such concentrates. A reply from "a senior DoH official" gave the view that Plasma derived concentrates were "no less safe" than the recombinant product and added that the current Recombinant product contained plasma derived albumin and " was not without side-effects".

Subsequent events suggest that this letter was appropriate, although, at the time, some members were opposed to sending the letter in the name of UKHCDO. There may be a record in the UKHCDO archives of the correspondence and the difficulty it created.

v) I am not aware of my involvement in any UKHCDO policies, guidance, actions or decisions relating to the risks of infection associated with the use of blood products, save for the publication of the 8Y study in 1988 and referred to above, which was effectively managed by UKHCDO.

vi) I am not aware of my involvement in any UKHCDO policies, guidance, actions or decisions relating to the sharing of information about such risks with patients or their families, save for the discussions already referred to relating to consent for the database itself.

vii) The Inquiry has already sent me some of my correspondence on consent relating to product use and this is referred to elsewhere. As Chairman of UKHCDO I attempted, unsuccessfully, to reach a consensus on obtaining consent for treatment with factor concentrates, at least for first exposure and on changing products.

viii) The Inquiry has already sent me some of my correspondence relating to provision of heat-treated concentrate and this has been discussed elsewhere. I took part in the 8Y study in 1988 and I made a personal request for an early heat-treated product in 1985. (That request was directed via the Oxford Haemophilia Centre but not to UKHCDO).

ix) I am not aware of my involvement in any UKHCDO policies, guidance, actions or decisions relating to the other measures to reduce risk.

x) As the immediate Past Chairman of UKHCDO I supported Professor Ludlam in the switch from UK to USA sourced plasma, as the nvCJD crisis developed. I was aware of and had to take action locally, over the identification of patients who had received products that might have been implicated as nvCJD risks, because of the donors who had contributed to the plasma pools. This work was extremely difficult and involved complex and sensitive personal communications with patients and parents, especially as the crisis coincided with reduced availability of recombinant

products. The process of identification was certainly facilitated by UKHCDO as part of their adverse events recognition activity.

xi) I do not recall playing a significant role in advising on the selection of treatments for HIV and hepatitis C. I believe that I relied on local expertise for both services and in addition relied on the expertise of The Royal Free Hospital but not on UKHCDO. The interferon publication, for which I was a co-author was a Royal Free based study.

SECTION 9: PHARMACEUTICAL COMPANIES/MEDICAL RESEARCH/CLINICAL TRIALS

135. **Advisory and consultancy services**

Ipsen Fund

From 2002-2006 I was a member of the Ipsen Fund Scientific Advisory Board. (see Annual Declaration of Interests in the Pharmaceutical Industry (BART0000869.) This was a remunerated role in which a panel of experts assessed and advised Ipsen on academic grants for research work. The applications were entirely general and not associated with haemophilia or its care. The reason for the declaration (and my selection to advise) was that Speywood (a part of Ipsen) had produced porcine factor VIII and I had used this product successfully for some patients with haemophilia A or acquired haemophilia with weak inhibitors to factor VIII, particularly in the 1980s.

By the time I was asked to sit on the panel, production and use of plasma derived porcine factor VIII had ceased but the Ipsen Company thought that I was a suitable person to advise them.

Baxter Healthcare

In 2005 I was invited by Professors Mannucci, Ludlam and Astermark to participate in a project to address haemophilia care in Europe with the title "Inter Disciplinary Working Group" [IDWG]). The initiative was funded by Baxter Healthcare. My role was to chair meetings of haematologists from all over Europe to define, write up and then publish the "European Principles of Haemophilia Care". These principles were well received and adopted by the European Haemophilia Consortium (EHC) and by the World Federation of Haemophilia (WFH).

The work of this group also led to the EUHASS adverse events initiative chaired by Professor Michael Makris, a training curriculum for haematology in Europe led by Professor Jan Astermark and the founding of the European Association for Haemophilia and Allied Disorders (EAHAD), of which I was the first Company Secretary.

Scottish National Blood transfusion Service (SNBTS)

My chairmanship of the Safety Committee of SNBTS can be found in my curriculum vitae and is only recorded here because it appears on the UKHCDO Annual Declaration of Interests in the Pharmaceutical Industry for 2003. (SNBTS is part of the NHS).

Retirement

I retired from the post of Director of the Royal London Haemophilia Centre at the end of 2006 and was succeeded by Professor John Pasi. During the spring of 2005 I was granted a three-month sabbatical by Queen Mary and Professor Pasi was in charge for this period. (At that time my wife was British Ambassador to the Holy See and was resident in Rome, where I was appointed Visiting Professor at Universita' degli Studi di Roma "La Sapienza").

After my retirement. from the NHS in April 2007 I continued to see patients once a week in a clinic at The London until the staffing of the haemophilia Centre had stabilised.

I retired from all clinical practice in September 2009, after completing 40 years of service in the NHS.

Wyeth Europa and Pfizer Specialty Care

On retirement from the NHS, from 2008 to 2010 I acted as a consultant and Medical Director Haemophilia to Wyeth Europa in a remunerated consultancy. I led and coordinated their European haemophilia team, giving advice, promoting academic sponsorship of meetings of health care professionals and speaking at meetings in Europe and beyond. In this role I was also responsible for much of the company's relationship with the European Haemophilia Consortium (EHC) and the European Medicines Agency (EMA).

In 2010 Wyeth were taken over by Pfizer and my consultancy was transferred to Pfizer Specialty Care (Europe) as Director Medical and Scientific Affairs (Haemophilia). My role was to continue to build the Pfizer haemophilia team and my responsibilities were very similar to those of my time with Wyeth. I retired from my consultancy in 2015 but continued to work with them occasionally until 2019.

136. **Remunerated roles**

Ipsen Fund (see above)

From 2002-2006 I was a member of the Ipsen Fund Scientific Advisory Board. (see Annual Declaration of Interests in the Pharmaceutical Industry: BART0000869.) The declaration states that the interest was "personally remunerated" but I no longer have a record of this.

Inter Disciplinary Working Group IDWG (Baxter)

IDWG meetings took place over two or three years from 2005 and involved discussions in Rome and Brussels and a final meeting in Vienna in 2008 to create the European Association of Haemophilia and Allied Disorders. The work of the Interdisciplinary Working Group was supported by an unrestricted grant provided by Baxter, who played no part in the academic discussions. I am not sure whether the consultancy was remunerated and I no longer have records for the period but the work did not include any discussion of individual products and factor concentrates have been purchased centrally by tender in the United Kingdom since 2005.

Wyeth and Pfizer (see above)

Following my retirement from the NHS I accepted a consultancy for Wyeth and then Pfizer from 2008 to 2015/19 for which I was remunerated (see 135 above). Neither company was, strictly speaking, involved in the "manufacture or sale of blood products", since their portfolio consisted of recombinant products only.

137. **Advisory Boards, Panels or Committees**

I cannot recall being a formal member of an advisory panel, board or committee of a pharmaceutical company, except as stated above in 135 and 136. I may have attended some advisory meetings for pharmaceutical companies over the years but have no recollection or records of which companies, the dates of any meetings or any remuneration.

I have attended many academic meetings sponsored by pharmaceutical companies over the years, often during annual meetings of academic societies and at other times. I can, for example, recall meetings organised by Octa in Vienna and by Novo Nordisk in Copenhagen. In 2003 (BART0000869) I declared attendance at meetings supported by Aventis, Baxter and BPL but I have no record of them and do not believe that I was remunerated for my attendance. Hospitality was usually offered on these occasions and I believe that all haemophilia centre directors attended

them. Staff members of the centre were also supported to attend meetings in 2003 and this was not unusual.

138. **Financial incentives**

I have never received financial incentives from pharmaceutical companies to use certain blood products.

139. **Non- Financial incentives**

I have never received non-financial incentives from pharmaceutical companies to use certain blood products.

140. **Funding**

I have never knowingly received any funding to prescribe, supply, administer, recommend, buy or sell any blood product from a pharmaceutical company.

The absence of VAT on recombinant factor concentrates delivered to the home, as opposed to the hospital (**home delivery**) was a financial incentive for this practice but there was no financial advantage to any particular pharmaceutical company. I believe that this advantage facilitated the development of a home delivery programme and was known to and understood by the Trust and the purchasing authorities.

141. **Regulations, Requirements and Guidelines**

I do not recall when a decision was made to make an annual "declaration of interests" to UKHCDO and BART0000869, provided by the Inquiry, is an example.

I am not familiar with the details of regulations or requirements or guidelines concerning declaratory procedures for involvement with a pharmaceutical company that have developed over a 40-year period. I believe that I have always abided by current regulations, requirements or guidelines but I cannot comment in detail about a matter of which I have no recollection or record.

142. and 143. **Medical research**

NHS

I have already written about my work for BPL, which I regarded as being part of the NHS.

The Inquiry has sent evidence of my participation in an MRC study of rapid reversal of oral anticoagulants from 1982. This was an NHS product.

My experience of an early heat-treated NHS concentrate manufactured in Oxford is a matter of record.

Commercial

Speywood

I used porcine factor VIII (Speywood) to treat a patient with a weak inhibitor to factor VIII in 1983. I published my findings in a medical journal.

Alpha

I have already mentioned my possible participation in a study of an early heat-treated factor VIII product called Profilate (Alpha) that I believe was organised by Dr Peter Kernoff (deceased) in the late 1980s but I have no written record of this.

Baxter

I have already stated that I contributed patients to a formal study of the clinical use of recombinant factor IX concentrate and, at the time, the product was marketed by Baxter. Professor Pasi, who is now Director of the Haemophilia Centre, may be able to provide information from records held at the Haemophilia Centre, since he is shown, in the publication, as the contributor from The Royal London Hospital.

Novo Nordisk

Novo Nordisk is a Danish pharmaceutical company which manufactures recombinant factor VIIa (rVIIa, NovoSeven) which is not, strictly speaking, a blood product, since the factor is genetically engineered and then expressed in mammalian cells.

At The Royal London Hospital there is a significant population of people with heritable factor VII deficiency (because of consanguinity in an immigrant population) and there is also a major trauma centre and cardiac surgery department.

While I was in practice, patients with factor VII deficiency were treated with rVIIa and the haemophilia centre and/or haematology department were sometimes requested to authorise the use of rVIIa for uncontrollable bleeding in the Emergency Department or the operating theatres (and often out of hours). I have no record of what consent was obtained in these circumstances and I do not believe that any research was undertaken. Some information from The Royal London (and/or other haemophilia centres) may have been used in the granting of a licence for the management of congenital factor VII deficiency and/or to support compassionate use for uncontrollable bleeding, but I have no record of this.

I do not recall providing any other pharmaceutical company with results from any medical research studies that I have undertaken.

144. **Funding**

I do not recall receiving funding from a pharmaceutical company for medical research. There may be information at the Haemophilia Centre or in Professor Pasi's records of the way in which participation in the Baxter recombinant factor IX study was conducted, with particular reference to any administrative funding support that may have been received.

SECTION 10: VCJD

145. **Awareness**

I became aware of the risk of transmission of nvCJD in the late 1990s through my position of Past Chairman of UKHCDO and my regular reading of the New England Journal of Medicine.

146. **Information for patients**

I do not recall the exact details. I believe that we were informed of the patients at risk through the Blood Transfusion Service and information documents were produced for patients, which I think must have been prepared centrally.

147. – 150. **Process**

I cannot recall the exact process for informing patients, but I know that written material was distributed both in person and probably by post as soon as information was available. Detailed information was given on pre-prepared information sheets, but personal contact was vital. What I do recall was the extreme difficulty in knowing what to say at a personal level, especially to the parents of children. The uncertainty was extreme because we simply did not know the true risk, if any, of clinical disease or the possible timescale and there was no clear view of the problem

that could be communicated. This was a very uncomfortable reminder of the agonising decisions which had to be made in factor allocation and communication in the 1980s.

I made the decision to treat all children with recombinant factors, shortly before the government made a similar decision and eventually a "recombinant for all" policy was correctly introduced. The problem was compounded by the sudden failure of recombinant factor VIII production in the USA, so that some people with haemophilia A had to go back on to plasma derived products, although children were mostly protected from switching by the allocation to them of the limited supplies of recombinant concentrates that were available.

151. **Measures**

I cannot easily answer this question, since I do not have access to any files at The Royal London Hospital. I believe that Professor Pasi should be able to answer the question from the Haemophilia Centre's records.

SECTION 11: INVOLVEMENT WITH THE FINANCIAL SUPPORT SCHEMES

152. **McFarlane and Eileen Trusts. Caxton Foundation and Skipton Fund**

I provided certified documents to support the applications of patients from The Royal London Hospital for assistance from the McFarlane Trust and the Skipton Fund. I do not believe that I have had any contact with or provided documentation for the Eileen Trust or the Caxton Foundation.

153. **Information**

The Haemophilia Centre and its staff informed patients fully about the McFarlane Trust and the Skipton Fund. I am not familiar with the Eileen Trust and I believe that the Caxton Foundation came into being after my retirement.

154. **Policy**

I do not recall any written policy or guidance for staff members in relation to referring patients to the trusts and funds for support.

155. **Type of information provided**

I have no precise record or recollection of this, but I do remember that I personally completed many forms on the behalf of my patients. Information may be available from Professor Pasi at the Haemophilia Centre.

156. **Gateway and eligibility**

I recall that I completed the necessary forms, as required, and sent them off to be approved. (See 155). I recall two cases where patients were known to have been infected overseas before arriving in the UK and I may therefore have been unable to confirm eligibility.

157. **Determination of applications**

I have no recollection of my or staff involvement in determining applications made by patients in relation to the trusts and funds.

158. **My experience**

It is now over ten years since I had any contact with patients at The Royal London Hospital, but I remember that I and they, were generally satisfied with the performance of the McFarlane Trust.

I have a rather uncertain memory of dissatisfaction with the bureaucracy of the Skipton Fund, but I cannot give details at this distance in time.

SECTION 12: OTHER ORGANISATIONS

159. **Haemophilia Society**

I have been a subscribing member of the Haemophilia Society for 45 years and remember being present at their Silver Jubilee in 1975. I spoke at their meetings and wrote for their journal from as early as 1982. My curriculum vitae states that I was a Member of their Medical Advisory Board from 1982 to 2007 but I do not believe that I was called on to advise them formally in recent years. It may be that my Advisory Board membership ended without my knowledge at some point. When I did advise the Society, I always found them to be well informed, friendly and supportive of their members and I have always admired the work they do and have done for people with haemophilia and allied disorders. The tragedy of infected blood has undoubtedly placed a great strain on the work of the Society, because they have had to look back to the problems of the past at the same time as they prepare their membership for the opportunities offered by the future.

I gave evidence to the Archer Inquiry in 2008 at the specific request of the late Reverend Alan Tanner (a founding member and vice-president of the Haemophilia Society, chair of their board of trustees for 22 years, as well as past chairman of the World Federation of Haemophilia, and the Macfarlane and Eileen Trusts). For many years I have also done my best to attend the Annual Service of Thanksgiving and Remembrance for those who have died from infected blood. At Alan Tanner's request I used to read a lesson or poem at this service.

In 2019 the Haemophilia Society's Chief Executive, Ms Liz Carroll, asked me to see the son of one of my former patients, as he wished to discuss his father's case. I agreed to the meeting which took place in the Haemophilia Society offices in her presence and she took a note. She later told me that the meeting had been helpful.

SECTION 13: OTHER ISSUES

160. **Introduction of Recombinant Products**

I introduced recombinant products for children just before The Secretary of State in 1998, Mr Frank Dobson, issued a policy, I believe in February, to provide recombinant concentrate for children and previously untreated patients. I introduced recombinant products for children just before this statement because I felt that I could not tell parents that their children might have been exposed to nvCJD when a product prepared without plasma was available. This decision was complicated by the fact that, at that time, human albumen was still present in recombinant products and also that plasma derived from the USA was almost certainly prion free. I remember informing the Trust's Medical Director of my decision and he concurred. Recombinant product for adults was then introduced according to government policy.

161. **Complaints**

In 1990 I was required to prepare the defence of the Trust for approximately 30 law suits relating to the campaign for compensation concerning the HIV infection of blood products. I worked with The London Hospital's lawyers (Beachcroft Stanley) until the suits were withdrawn as a result of the McFarlane Trust being set up by the John Major government. I have retained no information from this period.

I am not aware of any complaints of any kind concerning my professional or personal conduct ever having been made to my 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. The Barts Health NHS Trust, Medical Defence Union and General Medical Council should be able to confirm this.

On the contrary, I have a personal dossier of messages of appreciation from patients.

This statement excludes the Witness Statements I have received from the Infected Blood Inquiry.

162. **Other Issues relevant to the Infected Blood Inquiry**

A global tragedy

I believe that the idea that the infected blood tragedy was, in some way, avoidable is not justified so long as blood products were used for treatment. I draw the Inquiry's attention to the fact that the same problems arose within the whole of the developed world, including North America, Western Europe, Australia, New Zealand and Japan.

Who was affected?

I am disappointed that the Terms of Reference of the Inquiry do not appear to include all those who were "affected" by the tragedy of infected blood. Nurses, laboratory staff, professionals allied to medicine and medical staff, all had to manage a problem that concerned a number of initially unknown transmissible agents in unprecedented circumstances over a fifty-year period from 1970 until the present day.

They had no means of knowing the extent to which they were also at risk of infection and had to deal with problems of diagnosis, treatment, counselling, breaking bad news and bereavement, for which they had little, if any, training. There was little recognition at the time that staff had anxiety and needs of their own and none has been apparent in recent years.

The nature of "mild (and moderate) haemophilia"

There has been an understandable tendency for the haemophilia community to equate "mild haemophilia" with mild bleeding. This is very far from being true and I have cared for many patients with "mild haemophilia" who have had catastrophic bleeding. For example, I once saw a patient, who proved to have "mild haemophilia" who was operated on in his seventies for prostate enlargement and was referred to me when he nearly bled to death. It is possible to go through life without bleeding problems and yet be diagnosed with true haemophilia and require urgent and timely blood product and concentrate support.

The position in 1984/85

It is clear that, by 1984/85 HIV had also entered the British donor pool and we later became aware that some patients became HIV positive and developed AIDS from British sourced products.

Early heat-treated concentrates had failed to prevent HCV infection and it later became apparent that some early heat-treated factor concentrates were capable of transmitting HIV infection, (probably because of heavy contamination and inadequate viral inactivation), until 1986/87.

Inhibitors

It is important to understand that inhibitor development in haemophilia A or B has been a very serious problem which, in the past, could render people with haemophilia almost untreatable. There are some specific genetic mutations which cause apparently mild or moderate haemophilia but are associated with a very high risk of inhibitor development after replacement therapy, leading to major treatment and lifestyle difficulties.

Laboratory tests

The early tests for HIV and HCV infection were not reliable because of problems with both specificity and sensitivity. Those of us who were trying to grapple with a rapidly moving and uncertain epidemic had no reference points on which to rely, even when the first tests became available. Today, in the midst of the Covid 19 pandemic, there is much discussion about antigen and antibody testing (which we did not possess at the beginning of the crises of the 1980s). The uncertainty of the meaning of test results is evident today in exactly the same way as was the case nearly 40 years ago.

The pharmaceutical industry and the haemophilia community

I have spent the last 50 years in various aspects of haemophilia care and am proud to have worked for 40 years in and for the NHS. During that time the relationship with pharmaceutical companies has been difficult and complex but without the industry I believe that much less progress would have been made in this field.

Examples are, a) the chemistry required for plasma fractionation, b) development of viral inactivation procedures, c) the chemical separation and structural identity of coagulation factors d) the genetic identity of haemophilia A and B and vWD, e) the preparation of various recombinant coagulation factors and f) recent research leading to revolutionary solutions to haemophilia care, such as gene therapy.

When, after my retirement from the NHS, I acted as a consultant to Wyeth and Pfizer, I learned about modern practice in the industry and its regulation and I tried to create and develop an educational and academic approach to the company's relationship with European care services, including those of the United Kingdom.

Today the media is full of the importance of collaborative working between the NHS, UK academic laboratories and the pharmaceutical industry to develop laboratory tests and to prepare, validate and produce an effective vaccine against coronavirus. I do not believe that anyone questions the importance of this work.

I am more than ever convinced of the value of appropriate collaboration between governments, patient representatives, healthcare systems, physicians, professions allied to medicine, and industry in optimising haemophilia care in the future.

STATEMENT OF TRUTH

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

I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

GRO-C

Signed: .....

Name: .....Brian T. COLVIN.....

Dated: .....28th August 2020.....

Table of exhibits:

Date	Notes/Description	Exhibit Number
August 2019	Curriculum Vitae for Professor Brian T Colvin	WITN3343008
2 March 2020	General Rule 9 Request	WITN3343009

Witness Name: Dr Brian Trevor Colvin
Statement No.:WITN3343007
Exhibit:WITN3343008-9
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INFECTED BLOOD INQUIRY

WITNESS STATEMENT OF

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