Witness Name: Frank Boulton
Statement No.: WITN3456002
Exhibits: WITN3456003-
WITN3456006
Dated: 26 October 2021

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DR FRANK BOULTON

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 11 June 2021.

I, Dr Frank Boulton, will say as follows:

Section 1: Introduction

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

1. Name: Frank Ernest Boulton
2. Address: C/o NHS Blood and Transplant, 500, North Bristol Park, Filton, Bristol, BS34 7QH
3. Date of birth: GRO-C 1941
4. Professional qualifications: MD (London University), FRCPath, FRCPEd

2. **Please set out your employment history with dates if possible, including the various roles and responsibilities that you have held throughout your career.**

5. Employment history, roles and responsibilities

   a. Trainee pathologist St Thomas' Hospital 1967 to 1970

   b. Senior Registrar in haematology, The London Hospital, 1971 to 1973 (Dr George Jenkins and Dr Adam Turnbull)

   c. Senior Lecturer, The London Hospital Medical College, 1973 to 1975 (Prof George Jenkins). Under Prof Jenkins I began to expand the clinical service to local haemophiliacs .

   d. Senior Lecturer and honorary consultant haematologist, University of Liverpool and Royal Liverpool Hospitals 1975 to 1980 (Prof Alastair Bellingham). Prof Bellingham delegated to me the responsibility for the clinical and laboratory service to haemophiliacs – children and adults, although care for children admitted to hospital was shared with Dr John Martin of Alder Hey Hospital.

   e. Consultant haematologist, Edinburgh and South East Scotland Region Blood Transfusion Service, Royal Infirmary of Edinburgh, 1980 to 1990 – deputy Director from 1982 (Dr Brian McClelland, Regional Director; Dr John Cash, SNBTS Medical and Scientific Director). I had responsibilities for the blood products laboratory which included the production of cryoprecipitate, and the supplies of all 'wet' blood products to Regional hospitals in Lothian and the Borders (whole blood, red cell concentrates, platelet concentrates, leucocyte concentrates, fresh frozen plasma (FFP) and cryoprecipitate for clinical use); and the supply of FFP for fractionation at the Plasma

Fractionation Centre (PFC) recently built at Liberton Hospital, Edinburgh. The clinical blood banking services for the RIE and associated hospitals was also my direct responsibility: the Western General Hospital and the more outlying hospitals (St Johns), Peel (Melrose) had their own blood banks administered by clinical and laboratory staff in those hospitals. The day-to-day work of the EBTS/RIE blood bank was conducted by specialist Medical Laboratory Scientists. From 1982, as Deputy Director I became responsible for the clinical laboratory serological diagnostic services run by specialist Medical Laboratory Scientists: most of this work was for antenatal serology associated with alloimmune haemolytic disease of the newborn ('rhesus babies'). This was linked to the supply of blood and blood products, and anti-D immunoglobulin when indicated, for such babies. For the last year of my appointment there I transferred to take charge of the donation sessions and the care and selection of blood donors.

f. Medical Director, Wessex Regional Blood Transfusion Service, Wessex Regional Health Authority, Southampton, 1990 to 1995 (Chief Executive Officer from 1992 to 1995), (Dr Graham Winyard, Wessex RHA Medical Director and Mr Ken Jarrold, Chief Executive, Wessex RHA). Initially, Director responsibility for the WRTC was shared with a General Manager, Mr Jim Smith, who was recruited in 1988 from the managerial staff at the RHA. A year or so after my appointment (in October 1990), Mr Smith was redeployed back to the RHA and I was asked by Dr Winyard to take sole Directorial responsibilities as 'Chief Executive Officer'. This was my role at the WRTC until officially taken over by the NBA in 1995.

g. Consultant haematologist, 1995-2006, National Blood Authority based at Wessex RTC, Southampton. WRTC was incorporated into the South Western Region of the NBA and I became accountable to Dr Tim

Wallington, based at Bristol, and to Mr Gary Austen who was General Manager there. During this time, I continued to liaise with the clinical blood banking services in the Wessex Region, and participated in clinical haematology meetings (including paediatric haematology) and rounds at Southampton General Hospital (University of Southampton Hospitals Trust). Specifically, I participated in the training of newly appointed medical staff (junior doctors) in how to use the hospital's blood bank. These occasions were twice each year during the first week of their appointments as 'house doctors' and – later – as F1 and F2 pre-registration doctors. This teaching came to be conducted in collaboration with the Southampton General Hospital (SGH) blood bank nursing officer and proved a useful continuing link with the work of the SGH blood bank staff.

h. Honorary Civilian Consultant Advisor to HM Armed Forces on Blood Transfusion. I accepted this honorary unremunerated position in 2000 and retained it until my retirement. This involved attending meetings at Millbank (I think three during my time) and giving occasional ad hoc advice to Medical Corps field operations overseas by audiolink.

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

6. Membership of relevant committees, parties, societies or groups, with dates:

a. As a Fellow of the Royal College of Pathologists, I joined their Blood Transfusion subcommittee which included identifying issues relevant to the training in transfusion for candidates for the haematology examination for Membership of the RCPath. I was also a regular examiner of such candidates for the practical examination in blood

transfusion techniques and practices for most of my time at WRTC, including after the establishment of the NBA.

b. I joined the British Society for Haematology as a trainee at the London Hospital in 1971. I have retained my membership.

    i. In the year 2000 I was appointed by the BSH as convenor of the BSH task force for clinical standards in blood transfusion. This involved preparing and publishing Guidelines for hospital staff conducting the transfusion of blood and blood products to patients.

c. I was a founder member of the British Society of Haemostasis and Thrombosis (BSHT) in 1981. My membership lapsed on my retirement.

d. In 1994 I joined the UK Standing Advisory Committee on the Selection of Donors, becoming its Secretary and, from the late 1990s the Chair of the SACSD when we added 'Care of Donors' which changed the acronym to 'SACCSD'. This was specifically to produce Guidelines for the selection of donors and the production of information sheets for donation collecting staff in the form of a 'Red Book' (which was updated in 2002) and regularly revised 'A to Z' guidelines which were very detailed. This work was conducted in close association with the SACTTI, and later with the SAC on Tissue Banks (tendons, Corneas, etc). In association with SACTTI, I attended meetings concerned with the risks of transfusion-transmitted prions associated with the outbreak of BSE and vCJD in the mid-1990s.

e. I was a founder member of the British Blood Transfusion Society and was elected President for the years 2005 to 2007. This is a multi-professional Society and most of its Board Members were experienced senior scientists as well as medical doctors. Wessex RTC

hosted the annual meeting of the BBTS in Southampton in 1994. In 2000 I helped to initiate the BBTS 'Special Interest Group' in Hospital Based Transfusion Practice. I have retained my membership of the BBTS.

f. I also joined the International Society of Blood Transfusion (ISBT) in the 1980s and maintained my membership while working for the NBA. During this time I also became an official consultant on blood transfusion to the WHO and attended meetings in Geneva. I allowed my ISBT membership to lapse a few years after my retirement in 2006.

4. Please explain how you kept abreast of medical and scientific development and research in your field in the course of your career.

7. Continuing professional development:

a. I have been able to keep abreast of medical and scientific developments and research through attending conferences of the professional societies to which I belonged, keeping up to date with medical literature particularly the major journals: BMJ, Lancet, the British Journal of Haematology, Transfusion, and Vox sanguinis.

b. I still subscribe to the BMJ, Lancet and BJH, and continue to take an interest in ongoing medical developments including the clinical complications of bleeding and clotting disorders caused by covid-19 and vaccinations. Of significant concern is continuing the supply of 'safe' blood for UK patients during the ongoing pandemic and possible challenges during the coming winter. (I read the article by Stanworth et al, Lancet October 2020, with great interest) RLIT0000717).

c. I still teach medical students and have led 'Student Selected Courses' for third year medical students at Southampton University

on Clinical Haematology and Blood Transfusion each year for the past 30 years. Each course consists now of ten sessions once a week in two blocks each year, each session lasting two hours. Last year (up to June 2021) I was assisted by another consultant haematologist in the Region. Since March 2020 the courses have been delivered online. In leading such courses, it is essential to keep up to date with the literature and with clinical experience: for me the latter has been helped by my colleague referred to above.

5. **Apart from the Penrose Inquiry, please confirm whether you have provided evidence or have been involved in any other inquiries, investigations, criminal or civil litigation in relation to the human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Creutzfeldt-Jakob disease ("vCJD") in blood and/or blood products. Please provide details of your involvement.**

8. Evidence to other official Inquiries or civil litigations etc.:

   a. Apart from the Penrose Inquiry, I have not been involved in any other Inquiry relating to the transmission of HIV, HBC, HCV or prions by the transfusion of blood or blood products.

   b. I was a witness to a Coroner's inquiry into the post-transfusion death in 1998 of a patient who contracted a transfusion-transmitted infection of the bacteria *Serratia liquefaciens*. This case was reported in the journal 'Transfusion Medicine' in 1998 - doi: 10.1046/j.1365-3148.1998.00119.x. This case was of some interest at the time as a few other sporadic cases of blood transfusions contaminated by *Serratia* (which is an environmental contaminant) were being reported. This case did not result in further enquiries or litigation.

Section 2: Decisions and actions of the Liverpool Haemophilia Centre

6. How many patients with bleeding disorders were under the care of Liverpool Haemophilia Centre ("Liverpool HC") between 1975 and 1980? (If you are able to give exact rather than approximate figures, please do so). In answering this question you may be assisted by the Liverpool Annual Returns for 1976—1980 (HCDO0001093, HCDO0000081_004, HCDO0001178, HCDO0001275, HCDO0001344 and HCDO0001440).

9. I have kept no personal data but from the documents supplied:

a. No return for 1975 – but my appointment there began in October 1975
b. 1976 – 48 with F VIII deficiency; 6 with vWd; 7 with F IX deficiency
c. 1977 – 56 with F VIII deficiency; 3 with vWd; 8 with FIX deficiency
d. 1978 – 58 with F VIII deficiency, 1 with vWd; 4 with FIX deficiency
e. 1979 – 49 with FVIII deficiency; 1 with vWd; 5 with FIX deficiency

10. These numbers accord with my general recollection.

Hepatitis B

7. How many patients at Liverpool HC were infected with hepatitis B?

11. The documents show that 8 people were recorded as having jaundice but two of these may be duplicated (1977 and 1978). One extra – a boy – was confirmed to be positive for HBsAg but was not jaundiced. All were F VIII deficient haemophiliacs; none had F IX deficiency or vWD.

8. Were patients infected with hepatitis B in consequence of their treatment with blood products informed of their infection? If so, how?

12. I cannot say for definite but my policy was to inform all such patients or the parents of patients who were minors. I may well not have met some of them if they were diagnosed before I came to Liverpool. Three of them were on home therapy – judging by the partially redacted dob record, two were teenagers and one was a child. The child was the confirmed HBsAg positive and his parents would have been informed but I cannot confirm that. (It might help if more details of patient identity were to be made available to me.) One man with mild F VIII deficiency (12%) who had a vasectomy under Kryobulin commercial F VIII cover was reported belatedly to me to have contracted a very mild form of hepatitis while I was out of the country. I believe he may be identified as the entry in the table in form A (2) second page 7th row – dob - - 32; basic F VIII 12%; no inhibitor; Jaundice 'YES' (my handwriting, after crossing out a 'no' entry); not on regular home therapy.

9. What information was provided to patients infected with hepatitis B about the infection, its significance, prognosis, treatment options and management? What if any involvement did you have in this process?

13. Apart from the man who had a vasectomy under Kryobulin cover, another patient documented to have had hepatitis B (who was HBsAg positive in 1978, but was not jaundiced) was the boy on home therapy. He received cryoprecipitate for hospital treatment and commercial F VIII concentrate (Factorate) from just one manufacturer in my time. I cannot recall why he was tested for hep B. My policy when advising and training parents administering home therapy included information on the risks, which would have included the possibility of developing inhibitory antibodies to FVIII and also of contracting viral hepatitis from the F VIII product preferred for HT (home treatment). This was usually a commercial freeze-dried powdered concentrate product as they were easier to administer and dissolved more readily in the distilled water also supplied than the NHS BPL product.

14. The care of boys with haemophilia was shared with Dr John Martin, Consultant Paediatric Haematologist at Alder Hey Hospital. We shared a regular (monthly) integrated clinic at the Liverpool Royal Infirmary/Royal Liverpool Hospital seeing patients and their parents in the company of dentists, occupational therapists and physiotherapists during which we discussed the principles of haemophilia care which would have included the risks of transfusion-transmitted jaundice. I have no records to confirm this practice but can testify that such a system, which was conceptually quite advanced at the time, was in operation during my tenure at Liverpool. The haemostasis diagnostic laboratory at the LRI was part of my responsibility for patients of all ages in Merseyside.

15. I also attended meetings of the local Haemophilia Society – set up by the father of one of the haemophilic boys with my active support. Home therapy was a topic at such meetings and although the emphasis was undoubtedly on the virtues of F VIII / IX replacement therapy and its enhancement by a home-treatment regime, the possibilities of jaundice were also mentioned although by modern expectations the risks were probably under-emphasised.

16. Because HBsAg positivity not only marks infectivity, particularly by parenteral spread, and because home therapy involved preparing potentially infectious blood products, parents were instructed to avoid needle-stick injuries to themselves: they would also have been advised that an injury to them from a needle after it had been used for injection to the boy also carried a risk of virus transmission. I have little evidence that any parents really understood the significance of such points which, at the time, seemed to be of secondary importance to the therapeutic benefit to the patient of receiving effective haemostasis.

NANB Hepatitis

10. Were patients infected with NANB hepatitis informed of their infection and if so, how and by whom?

17. As far as I can recollect, no patients at Liverpool were found to have NANB hepatitis. I was very aware of the existence of viruses other than Hep A and Hep B which could infect the livers of people (and chimpanzees) exposed to blood products and observed possible 'cases' during my specialist training. I was also aware of the work of Dr Craske of Manchester. By 1972 or so, transfusion-transmissible hepatitis should have been common knowledge to haematologists as well as hepatologists. The most common NANB virus – hepatitis C – was not identified until the late 1980s and diagnostic tests only became available in 1990 / 1991.

11. What information was provided to patients infected with NANB hepatitis about the infection, its significance, prognosis, treatment options and management? What if any involvement did you have in this process?

18. Meaningful discussions about NANB would have been difficult before 1980 as so little was known about the pathology of the then putative viral origin: I was not employed at the Liverpool Centre after 1980 so I do not know the position after then.

Informing patients

12. Were the results of testing for hepatitis (of all kinds) notified to patients promptly, or were there delays in informing patients of their diagnosis? If there were delays in informing patients, please explain why.

19. I cannot recall. Some parents may have been informed at the next integrated clinic with Dr Martin – which may have been expedited – but I have no recollection of any specific episode of this sort.

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

20. Transfusionists during WW2 became aware of 'homologous serum jaundice' associated with transfusions of freeze-dried plasma or plasma-derived vaccines, but the low apparent incidence (a few percent) and the mostly subclinical apparent effects made it difficult to appreciate its true significance, and there was little or no understanding of long-term effects such as cirrhosis (which was mostly diagnosed post-mortem). The population-wide increasing incidence of cirrhosis found at autopsy during the 1970s was mostly attributed to rising alcohol consumption, but some physicians were becoming uneasy about possible long-term implications of serum jaundice. The World In Action TV programme in 1975 drew attention to the dangers of 'skid row' blood donations and warned that such donations posed increased risks especially if their plasma was pooled for preparing factory-scale quantities of blood products such as F VIII and F IX. It also pointed out that the UK transfusion services' blood donors (some of whom were prisoners) are not hepatitis-transmitting risk-free either. (Donations collected from prisoners were stopped by the mid-1980s.)

21. In the late 1970s, Dr Eric Preston published data showing alarmingly high incidences of cirrhosis in the livers (taken, rather daringly, by biopsy) of haemophilic men. This advanced our appreciation of the possible long-term effects of chronic hepatitis, but many haemophilia practitioners were reluctant to monitor haemophiliacs' liver function by biopsy although Preston had shown that blood tests of liver enzyme activity were consistent with the biopsy findings. My recollection is that by 1980 the (pre-AIDS) haemophilia community was becoming more concerned about

transfusion-transmitted hepatitis but the drive for 'bleeding-free independence' for haemophilic children usually over-rode such concerns. Hence, the understanding of the public health implications of hepatitis B and NANB were still poorly developed – not enough to override the clinical demand for F VIII even though this topic was occasionally presented to members of the Liverpool Haemophilia Society (but admittedly probably somewhat underplayed).

22. The commercial product most strongly criticised by World In Action was Hyland's Hemofil.

23. For 1976, Liverpool HC's largest commercial supplier was Immuno Kryobulin (365,545 units, c 42% total F VIII supply compared with 53% from Liverpool RTC cryoprecipitate and 1.5% NHS F VIII concentrate). Kryobulin was sourced from Paid donors from Europe (mostly Austria).

24. For 1979. Liverpool HC's largest commercial supplier was Armour's 'Factorate' (550000 units, c 41% total F VIII supply compared with 47% from Liverpool RTC cryoprecipitate and 1.6% from NHS F VIII concentrate). (see the Table attached to Q 38).

25. So we tried to meet the public health concerns by maximising cryoprecipitate use for 'routine' hospital care and taking the perceived least undesirable commercial concentrate (in terms of viral transmission risk) which was also the most easy for patients on home therapy and the most consistent for high doses needed to cover surgery or bleeding episodes in patients with inhibitors.

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

26. Patients' and parents' appreciation of the World In Action programme probably led them to emphasise the undesirability of 'skid row' derivatives

but we told them of the possibility of transmission of other infections though detailed individual discussions were probably infrequent. Patients and parents were probably informed mostly through their attendance at meetings of the local Haemophilia Society which, though often well attended, may well not have reached all the interested parties. None of these meetings were 'sponsored' by any commercial or pharmaceutical agency.

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

27. This was mostly provided in the home treatment setting. Other modes of transmission – such as sexually – were rarely mentioned and I don't remember discussing the risk of sexual transmission of hep B with patients or parents although I can imagine circumstances when this might have been appropriate.

Consent

16. How often were blood samples taken from patients attending Liverpool HC and for what purposes?

28. Blood samples were only taken for initial diagnostic purposes or for monitoring the effect of treatment (factor recovery in the patient's circulating blood). Every bleeding episode requiring hospital treatment would have had 'before and after infusion' assays of factor levels in the patient's blood. Blood samples would also have been required for monitoring patients' liver enzymes (as a test of liver function) or general screening (electrolytes and renal function, etc), but I cannot recollect how often this occurred.

17. What information was given to patients about the purposes for which blood samples were taken?

29. Patients and parents would have been told the results of factor recovery tests, including before and after administering DDAVP to mild haemophiliacs (or patients with vWD). I cannot recall how much information was given to adults or the parents of minors from whom samples were taken for HBV but am confident that they would have been informed of the need to exclude any condition meriting such tests. As far as I know, no samples taken from patients during my time at Liverpool HC were subsequently tested for other viruses including for HIV or for HCV.

18. Were patients asked to consent to the storage and use of the samples? Was their consent recorded and, if so, how and where?

30. I do not recollect any blood samples being stored for such purposes, or whether consent for such storage was sought.

19. Did Liverpool HC have a bank of stored samples? If so, was that storage undertaken with patients' knowledge and consent?

31. I do not recall retaining or storing any blood samples after the cessation of the clinical management of any episode .

20. Were patients under your care or under the care of your colleagues at Liverpool HC treated with factor concentrates or other blood products without their express and informed consent? If so, how and why did this occur? What was your approach to obtaining consent to treatment? Was their consent recorded and, if so, how and where?

32. I always obtained patients' expressed and informed consent before treatment, but this was verbal and probably not specifically recorded at the

time, although any treatments would have been recorded in the patients' notes.

21. Were patients under your care ever tested for hepatitis or for any other purpose without their express and informed consent? If so, how and why did this occur? What was your approach to obtaining consent for testing? Was their consent recorded and if so how and where?

33. We obtained expressed consent generally as part of the discussion with patients or parents concerning the management of whatever clinical situation was presenting. This would have included tests for hepatitis if indicated but may not have been expressly recorded as such.

PUPS

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

34. The only 'PUPs' we cared for and treated would have been newly diagnosed patients, most of whom would have been young boys. I cannot recall any specific episode or 'actions' such as this, or of the type to which you refer, but expect that a few of the young newly diagnosed boys – of whom there were very few – would have been treated under my care or, more likely, under the excellent care of Dr John Martin at Alder Hey or the Children's Hospital in Myrtle Street.

Treatment of patients who had been infected with hepatitis

23. How was the care and treatment of patients with hepatitis managed at Liverpool HC? Please answer the following questions with reference to hepatitis B and NANB hepatitis respectively. In particular:

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

35. I recall no patients newly diagnosed with hepatitis during my time at Liverpool other than the boy found positive for HBsAg. I do not recall what happened to him – possibly because he might have been referred to specialist paediatricians responsible for liver disease.

b. What treatment options were offered during your tenure?

36. Not relevant.

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

37. I cannot recall, but pharmaceutical treatment options at that time were very limited.

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

38. I do not know.

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

39. I do not know.

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

40. I cannot recall – I think that most of the 6 or 7 patients recorded during my time were simply followed up in the integrated clinic.

27. What, if any, involvement did you or your patients have with clinical trials in relation to treatments for hepatitis? Please provide full details.

41. Not relevant.

Records

28. What was Liverpool HC policy with regards to recording information on death certificates when a patient had been infected with hepatitis? Were you involved with any inquests in relation to patients who had been infected with hepatitis as a consequence of their treatment? If so, please provide details.

42. No patients under my care at Liverpool died of, or with, hepatitis.

29. What were the retention policies of Liverpool HC in regards to medical records during the time you were practising there?

43. Records were retained in the Hospital's medical records department.

30. Did you:

a. maintain separate files for some or all patients? If so: why; where were those files located; and where are those files now?

44. No.

b. keep records or information (e.g. information being used for the purpose of research) about any of your patients at your home or anywhere other than at Liverpool? If so, why, what information and where is that information held now?

45. No.

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

46. No.

Selection, purchase, and use of blood products

32. In answering the following questions you might find it helpful to refer to the transcript of your oral evidence given to the Penrose Inquiry (PRSE0006024). It may also be helpful to refer to UK Haemophilia Centre Directors ("UKHCDO") meetings held between 1975 to 1979 (OXUH0003735, PRSE0001002, HSOC0010549 and CBLA0001028).

a. To the best of your knowledge, what decisions and actions were taken, and what policies were formulated by Liverpool HC, regarding the selection, purchase and use of blood products (in particular factor concentrates) during the time that you worked there?

47. The UK Haemophilia Centre Directors had started convening for mutual discussions and advice-sharing from the late 1960s. By 1975, when I began my appointment at Liverpool, Centres submitted annual reports on their own practices and experiences including the amounts of various F VIII-rich products of NHS and commercial origin, cryoprecipitate (supplied

by Regional Transfusion Centres) and non-blood agents such as DDAVP. These meetings were invaluable. Commercial companies were not invited, but representatives from the various companies made themselves well-known to HCDs including myself. Acquisition policies for Liverpool HC were devolved to me by Professor Bellingham – in practice I made the final arrangements. BTS supplies of cryoprecipitate were reliable and made up almost half of total F VIII use. NHS F VIII from BPL at Elstree or PFL at Oxford made a minor contribution – less than 2% of all F VIII products including cryoprecipitate. The remaining supplies were commercial in origin. In 1976, the main commercial supply was of 'Kryobulin' from Immuno whose sources were paid blood donors of European origin. Although Hyland's 'Hemofil' was also available at comparable prices, Hemofil had featured prominently and adversely in the World In Action programme of 1975 so I obtained only small quantities. By 1979, Armour's 'Factorate' became the major supply and supported the expanding home therapy programme being developed at Liverpool. It was also the main supply of F VIII for haemophiliacs with inhibitors although non-F VIII products (such as 'FEIBA') were also used for haemophiliacs with F VIII inhibitors (who used about 3% of the total supply of 1.3 million units of VIII in 1979).

b. How, on what basis, and by whom, were decisions made about the selection and purchase of blood products? If the responsibility for the selection and purchase of blood products lay with an organisation other than Liverpool HC, please specify which organisation and provide as much information as you can about its decision-making.

48. I carried the sole responsibility for selecting the commercial concentrates but had been given a guiding budget for their purchases by the Treasury Department of the LRI (£40,000 a year). In 1977 (I believe) I incurred costs of £50,000 which, however, was acceptable to the Treasurer. This enabled me to procure about 500,000 units of commercial F VIII which was about

half the annual consumption (the total included cryoprecipitate, the amount being estimated from the periodic monitoring of the F VIII content by the RTC at about 70 iu F VIII per pack as it was naturally not possible to assay each pack of cryoprecipitate).

c. What (if any) other bodies or organisations or individuals (e.g. other centres in the same region, or the Regional Health Authority) were involved in the arrangements for the selection, purchase or use of blood products?

49. I selected: the LRI purchased.

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

50. In practice, there was little to choose between each commercial product on the grounds of ease of use (particularly for home therapy) although by 1979 Armour Factorate became the home therapy (HT) product of choice for Liverpool HC; as far as I remember, HT patients liked it for its solubility in the water also provided for each vial which made it easier to administer by i.v infection. It seemed that there was little variation in the risk of transmitting hepatitis between the various commercial products.

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

51. None.

f. What, if any, involvement did you have?

52. For both these points, see my answers above.

33. What products or treatments were generally used for treating (i) patients with severe haemophilia A; (ii) patients with moderate haemophilia A; (iii) patients with mild haemophilia A; (iv) patients with haemophilia B; (v) patients with von Willebrand's disease? In answering this question you might find it helpful to refer to the Liverpool HC Annual Returns (HCDO0001093, HCDO0000081_004, HCDO0001178, HCDO0001275, HCDO0001344 and HCDO0001440).

53. (i) - Cryoprecipitate; NHS factor VIII concentrate ('Elstree'), commercial freeze-dried standardised factor VIII concentrates, especially for home therapy Cryoprecipitate.

54. (ii) and (iii) - Cryoprecipitate – but one mildly affected haemophilic was given commercial factor VIII to cover vasectomy. I think I only became aware of this after the event – I would have preferred cryoprecipitate or DDAVP if that option had been available.

55. (iv) - Oxford NHS F IX.

56. (v) - Cryoprecipitate and / or DDAVP (when this was discovered). In 1977, a patient in North Wales with severe (probably homozygous) vWd had profuse bleeding from his vocal cords (he was a folk singer) which required large amounts of cryoprecipitate and one treatment episode with Immuno Kryobulin before coming under control. DDAVP was ineffective.

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

57. Home therapy patients and patients with inhibitors were treated with commercial F VIII concentrates.

58. Patients in hospital received cryoprecipitate mainly; more mildly affected patients were offered DDAVP when it became available. Patients were informed about the alternatives – especially DDAVP and consented verbally.

35. The Inquiry understands that there was no Haemophilia Reference Centre in North Wales and that patients were treated within local general hospitals or referred to Liverpool HC (see TREL0000311_027, a letter from you to Dr P Kirk dated 26 July 1977). Please describe, insofar as you are able to, your understanding of the relationship between Liverpool HC and North Wales in the context of haemophilia care; and whether the relationship had any impact on the decisions made by Liverpool HC regarding the selection, purchase and use of blood products to treat haemophiliacs.

59. I can only recall the background to this letter rather imprecisely. It seems that this patient, whose hometown was GRO-A was resident at Treloar in the care of Dr Kirk where his routine treatment included 'Lister F VIII'. While holidaying at his home in GRO-A in July 1977, he presumably had a bleed for which he attended the local hospital and received cryoprecipitate which presumably came from Liverpool. The GRO-A haematology department's technician seems to have asked the Manchester Regional Centre for a supply of Lister F VIII and (presumably) received a small supply from the Manchester Director Dr Wensley (there is an indication in my letter that Dr Wensley wrote to me about this); this was presumably deemed insufficient and the technician approached Treloar for a supply of more Lister F VIII. It is not clear why GRO-A asked Manchester but presumably the technician did not realise that the Liverpool Regional BTS which supplied all blood and blood products including cryoprecipitate to Merseyside and all of North Wales, including GRO-A was linked for haemophilia care with the Haemophilia Centre at Liverpool Royal Infirmary. The fact that the patient was not registered with the Liverpool HC may also have complicated GRO-A management – I have no information on that.

60. So to clarify: the area covered by the Merseyside and N Wales Regional BTS was the same as that covered by the Haemophilia Centre at the Liverpool Royal Infirmary, and the LRI HC staff were in regular communication with colleagues at the Merseyside and N Wales RBTS – including at Medical Consultant level. The selection, purchase and use of blood products for haemophiliacs in N Wales was in theory co-ordinated between the staff of the RTC and the Liverpool HC. Occasionally, through misunderstandings as exemplified by this episode, such arrangements broke down.

36. What was the relationship between Liverpool HC and the pharmaceutical companies manufacturing/supplying blood products? What influence, if any, did that relationship have on Liverpool HC's decisions and actions? In answering this question, please describe the kinds of interactions and communications (such as visits from sales representatives) you had with pharmaceutical companies which supplied factor concentrates. You may be assisted by considering the following: Letter from David Williams (Speywood) to you dated 14 February 1979 regarding Koate (IPSN0000337_024); Letter from David Williams (Speywood) to you dated 3 August 1979 regarding Koate (IPSN0000337_016).

61. See my answer to Q 32.

62. Sales Representatives of pharmaceutical companies supplying F VIII were very active with all UK HCDs at this time: Speywood were no different. The offer of reduced-price Cutter Koate for 1979 mentioned in doc IPSN0000337_016 seems to have been followed by an order for the 150,000 units used that year. I cannot recall the precise circumstances or the context of the comments about the rabbits in that 016 letter. We never used porcine F VIII concentrate (Speywood's speciality) but we did have patients with inhibitors who were potential candidates for that product.

37. What alternative treatments to factor concentrates were available during your time as Director of Liverpool HC for people with bleeding disorders? What were, in your view, the advantages and disadvantages of those alternative treatments? What use did Liverpool HC make of them? Do you consider that they should have been used in preference to factor concentrates so as to reduce the risk of infection? If not, why?

63. For haemophiliacs and people with von Willebrand's Syndrome, cryoprecipitate was the only alternative to factor concentrates until DDAVP became available from 1978 for mild haemophilia and for vWD. 40% of all the transfused F VIII in 1979 was as cryoprecipitate. The demand for F VIII far exceeded the supply of UK blood donor-derived F VIII even working at full capacity. However, cryoprecipitate is quite difficult to re-formulate as an intravenous transfusible material: each treatment episode requires several single frozen units to be carefully thawed and pooled, either on the ward or in the haematology laboratories, and administered immediately as it has a short shelf life. There is also a significant risk of introducing environmental infectious material such as bacteria during preparation and administration. However, whenever sufficient quantities of cryoprecipitate were available, it would have been preferred for hospital use except for large repeated doses such as for major injuries and/or surgery.

38. What was Liverpool HC's policy and approach to:

a. the use of cryoprecipitate for the treatment of patients with bleeding disorders? Did that policy and approach change over time and if so how?

64. See Q 37 and the table below (at b.) on numbers of patients and therapeutic materials.

65. In 1976 approx 460,000 iu F VIII was administered as cryoprecipitate, 53% total F VIII given that year.

66. In 1979 approx 630,000 iu F VIII were administered as cryoprecipitate, 41% total F VIII.

b. home treatment? When was home treatment introduced? Did the policy and approach change over time and if so how?

67. Home treatment was started by my predecessor. The numbers of Haemophilia A patients on home therapy almost doubled in my time (from 15 to 27).

Table. Liverpool Royal Infirmary Haemophilia Centre, numbers of patients treated and therapeutic materials used 1976 – 1979.
Note, some paediatric patients were treated at Alder Hey Children's Hospital.

	1976	1977	1978	1979
Numbers treated				
Haemophilia A	48	56	58	49
vWd**	6	3	1	1
Total iu of Cryoprecipitate used each year (assuming ~ 70 iu/pack)				
Haemophilia A	452,000	700,000	665,000	630,000
For people with vWd**	8,000	52,000 +	560	560
Total iu NHS F VIII used each year				
Haemophilia A	12,532	13,060	76,015	220,000

For people with vWd**	0	0	0	0
Total iu of Commercial F VIII used each year – *by commercial type*				
For Haemophilia A	387,665	444,260	589436	700,750
Abbott	*11,826*	*0*	*0*	*0*
Hyland Hemofil	*8,809*	*83,800*	*0*	*0*
Immuno Kryobulin	*365,545*	*94,407*	*0*	*750*
Armour	*1,485*	*58,723*	*487,544*	*550,000*
Cutter Koate	*0*	*207,330*	*101,892*	*150,000*
For people with vWd**	0	1,164 (*Immuno*) +	0	0
Total F VIII given (iu)	**860,197**	**1,210,484**	**1,331,011**	**1,551,310**
Number of people on home therapy				
Haemophilia A	15	19	20	27
Haemophilia B	1	1	1	1
Number with jaundice (All had haemophilia A)	2	3 (1 duplicated from 1976?)	3 (1 duplicated from 1977?)	0
Number with Jaundice on HT	1	2	1	

** vWd = von Willebrand disease

+ One of the three people with vWd in 1977 received most of the 52,000 iu of cryoprecipitate and all the 1,164 iu of Immuno F VIII concentrate

c. prophylactic treatment? To what extent and when was treatment provided on a prophylactic basis? Did the policy and approach change over time and if so how?

68. I did not adopt a general prophylactic policy, i.e., regular doses to prevent excessive bleeding from day-to-day activities although planned surgical procedures including traumatic dental extractions would have been covered. Even for home therapy I only recommended treatment for specific bleeding episodes.

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

69. Please explain 'external parties'. I received no benefits from commercial interests. Dr Peter Jones' "Living with Haemophilia" certainly impressed the haemophilia community and parents and put some pressure on HCDs, including me, for expanding supplies for increasingly generous home therapy.

39. What was Liverpool HC's policy and approach in relation to the use of factor concentrates for children? Did the policy and approach change over time and if so how? You may find it helpful to consider the letter from you to Dr P Kirk of Lord Treloar Hospital dated 26 July 1977 where you note that cryoprecipitate was an adequate therapy for a particular patient (TREL0000311_027).

70. See my answer to Q 35. As I was not made aware precisely of this patient's clinical presentation at that time, I cannot comment on why NHS concentrate (which was nationally in very short supply at the time) was preferred. My letter indicates that cryo had been adequate for treating previous episodes, but I cannot (and probably did not) know whether it would have been sufficient for this presenting episode.

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

71. Of patients with basic F VIII concentrations of more than 2%.

72. In 1977, of ten patients: one had only DDAVP; 8 had cryo; one had 'Koate'.

73. In 1978, of five patients, all had just cryoprecipitate.

74. In 1979, of seven patients: three had just cryo; 2 had cryo + DDAVP; one had cryo plus 'factorate'; one had just 'factorate'. I cannot recall the clinical circumstances.

75. See also my answer to Q8 above.

41. What viruses or infections, other than HCV and HBV, were transmitted to patients at Liverpool in consequence of the use of blood products between 1975 and 1980?

76. I am not aware of any such transmissions

Liverpool HC's relationship with local RTCs

42. Please describe Liverpool's relationship, and your own involvement, with the local RTC.

77. The Merseyside and North Wales Regional Blood Transfusion Centre based in Liverpool was the sole supplier of blood and blood products to the Liverpool Royal Infirmary's Blood Bank of which I was the consultant in charge. This included the supply of cryoprecipitate. They may also have been the conduit for the supplies of NHS F VIII concentrate. I had good professional relationships with the scientific and clinical staff of the MNWRTC.

43. Please explain whether the RTC supplied Liverpool HC with cryoprecipitate and with NHS factor concentrates and whether (and, if so, to what extent and with what frequency) there were shortages or other difficulties in obtaining sufficient supplies.

78. The supplies of cryoprecipitate were regular and frequent. As to NHS factor concentrates, I am unsure - see the answer to Q42. The day-to-day running was coordinated by senior scientific staff at both locations.

44. Please confirm whether the RTC had any involvement in supplying commercial factor concentrates or whether those were obtained from the pharmaceutical companies directly.

79. Commercial factor concentrates were supplied solely from pharmaceutical companies.

Knowledge of risk at Liverpool HC

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

80. My training in haematology included a 6-month secondment to the North East London Transfusion Centre at Brentwood where I became familiar with the then current state of understanding of infections transmissible by blood transfusions and the methods of routine testing for syphilis and hepatitis B. We were aware that there were infectious agents other than hepatitis A and hepatitis B viruses which could cause hepatitis for which no test was yet available, and that occasional haemophiliacs could suffer more than one episode of hepatitis after receiving F VIII concentrates. I was also made familiar with the early work of Dr Craske at Manchester. The HCDO meetings and community were also valuable sources of information.

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

81. I met Prof Bellingham frequently to discuss various aspects of haematological care including haemophilia. Both of us recognised that blood and blood products were associated with infections including hepatitis, and that the mode of preparing cryoprecipitate led to risks of environmental contamination. No formal recorded assessment procedure was adopted. The pooled nature of F VIII concentrates was also recognised as a risk factor including from NHS sources as well as the probably increased risk from commercial sources (see the answer to the next question).

47. What was your understanding of the relative risks of infection from commercially supplied factor concentrates and NHS factor concentrates?

82. We understood that commercial concentrates were likely to carry more risk than NHS concentrates, but the degree of increase was not clear.

48. How did you keep up-to-date with relevant scientific and medical developments in knowledge? What journals did you regularly read?

83. Among the conferences I attended were several of the British Society of Haematology and meetings of the Haemostasis Club in London.

84. Journals included BMJ, Lancet, British Journal of Haematology, New England Journal of Medicine, Blood, and Nature.

85. I also kept up-to-date reading textbooks such as PL Mollison's 'Blood Transfusion in Clinical Medicine'.

86. The LRI had regular clinical meetings at which a wide variety of clinical presentations were made. These included developments in haemophilia care such as DDAVP.

49. When you began work as Director at Liverpool HC, what was your knowledge and understanding of:

a. the risks of the transmission of hepatitis (including hepatitis B and NANB hepatitis/hepatitis C) from blood and blood products?

87. I knew that patients transfused with blood risked contracting hepatitis from the transfused material whether this was derived from single-donor materials, small pools such as cryoprecipitate, or larger pools such as factor concentrates; and that the degree of risk was associated with the pool sizes. The degree of risk was unknown but that from single-donor product was known to be very rare after the introduction of Hepatitis B screening tests on donated blood. Nevertheless, I was also aware that some F VIII concentrates – even though collected from donations screening negative for Hep B – could transmit not only hep B (due to false negative screening tests) but also another separate agent capable of transmitting hepatitis, this phenomenon being attributed to non-A non-B virus(es) as yet unidentifiable. Late in my time at Liverpool we became aware of reports of a strange form of exacerbation of hepatitis B due to superimposed infection characterised by an antigen called the 'delta antigen'. The significance of this finding for haemophiliacs was not appreciated at this time.

b. the nature and severity of the different forms of blood borne viral hepatitis?

88. The hepatocellular cancer potential of chronic Hep B infection was well appreciated, so concern was always expressed when a haemophiliac was

found to be a carrier of hep B. Until the publications from Preston et al in the late 1970's, we had little appreciation of the potential chronicity of NANB hepatitis. It was often anticipated at that stage – perhaps more in hope than expectation – that NANB hepatitis would be self-limiting and mild in most infected people.

c. What were the sources of your knowledge? How did that knowledge and understanding develop over time?

89. See my answer to Q 48 and 45.

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

90. We made no further specific enquiries nor investigations at Liverpool. In my letter to Dr Biggs of 23 September 1977 (doc HCDO0001093), I refer to my regret at not being able to participate in Dr Kirk's 'jaundice survey' which was 'a bit regrettable as two of our patients have had some form of hepatitis during 1976/77' but I did add some information in that letter. One patient was a mild haemophilic undergoing a vasectomy and the treating 'doctors' were supplied inappropriately with Kryobulin, while I was informed about the other patient with 'only a very mild form of hepatitis' only after a considerable delay (see my answer to Q8).

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

91. We tried to prioritise the use of cryoprecipitate for hospital-based care; we used non-blood-based treatments such as DDAVP for mildly affected haemophiliacs with mild bleeds or about to undergo dental treatment when Epsikapron – a fibrinolytic inhibitor – was used along with prophylactic

antibiotics. Until the late 1970's the supply of NHS F VIII concentrate was very limited.

52. What was your understanding of the nature and severity of the different forms of blood borne viral hepatitis and how did that understanding develop over time?

92. I think I have addressed these issues in the answers above.

Reduction of and response to risk

53. Did you or your colleagues at Liverpool HC take steps to ensure that patients were informed and educated about the risks of hepatitis? If so, what steps? What information was provided to patients, and when, about such risks?

93. The risks of hepatitis transmission from factor replacement blood products were discussed with patients and parents at diagnosis of new patients, but the main interest was on the ability to control life-affecting bleeds which were usually seen as the most immediate threats. These risks were re-iterated when patients/parents were introduced to home therapy.

54. What, if any, actions did you and/or Liverpool HC take to reduce the risk to your patients of being infected with hepatitis? What changes (if any) did you make to the way in which patients were treated?

94. The purchase of the Immuno product Kryobulin, which at that time used Austrian donors (who were, nonetheless, remunerated) in the hope that the risks of transmitting hepatitis were lower than in products of N American origin. We realised later that this was probably a misplaced assumption, and a batch of Kryobulin was implicated in the hepatitis

contracted by the mild haemophiliac to cover his vasectomy. The use of Kryobulin dropped considerably after that episode.

55. Did you or your colleagues at Liverpool HC revert to treatment with cryoprecipitate for some or all of the patients in response to the risk of infection? If so, how was it determined which patients would be offered a return to cryoprecipitate and which would not? If not, why not?

95. For home therapy and for elective surgery on severely affected haemophiliacs, reversion to cryoprecipitate was not regarded as an option. Each year, about 30% of the haemophiliacs received cryoprecipitate only: these were mostly but not exclusively mildly affected.

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

96. I believe that our decisions and actions were mostly appropriate for the time although errors were made, such as the mild haemophiliac who had a vasectomy. That man would probably have been offered DDAVP if it had been available at that time.

97. Quite apart from the complication of transfusion transmitted infection, the management of haemophilia was – and even in today's circumstances is – much more complex than the mere replacement of a dysfunctional clotting system. Nevertheless, the availability from the mid-1960s of even a limited amount of F VIII for haemophilia A, either from cryoprecipitate or from lyophilised fractions of fresh plasma, was a sea-change. This was broadly illustrated by changes in the general 'personality', attitudes and behaviour of haemophiliacs. Those who had grown up before the mid-1960s when freshly donated whole blood was the only source of transfusible material

(which was relatively scarce and the volume transfused was limited by the circulatory capacity) had matured into inactive men often crippled and suffering chronic pain from repeated bleeds into joints and muscles, with limited education and employment prospects, and grateful for any care which alleviated pain and controlled the imminence of fatal haemorrhages. Such men were often habituated if not addicted to analgesics and even opiates; they were pleased to get any form of effective pain relief. They tended to be 'low-demanders' not only of replacement therapies but also of psychological support – they had grown up with lower expectations and in their way were more resilient. There were notable exceptions – some took a more defiant 'devil-may-care' attitude and worried their parents, especially their mothers, some of whom had quite a 'guilt complex' as they felt responsible for transmitting defective maternal genes. The rapid but not immediate expansion of access to more effective haemostasis led boys with haemophilia born after the mid-1960s to have greater expectations and demand more treatment – which was psychologically more complex – as, understandably, did their parents. We physicians responsible for haemophilia families had to learn novel and multifunctional approaches to their care and requirements. Dr John Martin was a leader in promoting multi-specialist clinics for haemophilic boys and their families at which for example nurses, occupational therapists, physiotherapists and dentists were also present to encourage the development of a healthy outlook in dealing with their disabilities.

Section 3: My roles at the Scottish and English blood services

Edinburgh and South East Scotland Blood Transfusion Service

57. Please describe the roles, functions and responsibilities you had at the Edinburgh and South-East Scotland Blood Transfusion Service (EBTS)

98. The following is a brief account to the best of my recollection of the accommodation of the EBTS Centre when I arrived in 1980, and my duties there. Details should be confirmed from records.

99. When my consultant colleagues at the EBTS, Dr S Urbaniak (Deputy Director) and Dr B McClelland (Director) were absent or on leave, I covered all their consultant duties including donor and Cell-separator Unit managements, and the training of junior medical staff, some of whom were rotated in from hospital haematology departments in the City, and all the out-of-hours on-call work.

100. The EBTS was accommodated within the former Royal Infirmary of Edinburgh in Lauriston Place. The main laboratories were based in the South Block and included the Regional Blood Bank, the Clinical Cell Separator Unit, serology laboratories including a routine ante-natal service, a clinical and research haemostasis laboratory, canteen, and the offices of the three consultants and their secretaries. Other activities were housed in the basement of a building in Archibald Place, and in separate accommodation in a building off Lauriston Place - see below.

during your period as:

a. Consultant in Haematology and Blood Transfusion

101. This period was for the years 1980 – 1982. My main responsibilities were as follows:

i. The Regional Blood Bank, both the technical performance (which was under the direction of the Chief MLSO) and the clinical use – which required frequent liaison with ward and operating theatre staff. The Regional Blood Bank organised the supply of whole blood and products (red cell concentrate, platelet concentrates, Fresh Frozen

Plasma, cryoprecipitate, etc.,) for all the hospitals in the Region (Lothian and Borders), and in addition provided the serological compatibility services for patients receiving blood transfusions within the Royal Infirmary Complex (including the RIE, the Royal Hospital for Sick Children, Princess Margaret Rose Hospital (orthopaedics), the City Hospital, the Astley Ainslie Hospital, the Elsie Inglis Hospital, the Bruntsfield Hospital, etc). As the blood bank stored and supplied cryoprecipitate for use by the Edinburgh Haemophilia Centre, I was ultimately responsible for ensuring an efficient and adequate supply. This included F VIII made by the Scottish Plasma Fractionation Centre (PFC) at Liberton which also passed through the Regional Blood Bank - almost solely for the Haemophilia Centre in the Haematology Department, the laboratories of which were conveniently sited in a neighbouring block in the RIE.

ii. A haemostasis laboratory within the main South Block of the RIE which provided a clinical service for the investigation of non-haemophilic bleeding disorders of patients in the RIE and associated hospitals. This was particularly useful to help the management of patients experiencing excessive bleeding during or after major surgery including cardiac. The haemostasis laboratory was also used for in vitro quality monitoring of haemostasis-promoting blood products supplied to the EBTS Blood Bank - principally FFP, cryoprecipitate, platelet concentrates; and was also a back-up for quality monitoring of factor concentrates made at the Scottish Plasma Fractionation Centre (PFC) at Liberton.

iii. The Blood Products Unit, which prepared blood components from whole blood - red cell concentrates, FFP and Cryoprecipitate. In 1980, these activities were conducted in laboratories in the basement of an old building in Archibald Place on the north-west side of the RIE site, from which they were transported to the Blood Bank. The Blood

Products Unit moved in 1982 to separate and much improved accommodation at Livingstone House, Cowgate, where I continued to be responsible for the clinical oversight of these services which were managed by a Chief MLSO.

iv. In 1980, Donor services were accommodated and organised from a separate facility in an old building in Lauriston Place which included a service for the donation of hyperimmune anti-D plasma by manual apheresis.

v. A major upgrade of accommodation for the Donor services and the serology and tissue typing laboratories allowed these services to be moved to facilities in the newly erected Lauriston Building in about 1984. The Donor services are still there.

b. Deputy Director

102. In 1982 Dr Urbaniak moved to Aberdeen and I was appointed Deputy Director: around then Dr PL Yap and Dr Anne Smith were appointed as consultants: around 1985, Dr Gillon joined the consultant staff after Dr Smith moved to another appointment. After 1982 my responsibilities described in a. above continued, but with Dr Urbaniak's departure I was in clinical charge of the 'Cell Separator Unit' which mostly applied to (non-haemophiliac patients) patients requiring plasma exchange until the arrival of Dr Gillon who, as far as I remember, took over the responsibilities of the CSU. From 1982, I also took over the clinical side of the antenatal serology laboratory services.

and explain how these changed over time.

103. In 1981 the Lauriston building, which initially was meant to be the first phase of a renovated RIE, was officially opened. After a delay of – as I

recollect – more than a year, facilities there were provided for a new suite for collecting blood donations and updating the whole administrative system of donations session organisation. The public and blood donors gained access from an entrance in Lauriston Place. Behind this suite the laboratories for special investigations including blood serology (including antenatal serology) remained part of my responsibilities.

58. Please describe the organisation of the EBTS during the time you worked there, including:

a. its structure and staffing;

104. Medical staff: consultants (as above): three Associate Specialists: one Senior Registrar: one (rotating and occasional) trainee senior registrar in haematology (part of the Edinburgh rotation of senior registrars in haematology).

105. Research Staff – two or three Clinical Scientists.

106. Scientists (formerly Medical Laboratory Scientific Officers' - MLSO')

a) One Principal
b) Two or three Deputy Principals
c) Five Chief
d) Several Senior
e) Several MLSOs and trainees.

107. Nursing staff

a) One Principal Nurse.
b) Senior Nursing Sisters – one for the Cell Separator Unit, one for the blood collection sessions.
c) Registered Nurses in charge of collection session teams.
d) State Enrolled Nurses on collection session teams.

108. Administrative staff and secretaries (a secretary was assigned to each consultant).

109. Transport staff (drivers of vehicles delivering blood and products to hospitals, and for staff attending outside donation collection sessions).

b. to whom you were accountable;

110. Dr Brian McCclelland, Director of the EBTS.

c. how the centre was funded;

111. The Common Services Agency of the Scottish Home and Health Department, of which the SNBTS with its Regional Centres was a 'Division'.

d. its remit, including the geographical area it covered and the hospitals within its area.

112. The supply of blood and blood products to all the clinical services (including private hospitals) within the Lothian and Borders Regional Health Boards, from Melrose to Livingstone (South East Scotland and Edinburgh Blood Transfusion Service).

e. information as to whom the centre was answerable to at the Scottish National Blood Transfusion Service ("SNBTS"), if anyone;

113. Professor John Cash: in the last few months of my time with SNBTS, a reorganisation of the SNBTS had created a Management Board which included the Medical and Scientific Directors and a General Manager.

f. whether the EBTS was associated or linked with other regional centers within the SNBTS and, if so, how and for what purpose;

114. The other Regional Centres were based in Glasgow, Dundee, Aberdeen and Inverness. The consultant staff of all Centres were in frequent contact and met annually (as far as I can recollect) at meetings coordinated by Professor Cash.

g. whether the EBTS was subject to any form of regulation and if so, what;

115. Initially when I arrived, 'protection' under 'Crown Immunity' was still operative. We recognised that this was undesirable and welcomed visits by the Medicines' Inspectorate – usually Dr Mike Haythornthwaite, who was critical and helpful. Crown Immunity was removed in 1991, but throughout the 1980s we strove to achieve 'Good Manufacturing practices' under the guidance of the Medicines Inspectorate.

h. the EBTS's relationship with the Protein Fractionation Centre ("PFC"), and any other laboratory involved in the production of blood products or processing of blood. You may find PRSE0004328 of assistance; and

116. There was a historical and geographical link to the PFC which was sited in the grounds of Liberton Hospital: its predecessor 'Blood Products Unit' had been sited in the RIE since 1950 and moved to Liberton in the mid-1970 s. By the 1980s the supply of F VIII concentrates from PFC and Scottish RTC production of cryoprecipitate enabled Scotland to achieve near self-sufficiency in F VIII although demand was constantly rising, but the ability to maintain high supplies was affected by the arrival of AIDS in the general community which included blood donors. As the PFC was constantly striving to improve its products, including means of neutralising

or removing the putative agents for AIDS and other infectious organisms, investigations – which included the incorporation of sucrose into the manufacturing process – were of interest and Dr Perry's letter to me was an acknowledgement of receiving an apparently helpful comment from me on this. This was merely an example of the positive professional relationship between the PFC Directorate and the Regional Directors and staff.

i. the approximate number of donations collected each year.

117. As far as I remember, about 60,000 donations were collected by the ESES BTS each year.

Wessex Regional Transfusion Centre

59. Please describe the roles, functions and responsibilities you had at the Wessex Regional Transfusion Centre (WRTC) during your period as:

a. Medical Director and Chief Executive and explain how these changed over time.

118. Several aspects of Qs 59 and 60 are addressed in document NHBT0009786_001. I took up my appointment at WRTC in September 1990. This was as 'Co-Director' with an administrator who had been appointed about a year previously by the Wessex RHA. After a year or so, I was appointed as 'Chief Executive Officer' with sole responsibility and the administrator was redeployed within the RHA HQ. I remained as CEO until the merger of the WBTS, along with the other English Regions (and N Wales) into the new National Blood Authority based at Watford under the Managing Director Mr John Adey and the National Medical Director Dr Harold Gunson, who was based at Manchester. Dr Robinson became

medical Director in 1994 and Martin Gorham became Chief Executive in 1997. This arrangement remained until my retirement in 2006.

119. As WBTS Director I was responsible for all aspects of the collection of blood from Wessex-resident donors and supply of all blood and blood products to all hospitals in Wessex. I have been shown reports submitted by the WRTC to Wessex RHA covering the period 1979 to 1988: this was the first time I had seen them as I joined WRTC in October 1990. The reports for the last two years (1986-1987 and 1987-1988) reflect quite well the state of the WRTC when I joined, staff-wise and productivity-wise.

120. Unlike my appointment at Edinburgh, I had no responsibility for providing a clinical service – such as haemostasis advice or haemophilia care – apart from the reference services called upon to supply blood for specific patients with problems of incompatibility to transfusions of most standard blood donations and an antenatal serology service for the Southampton General Hospital which was transferred to the SGH (at their request) in 1993. There was also a residual clinical therapeutic plasmapheresis service, conducted in the apheresis suite, for two patients - one with SLE (Systemic Lupus Erythematosus), and one with polyarteritis nodosa.

121. In 1991, I closed the therapeutic plasmapheresis service due to the poor access of the WRTC facilities to the emergency services ("crash trolley") provided by the Southampton General Hospital in the event of either of these (admittedly relatively healthy) patients suffering a significant adverse while being plasmapheresed at the WRTC.

122. WBTS also had responsibility for providing serological tissue typing facilities for the organ-transplant services, but as genetic typing methods became dominant and available from genetic diagnostic laboratories in the hospitals, this service from WRTC became obsolete in the late 1990s.

123. WRTC was also providing a clinical research service for patients experiencing recurrent miscarriages. This was quite elaborate, involving the determination of the blood groups and tissue types of the consenting patients and their partners (husbands), infusing patients with leucocytes from the husbands and following up the serological (immune) responses in the patient and their future obstetric record. In 1988-9, 37 couples made 101 visits. Under the advice of the Professor of Obstetrics Eric Thomas, and with RHA approval, I closed this programme in 1991.

60. Please describe the organisation of the WRTC during the time you worked there, including:

a. its structure and staffing;

124. To the best of my recollection:

- CEO (myself): two other medical consultants (one such appointment was vacant at the time of my arrival but was filled after two years); two associate specialists, and six donor session medical doctors.
- Two Clinical Scientist (one post terminated in 1996; the other became vacant in 1997 or 8 and was not filled)
- One Principal Medical Laboratory Scientist
- Three Deputy Principal Medical Laboratory Scientists
- Five chief medical laboratory scientists
- Several Senior Medical Laboratory Scientists, other medical laboratory scientists and trainees.
- One Principal General Manager (post terminated in 1991)
- One Senior administrator; one finance officer; two storemen
- One donor services manager and one assistant
- One Principal Nursing Officer
- Six Senior Nursing Officers
- Between 35 and 40 donor nurses

- Transport staff: there were seven or so drivers of cars delivering blood and blood products around the Region on a 24-hour basis, and from bleeding sessions to base during and after the sessions and a transport 'bus' to deliver staff and equipment to blood donation session venues.
- Domestic staff (cleaners) – mostly working at night. Around 1994 this service was privatised.
- A new administrator, finance officer and assistant quartermaster were appointed around 1993.

b. to whom you were accountable;

125. Dr Graham Winyard, Regional Medical Officer; and Mr Ken Jarrold, Chief Executive at the Wessex Regional Health Authority.

c. how the centre was funded;

1. The WRTC was funded by the Wessex RHA until 1994, when the NBA was established.

d. its remit, including the geographical area covered and the hospitals within its area;

126. The Wessex Region included Southampton, Portsmouth, Isle of Wight, Winchester, Bournemouth, Poole, Salisbury, Basingstoke (including the Lord Mayor Treloar School and Hospital), and Dorchester (and to private hospitals). I was also the first point of clinical contact for services in Jersey and Guernsey although the local hospitals there had their own blood collection and supply services.

e. information as to whom the centre was answerable to at the National Blood Transfusion Service ("NBTS"), if anyone;

127. Dr Harold Gunson, Director of the National Blood Transfusion Service for England and Wales; this was an advisory role and my relationship with Dr Gunson was more advisory than answerable.

f. whether the WRTC was associated or linked with other RTCs and, if so, how and for what purpose;

128. Only as a 'Federation' of Directors or equal status.

g. whether the WRTC was subject to any form of regulation and if so, what; and

129. Crown immunity was formally lifted in 1991 but informal relationships were already established with the Medicines Inspectorate which I fostered. We appointed one of the deputy Principal medical scientists as Quality Control Officer in 1991.

h. the WRTC's relationship with the Blood Products Laboratory ("BPL"), and any other laboratory involved in the production of blood products or processing of blood.

130. Supernatant plasma from freshly donated blood was sent regularly to the BPL which was the sole recipient of such plasma for fractionation.

Section 4: Blood collection

61. Please explain the system for blood collection at both the EBTS and the WRTC during your employment there and how it changed over time.

131. EBTS: before the opening of the Lauriston building donor services in about 1983, the main donors were those for anti-D bled in the Cell Separator Unit. Upon opening the Lauriston site, more regular donations were collected there – I cannot recall the numbers of donations collected there.

132. Outside sessions were the main sources – taken on a regular basis from communities all over Lothian and the Borders Region. Some communities had established a 'traditional' system run by an experienced organiser from the local community who was responsible for advertising and liaising with collection sites (church and village halls etc) but these were gradually professionalised and organised solely from the Centre by the late 1980s . Teams of about nine people, including a leader, doctor, clerk and several nurses would set up all equipment in a venue and run two 2½ hour sessions a day collecting up to 90 or 100 donations a day which were ferried in cooled vans back to the centre for processing and testing. The main change over time was the yield of plasma from each donation pack when the Optimal Additive Solution system was adopted from the mid-1980s.

133. At WRTC, the donor sessions worked on similar principles. Four or five teams were sent out each weekday (Mondays to Fridays) to sites throughout the Region including the Isle of Wight. Each team was accompanied by a medically qualified doctor who interviewed and venepunctured all the donors: each team aimed to collect up to 100 donations which over one year amounted to approximately 100,000 donations. Mostly through 'natural wastage', the relatively expensively remunerated doctors were replaced by trained State Registered Nurses by 1994. During this time, the contributions of local volunteer organisers, principally from the British Red Cross, was also wound down and discontinued, to the advantage of organisational professionalism and of donor confidentiality.

62. What, if any, steps did the EBTS and the WRTC take to publicise itself to potential donor populations in order to increase donations? How successful were these steps?

134. On the whole there was little difficulty in recruiting donors from the communities in either Region and blood supplies rarely fell to 'emergency' levels. There was regular publicity. With the arrival of AIDS there was increasing publicity regarding the need to exclude potentially infected donors and as the epidemiology emerged it seemed likely that exclusion for AIDS-associated risk factors would also minimise donations from those with undetectable hepatitis. At EBTS, by working closely with the MSM (men having sex with other men) communities, Dr McClelland succeeded in getting cooperation and understanding and almost certainly reducing the risks of recipients getting infected blood.

135. In Wessex, a panel of Group O Rh D negative donors had been recruited as 'universal donors' (i.e., their blood could be transfused to almost anyone) from communities associated with certain venues so that in emergencies, they could be called upon to donate their blood. In practice this was rarely necessary and the donors rarely used, so we abandoned that practice in the mid-1990s.

63. Please consider the following questions relating to the collection of blood by the EBTS from prisons, borstals, and other correctional institutions:

a. According to PRSE0002164, page 8, the EBTS ceased blood collection from prison donors in 1980. According to NHBT0057149_087, the NBTS stopped prison collections in 1986. What factors enabled the EBTS to stop collecting from prisons in 1980 and, notably, several years prior to the rest of the Scottish RTCs and the NBTS?

136. I was not party to these decisions which were taken before my appointment to the EBTS. I believe that the donation supply in Edinburgh was sufficient to allow ceasing donations from the prison communities relatively early.

b. When did the EBTS stop collecting blood from borstals and similar institutions? Prior to that date, how extensively did the EBTS collect blood from borstals and similar institutions? Please identify and set out the number of such institutions from which blood was collected, and the frequency of collections.

137. Again, I was not party to these decisions and did not have the relevant data.

c. Were there any financial advantages to collecting blood from borstals and similar detention institutions as compared to collecting blood from RTCs?

138. I doubt it. It probably originated from a well-intended desire to assist prisoner rehabilitation and improve prisoner morale.

d. What involvement, if any, did you have with this practice?

139. None.

64. Please describe the way in which donations were collected at the EBTS and the WRTC during your time there. In particular:

a. What were the staffing arrangements during blood donation sessions?

140. See my answer to Q 61.

b. Where did these sessions take place?

141. Mostly in local communities – see my previous answers.

c. How frequently could a person donate blood?

142. Maximum recommended was three times a year, but individual donors in each session 'panel' (i.e., specific regular venues) might be invited four times a year.

d. How were blood donors recruited?

143. Publicity, newspaper advertising, local radio stations, campaigns in colleges and workplaces, word-of-mouth, etc. These included health criteria. As well as risks associated with specific infections, donors were required to be in good health, weighing at least 8 stone, over 18 and under 65, and to have passed a screening test for anaemia. The rules were the same throughout the UK. The volume of blood collected was between 400 and 450 ml but this increased slightly over the years to average about 470 by the time I retired in 2006.

e. Did any of these matters alter during your tenure at either RTC? If so, how?

144. Pragmatic solutions to donor care and health questionnaires have always been necessary but the increasing incidence of detectable infections (hep B, HIV/AIDS, hep C, etc) required better design of donor questionnaires and training of the donor selection and bleeding staff, as well as better general information. The arrival of the Internet increased opportunities for good quality information services.

65. Did either the EBTS or the WRTC have donation collection targets that it was required to meet? If so, did the EBTS or the WRTC meet their donation collection targets during your tenure? If not, why not? What was done to improve blood collection? What more could or should have been done? What were the barriers?

145. EBTS: I believe the target was about 50,000 red cell products a year: in the event this was well exceeded because of the optimisation of fresh plasma procurement to enhance the annual delivery of plasma to the PFC, so altogether about 60,000 to 70,000 donations were collected.

146. WRTC. We had a target of about 100,000 'standard' donations annually. This target was usually met in my time.

Section 5: Plasma procurement and production of fresh frozen plasma

Production of fresh frozen plasma

66. The Inquiry understands that the EBTS and the WRTC procured plasma from blood donor sessions to produce fresh frozen plasma ("FFP") to provide to the PFC or BPL respectively. Please explain:

a. where this production of FFP took place at both RTCs;

147. EBTS – initially in specially adapted facilities on the site of the Royal Infirmary of Edinburgh in Archibald place, from 1982-3 at Livingston House, Cowgate.

148. WBTS – in purpose-designed facilities on the premises in the grounds of Southampton General Hospital.

b. broadly, the process that was undertaken, the capacity of the EBTS and the WRTC to manufacture FFP, and whether this changed during your tenure and why;

149. EBTS – supernatant plasma from freshly collected (within 8 hours) hard-centrifuged whole blood was separated into an empty plastic pack: at Archibald Place these packs were snap-frozen in baths of ethanol and dry ice; at Livingston House they were frozen rapidly in a 'blast freezer'.

150. At WBTS, similarly separated plasma was also frozen rapidly in a 'blast freezer'.

151. It was important to achieve temperatures below minus 70 deg C rapidly in order to preserve the integrity and function of the delicate clotting factor proteins in the plasma, and to store them in freezers at the same low temperatures.

c. what proportion of blood collections were allocated to this process and how this decision was made, and whether this changed over time;and

d. how quickly the EBTS and the WRTC could have increased its manufacture of FFP or cryoprecipitate, had it wished to.

152. Quantitatively, FFP for clinical use was a minor drive for freezing plasma at each site. All locally produced cryoprecipitate for clinical use was manufactured from FFP as its raw material; but the bulk of FFP was sent from both sites for fractionation at PFC for EBTS and BPL for WRTC.

153. A possible approach to the problem of HIV-infected fractionated factor VIII concentrate, when the scale of that problem became apparent in the early 1980's, might have been the abandonment of such concentrates and replacing them with cryoprecipitate. If the pattern of use by the Liverpool

Haemophilia Centre in the late 1970's (Table attached to Q38) is reasonably representative of the UK as a whole, the 200 or so packs of single-donor-equivalent cryoprecipitate given on average to each of the 50 or so haemophiliacs (with a very wide range of pack numbers to each haemophiliac, from zero up to many hundreds) represented about 40% of total F VIII units at that time. I calculate very approximately that the total number of donations from which cryoprecipitate was made each year at the Merseyside RBTC in the late 1970s would have been about 10,000 – which would have been up to 20% or so of all the donations collected. Commercial concentrates contributed about 45% of the f VIII concentrates in 1979 used by the Liverpool Haemophilia Centre, and NHS F VIII concentrates the remaining 15% or so.

154. Assuming that at that time very approximately half of the donations collected by the Merseyside RBTC were issued to patients as whole blood, and half as red cell concentrates, about 6 tonnes of fresh plasma would have been available, the bulk of which would have been for fractionation into NHS F VIII concentrate at Elstree but a small proportion would have been prepared as units of Fresh Frozen Plasma (FFP) for transfusion to non-haemophiliacs. In order to supplant the 45% or so of commercial F VIII concentrate used by the Liverpool Haemophilia Centre in 1979, another 12,000 or so donations would have been needed to be processed as cryoprecipitate, which would have eroded very deeply into the supply of plasma for F VIII fractionation at the BPL in Elstree and Oxford PFL.

155. The risk of transmitting viruses in fractionated F VIII prepared from pools of plasma donated by asymptomatically infected apparently healthy donors is much higher than that from single units of cryoprecipitate. I understand that commercial suppliers used pools from many tens of thousands of donors, and whereas the NHS suppliers may have used smaller pools of just thousands of donated plasma, the risk from the NHS pools was still substantially higher than that from single or low-pool-sized cryoprecipitate.

However, a severe haemophilic treated solely with cryoprecipitate may get exposed to more than a thousand donors in a decade or so; but this is still a substantially lower risk than exposure to products prepared from very high numbers of donations pooled before fractionation.

156. But it is much more complicated than simply substituting fractionated F VIII concentrates with cryoprecipitate, the manufacture of which is complex for Blood Bank Staff. Two episodes of high-speed centrifugation, two episodes of snap freezing, and two episodes of thawing in warm water are required. All these processes are accompanied by losses of F VIII yield (due to inherent instability of the F VIII molecule) and must therefore be conducted expeditiously and skilfully.

157. The average single pack of cryoprecipitate contains between about 20 and 80 ml of plasma with between about 20 and 100 i.u of F VIII (1 i.u being the F VIII activity in 1 ml of fresh plasma). It also contains all the other plasma proteins and has relatively high concentrations of fibrinogen, von Willebrand factor and fibronectin (which plays a major role in cell adhesion, growth, migration and differentiation). The contents of each pack are quite heterogeneous and not 'standardised' (in the sense of each pack being qualitatively equivalent). The last thawing process includes pooling the contents of the required number of packs to give the commonly used adult 'dose' of 500 i.u F VIII (e.g., 6 to 10 or so cryo packs). In order to maximise the amount of F VIII received by the patient, each pack was 'swilled out' with about 20 ml of pharmaceutical grade citrated saline solution passed from pack to pack. The final volume infused could therefore exceed 500ml. The 'swilling' and the thawing processes render the infusate vulnerable to environmental contamination and it was not unusual for patients to experience 'nonspecific' febrile episodes during or shortly after infusion. (Febrile episodes could also accompany the infusions of fractionated F VIII, but less frequently than the use of cryoprecipitate.) It may be noted that the other cryoprecipitated proteins

increase the indications for cryoprecipitate therapy to conditions other than haemophilia – up to 5% or more of the total cryoprecipitate use.

158. In summary, the preparation and use of cryoprecipitate is time-consuming, labour-intensive, and not popular with ward staff: I felt it was not suitable for home therapy. I remain of this opinion in spite of a letter in the Lancet of 20 July 1974 (p155) extolling its virtues. This was by Katherine Dormandy, Director of the HC at the Royal Free Hospital (who I remember well). I had gained extensive personal experience of the preparation and administration of cryoprecipitate and formed the personal opinion that the conditions for safe and effective storage and administration of cryoprecipitate at home was undesirable.

159. Methods of freeze-drying cryoprecipitate were developed in several centres, including Glasgow. There was some advocacy of using such preparations more widely, including for home therapy, but I understand that problems of practicability deterred such developments.

160. So in my opinion it would not have been feasible for the UK clinical services in the 1980's to have substituted cryoprecipitate for fractionated F VIII concentrates in any substantial quantities in order to maintain the level of clinical demand after the onset of HIV. I understand that the demand for cryoprecipitate from the Treloar Centre proved very challenging for the Wessex RTC in the mid 1970's. The quality of life, particularly for severely affected haemophiliacs, would have been substantially reduced even had all the fractionated supplies been met by cryoprecipitate (which I think would have been unrealistic anyway). Whether, with hindsight, more pressures and finances to maintain a safer supply of cruder and less reliable F VIII in the form of cryoprecipitate should have been developed is beyond my expertise.

161. Note, cryoprecipitate is not suitable for people with F IX deficiency: neither is DDAVP. In the absence of low-pool F IX concentrates, they would still have had to rely on treatment with FFP.

67. As far as you are aware, how was plasma procurement at the EBTS funded throughout the 1980s? You may find NHBT0001343 of assistance.

162. I don't see how NHBT0001343, which is a letter from me dated 1991 when I had moved to Southampton, relates to the funding of plasma procurement at EBTS in the 1980s. However, it was funded by the CSA/SHHD

68. Please describe the arrangements for supplying FFP and/or cryoprecipitate to hospitals and haemophilia centres within the regions covered by the EBTS and the WRTC.

163. At both places, FFP and cryoprecipitate for local clinical use was supplied by direct transport. The main haemophilia centres at both sites were located in the adjacent major teaching hospital (Royal Infirmary of Edinburgh (RIE) for EBTS and Southampton General Hospital (SGH) for WRTC).

Plasma targets

69. Did the EBTS and the WRTC have targets for the amount of plasma that had to be collected by the centre? If so, who set these targets and what were they? If not, why not? What was the purpose of the targets?

164. Targets. I cannot at the moment recollect the number of donations collected daily at Edinburgh but do recollect that during the earlier period of my appointment, the number of donations exceeded by a significant margin the number of red cell concentrates needed for transfusion: the

donations from which red cells were not used were, nevertheless, used as sources of fresh plasma for fractionating and for the local manufacture of FFP and of cryoprecipitate, the cryosupernatant (the material decanted off the precipitate but which still had other proteins such as albumin, F IX, and immunoglobulins) being retained and sent for fractionation).

165. For the English Regions, I believe that a 'pro rata' system of supplies of NHS (BPL) F VIII to regional hospitals was designed but it was difficult to apply. For Wessex, which had the Treloar College in its territory, a strict pro-rata system would have been unfair. However, I cannot recall how much the pro rata system was applied to the supply of NHS F VIII to haemophiliacs in Wessex in my time, but the Annual Report of the WRTC 1988-1989 indicates that during 1986-7, the 'target' of 18.6 tons of FFP for 'Elstree' was almost reached, and that they were hopeful that a target of 20.7 tons would be reached for 1989-90. It Is not clear how much donor plasmapheresis at WRTC contributed to these targets.

166. I also note that the WRTC return for 1987-8 indicates that 14.5 tonnes of FFP were sent for fractionation at BPL, and that the return for 1988-9 shows that 11,811 vials of NHS F VIII were received for Wessex hospitals: this indicates that at 250 iu per vial (which I think was the standard content) about 2,950,000 i.u. were sent to WRTC for the haemophiliacs in Wessex including Lord Mayor Treloar. A rough estimate indicates that the 14.5 tons of FFP sent to BPL for fractionation would, assuming a 20% or so recovery of F VIII in the final product (because of losses through transportation, storage, fractionation and processing), produce c2,900,000 i.u of F VIII. This crude analysis indicates that some form of pro rata supply of NHS F VIII was operating before I arrived and this probably continued while I was Director of WRTC. However, I believe that by the time I arrived, supplies of NHS Factor VIII may have been sent more directly to the haemophilia directors (Dr Morag Chisholm for Southampton

and Dr Tony Aronstam for Treloar), so WRTC was less involved in the local supplies of F VIII concentrate.

70. What impact did the setting of targets for the collection of plasma have on decision-making at the EBTS and the WRTC?

167. EBTS. The demand for plasma and plasma products tended to exceed the demand for red cells, so there was a relatively high out-dating rate of red cell products which were therefore not used, but I cannot remember how much plasma for fractionation was received by the PFC from EBTS.

168. For WRTC, the amount of plasma supplied (up to about 20 tonnes a year) was the best we could achieve.

71. What were the consequences if the targets were not met?

169. As far as I remember, targets were close to being met, but I have no direct knowledge of the amounts of therapeutic F VIII used in the Wessex hospitals during my time.

72. Were there any benefits to the EBTS and the WRTC if the targets were exceeded?

170. I am not precisely aware, but in principle, WRTC would have received NHS concentrate back pro-rata for the plasma supplied to Elstree. The haemophilia services at Treloar and the SGH would probably have been more aware.

73. In 1989, cross-charging was introduced in England and Wales to act as an incentive for RTCs to increase the amount of plasma being sent to BPL (see NHBT0057426_002). As far as you are aware, what effect (if any) did cross-charging have on the plasma supply in England and Wales?

171. This refers to NHBT0057426_002 which is undated but is probably 1988 or 1989 which was before I came to Southampton. I do not remember seeing this document before so I am at a disadvantage when trying to answer this. I do recollect general discussions about the oncoming 'cross charging' proposals at BPL, being aware that such a scheme was not being so considered in Scotland. This was a general issue I considered when applying for the Southampton post but my recollections are not very detailed. However, as far as I am aware, the application of cross-charging did not have a major effect on the plasma supply in England.

Plasmapheresis

74. As early as 1981, plasmapheresis was being considered as a means of increasing the plasma supply to help achieve self-sufficiency (CBLA0001287). Please explain, as far as you are able, what consideration both the EBTS and the WRTC gave to implementing plasmapheresis, including:

a. whether manual or machine plasmapheresis was preferred;

172. No major expansion of non-specific plasma collection by apheresis occurred at either venue. Specific high-titre anti-D plasma was collected initially by manual techniques but later by machine apheresis at EBTS.

b. the relative cost differences between each method;

173. I don't think this was a major issue although had any expansions occurred, the more expensive mechanised apheresis option would have been preferred.

c. the infrastructure, expertise and capacity of both RTCs to introduce plasmapheresis; and

174. There was expertise for apheresis collections at both sites but not the resources (equipment and staff) for expansion.

d. whether, in your view, plasmapheresis would increase the amount of available plasma.

175. This is partly addressed by the policy at EBTS at that time, of collecting more whole blood than was needed for supplying red cells, the 'excess' plasma being available for fractionation, the excess red cells being discarded upon reaching the 5-week expiry in the blood bank at the RIE site of the EBTS.

75. In a letter from you to Mr Perry of PFC in January 1985 (PRSE0000107), you indicate that Factor VIII deficient substrate plasma was collected from patients by plasmapheresis. Please set out the extent of the plasmapheresis programme at the EBTS during your tenure. As far as you are aware, did this programme differ from other RTCs? If so, why?

176. The letter from me to Bob Perry was more to explain the need for F VIII-depleted substrate plasma to be prepared artificially, rather than giving details of the quantity of plasma collected from whatever the number of haemophilic donors who were 'donating' their plasma by plasmapheresis. Note: this was purely for laboratory purposes as this was the main source of the essential F VIII deficient plasma used as a reagent for assaying F VIII activity in fractions of normal blood plasma or indeed in haemophiliacs receiving F VIII therapy to monitor their responses. I have no recollection of the numbers of haemophiliacs involved or the quantity of plasma obtained, but there would not have been very many haemophiliac 'donors': I assume that PFC records will have that sort of detail.

76. In 1989/90, it appears that the WRTC used their plasmapheresis machines for the collection of anti-D only, and that the machines and staff were being "greatly underutilised" (NHBT0003372). As to this:

a. Did you agree that plasmapheresis machines and staff were being underutilised at the beginning of your tenure at WRTC? If yes, what was the reason for this? If no, why not?

b. What steps, if any, were taken to increase the use of the machines and/or the duties of the staff?

177. I do not recall seeing doc 3372 before and do not remember being made specifically aware that Mr Moore had made that visit in July 1989. It does, however, give a fair picture of the general staffing structure and function when I took over in October 1990. Mr Moore's report that Mr Jim Smith had said that Dr Herborn was not highly regarded by the RHA (and that Mr Smith shared that alleged opinion of Dr Herborn) is a sad reflection of the dysfunction of the WBTC with the retirement of the previous Director, Dr Don Smith, in 1987-8. Mr Smith might have assumed that as Dr Herborn had not been appointed by the RHA to succeed Dr Smith as Director, he (Dr Herborn) might have been 'not highly regarded' by the RHA; but these allegations should be taken in the context that Mr Jim Smith was found by the RHA in late 1991 to be inadequate as a 'General Manager' and was redeployed within the RHA. Dr Herborn was hard-working and conscientious: as the sole medical consultant in the Centre at the time it would not have been fair to expect him to develop active policies around the donor apheresis strategy as there was so much else going on.

178. When I arrived October 1990 I soon realised that many other priorities had to be addressed:

- the donor records were completely paper-based and vulnerable to error so we began a process of computerisation eventually of all donor records. The previous attempt by Mr Jim Smith in the late 1980's to procure a computer system from the Cardiff centre was unsuccessful.
- the research scientists had not received any guidance for developing research programmes; it was my duty to remedy that as far as I could
- the session organisations needed re-appraisal – the more distant venues in East Dorset and the Isle of Wight needed better organisation
- The blood products facility (for preparing platelet concentrates, FFP and cryoprecipitate) needed updating – it was housed in the area originally designed as a 'bottle-washing' plant for sterilising the glass bottles into which blood was collected at the time when the Centre was opened in 1970)
- The stores which had been operating traditionally as a repository of equipment needed updating (it was replaced by a 'just-in-time' system which was more efficient).

179. Mr Moore was acting in good faith to maximise the input of fresh plasma for fractionation at BPL. The WRTC was the main source of cryoprecipitate for the Lord Mayor Treloar HC; although I cannot remember how much cryo was being sent to Treloar, the total demand for cryo remained quite high. The apheresis suite to which Mr Moore referred was sited in poorly resourced facilities used principally for collecting plasma donated by people with high concentrations of anti-D. These donors were occasionally boosted with small volumes of Rh D positive blood: this required careful appraisal. The suite was also used for two patients with chronic disorders amenable to therapeutic apheresis: although the patient workload was small, it required careful clinical management. The suite was also the only facility on the Centre's building for collecting standard blood donations from members of the general public: I believe that up to about ten donations a day were collected this way at that time, but this recollection is

probably inaccurate and may be wrong – records should show the true amounts.

180. Dr Herborn and Mr Dudderidge were of invaluable assistance to me in helping improve donation collection services and outside session organisation which – being the heart of the BTS – took priority over the development of apheresis donor services for supplying BPL.

181. So, under the circumstances at that time, I do not agree with Mr Moore's comments that the unit was 'vastly underutilized' although more plasma for BPL could have been collected had it been possible to prioritise such a policy.

182. I do recollect concerns that further developments such as an expanded apheresis suite might have overloaded the utility supplies (i.e., electricity) to the Centre although I have no written record. Later expansions were not, however, deterred.

77. In a 1989 visit note regarding the WRTC, R J Moore stated that the production of apheresis plasma could increase to 700kg in the year 1990/91 (NHBT0003372). Despite this, the production of apheresis plasma did not increase in 1991, remaining at a similar level to the previous year at approximately 68kg (NHBT0016101). Please explain, as far as you are able, why the WRTC did not increase its production of apheresis plasma during this period.

183. As is shown above and in document NHBT0016101, operating conditions at the Centre were difficult, and we were awaiting the outcome of our development proposals submitted to the WRHA five months earlier. I cannot recall now the details of our proposals.

184. It may be noted that although BPL had experienced several substantial upgrades during the 1980s, some scepticism among RTC Directors in

England and Wales about the efficacy of BPL and the achievement of 'self-sufficiency' probably remained. Apart from my correspondence with Dr Gunson [NHBT0016101] I do not recall any other correspondence with me about increasing the plasma output from the apheresis suite.

Use of plasma reduced blood and red cell concentrates

78. What steps, if any, did the EBTS and the WRTC take to persuade hospital clinicians to use less whole blood and more red cell concentrates and/or plasma reduced blood to release more plasma for fractionation?

185. EBTS. The most progress in this regard was with the cardiac surgeons who initially insisted that 'fresh whole blood' was needed to cover their open-heart surgical procedures – the usual request per procedure was for ten units of blood: the anaesthetists were more amenable to persuasion, but some surgeons were very reluctant. By attending the Cardiac Surgical Weekly Audit meetings, we were gradually able to encourage the surgeons to use more red cell concentrates and less red cell units overall. By the time I left in 1990, and with better intraoperative cell-recovery procedures, the demand for blood cover was considerably less.

186. WRTC. I was less involved directly with the Region's clinicians – blood use policies were the responsibility of the local haematologists, some of whom were more successful in persuading an overall decline in red cell product use by the surgeons. However, I used the unusual mantra whenever I could at meetings with clinical colleagues that it was 'my professional duty to cut off my nose to spite my face' – an allusion to the possible effect of 'cross-charging' for cell products in encouraging a 'commercial' blood supplier to profit by encouraging more use of blood; but I wanted to educate clinicians to use less blood, and particularly less whole blood in spite of the charges involved helping to fund the BTS. In the event, the advent of universal use of optimal additives for reconstituting red cell

products for transfusion and increasing overall plasma yields was probably more successful; ironically the educational effects of cross-charging were probably more effective at reducing blood use than my personal efforts in education.

Section 6: Arrangements for obtaining and allocating blood products

79. Please describe the arrangements in place in both the Edinburgh and South East Scotland region and the Wessex region for the purchase and holding of, and the allocation to haemophilia centres within each region, of (a) NHS factor concentrates and (b) imported factor concentrates and/or other blood products ("imported blood products"). You may find PRSE0001081 of assistance. In particular:

a. Please identify which haemophilia centres, if any, were supplied with such products by the EBTS and the WRTC, and over what period of time.

187. EBTS: supplied the HC at the RIE with NHS (SNBTS/PFC) concentrate only – we did not procure or supply any imported factor concentrates or other blood products.

188. WRTC: As far as I am aware, the haemophilia centres (Lord Mayor Treloar School and the Southampton General Hospital) were not supplied by the WRTC; they ordered such products directly from the manufacturers (BPL and commercial factor concentrate suppliers).

b. Please outline the respective responsibilities of the EBTS, the WRTC, PFC/BPL, and haemophilia centre directors, and how these responsibilities changed over time.

189. EBTS: responsibilities for supplying clotting factor materials were to produce FFP and cryoprecipitate to the haemophilia centres, and sending donor plasma to PFC for fractionation.

190. WRTC: similar.

191. There were no substantial changes in responsibilities over my times at either Centre, nor as far as I am aware, of the responsibilities of the Haemophilia Centre Directors at Edinburgh or at Southampton. I believe that the Haemophilia Centre at Treloar School/hospital closed sometime in the 1990's.

80. Please explain whether any forums were established between either RTC, PFC/BPL, and haemophilia centre directors to discuss and facilitate these arrangements. Were meetings held regularly? Were they minuted? If so, by whom? What was discussed at these meetings?

192. Doc PRSE0001081 is a minute of a meeting of such a forum in Scotland, which included EBTS and PFC. I have no clear recollection of this meeting although the documented PRSE0001081 minutes make sense.

193. There was no formal forum of meetings involving WRTC and BPL apart from the visit of Mr Moore in July 1989 – 15 months before I took up my appointment at WRTC.

81. As far as you are aware, were arrangements for the purchase, holding, and distribution of (a) NHS factor concentrates and (b) imported blood products similar in other regions, or was there a degree of regional differentiation (and if so, what)?

194. I am not aware of how much, if any, differences there were between the Regions except that in Scotland, one HC (Glasgow) procured relatively substantial quantities of imported F VIII concentrates.

82. Did you, or anyone else at the EBTS or the WRTC, contract directly with any pharmaceutical company involved in the manufacture and/or importation and/or sale of imported blood products? You may find PRSE0002222 and PRSE0002530 of assistance. If so, please describe:

a. how and by whom the decision was made to contract with the particular pharmaceutical company;

195. I believe that no such contracts were made by EBTS or the WRTC for commercially manufactured or imported blood products although the EBTS might have held occasional stocks of imported F VIII for the haemophilia centre at the RIE: If so, I cannot recall accurately whether this was funded by the CSA or the Lothian Health Board.

196. This correspondence appears to refer to a 'fishing trip' by the sales rep of Immuno giving some scanty details of a 'clean-up' process for clotting factor concentrate which had little or no bearing on SNBTS manufacturing.

b. the broad terms of the contractual agreements made; and

197. not known

c. the factors taken into account when determining whether to contract with one pharmaceutical company over another.

198. not known

83. Did the shortfall of NHS product coming from BPL have an impact on WRTC? Please provide details. How frequently did this occur? You may find NHBT0000534_003 of assistance.

199. The referred document (NHBT0000534_003) does not help me answer this question. Any such shortages in Wessex would have impacted on the Southampton Haemophilia Centre rather than the WRTC.

84. Was either the EBTS or the WRTC in any way responsible for decisions about the choice of product used to treat patients in hospitals, for example the choice between one imported factor concentrate over another?

200. EBTS - No, WRTC - No

85. Was either the EBTS or the WRTC in any way responsible for decisions about the choice of product used to treat patients in haemophilia centres, for example the choice between one imported factor concentrate over another? If yes, what were the deciding factors in the choice of product?

201. EBTS - No: WRTC - No

86. What, in your view, were the key factors influencing the choice between NHS blood products and imported blood products?

202. Relative safety; efficacy; convenience of administration; price (except for NHS product).

87. Please explain, in your view, the impact of clinical freedom on the relative use of NHS blood products and imported blood products in the UK.

203. In practice the application of 'clinical freedom' depends on what choices are available at any one time. For clotting factor replacement therapy over the period of this Inquiry, the circumstances and choices varied, so there is no simple answer. During my time at Liverpool, NHS F VIII concentrates were in very short supply (especially in 1976, 77 and 78: supplies in 1979 were better but still grossly inadequate) and no viral inactivation

procedures were available. There was little to choose between the various commercial choices – all carried the risk of Hep B and NANB, and others as yet unidentified.

204. The arrival of HIV/AIDS during my period in Edinburgh added pressure but the availability of good supplies of Scottish PFC product offered some attraction until it was found that at least one batch was implicated in 16 or so transmissions. Nevertheless, the PFC product was still preferred and for the haemophiliacs at Edinburgh a system agreed between myself and Dr Ludlam attempted to restrict the batches of F VIII ('batch dedication') to which each patient was exposed. I do not know what and how much of each F VIII concentrate was selected at Southampton.

205. In buying commercial concentrate, clinical freedom includes considering the taxpayer, but other criteria needed to be considered including ease of use and domestic storage considerations.

88. As far as you are aware, what influence did the pharmaceutical companies who supplied imported blood products to both the Edinburgh and South East Scotland and the Wessex region have on how they were used? For example, can you recall whether pharmaceutical companies provided advice on the implementation or use of the products?

206. I don't know, and wouldn't expect to, as I had no part in making decisions. Neither the ESEBTS nor the Wessex Region procured imported blood products for treating haemophiliacs. However, literature from the commercial manufacturers would have included how to prepare the constituents for intravenous administration and possibly suggested doses.

89. It appears that, in 1980, Dr Ludlam planned to expand home therapy programmes in the region (PRSE0006024, page 13). Please explain your

views in relation to home therapy programmes at the time, including whether you considered it important to expand them. In particular:

a. **What, in your view, were the key factors influencing the choice between PFC blood products and imported blood products in the development of this programme?**
b. **How, if at all, did the issue of PFC's low Factor VIII stocks affect the implementation of home therapy?**

207. I would like to see the letter from SNB0072566 to which p13 of PRSE6024 refers – presumably in the Penrose files. This was also presented to me during my evidence to the Penrose Inquiry. I don't have a copy; but in my evidence I stated that cryoprecipitate was 'messy' and unsuitable for home therapy. It seems that this letter was dated February 1980.

208. From the general content of PRSE6024 it is clear that I supported Dr Ludlam in his aim of developing and expanding the home treatment of haemophiliacs attending the Haemophilia Centre at the RIE.

209. I believe it was recognised even before he took up his post, that Dr Ludlam wanted to expand the availability of home treatment for the SE Scotland haemophilia community, and that demands for PFC 'intermediate' F VIII concentrates were likely to increase the risks of lowering PFC's stocks of F VIII. In the event, PFC usually kept pace with the rising demands but difficulties were more likely to arise when PFC had its occasional periods of 'shut-downs' for maintenance reasons, etc.

90. In June 1987, correspondence between Dr Ludlam, Professor Cash and you discussed the use of Z8 product whilst it was undergoing a clinical trial. Please answer the following questions with reference to that correspondence (PRSE0003825, LOTH0000010_038 and LOTH0000010_053):

210. Please note that many aspects of the issues addressed in Q90 are also addressed in my responses to Qs 127 to 133.

a. In PRSE0003825 (dated 11 June 1987), Dr. Ludlam suggested that Z8 had been issued with neither an approved product license nor a clinical trials exemption. If so, on what legal basis was Z8 issued at this time? Please could you elaborate with reference to LOTH0000010_053.

b. Why was Z8 introduced to patients without Dr Ludlam's knowledge?

211. Q90 a. and b.

212. In document PRSE0003825 dated 11 June 1987, Dr Ludlam complained that although 'we had agreed to discuss further evaluation of the new material' (Z8) he thought that there were still supplies of the older material and was surprised to find that while he was away (in Washington) that one of his patients had been used to trial some Z8 and that unfortunately he developed 'central chest tightness' during the infusion. Dr Ludlam also referred to discussions on compensation at a meeting at St Andrews House in February 1987 and that 'Mr Macniven' had given an undertaking that ABPI guidelines would apply to all test infusions 'sufficient to gain a Product License. Dr Ludlam goes on to say that the draft minutes of that meeting are not a true record. He went on to complain that he was 'now faced with a fait accompli over Z8' which 'comprised' (sic) his position and that he either has to accept the situation (by which he presumably means continue to use Z8) or go over to the purchase of commercial factor VIII (which would presumably have undergone virus inactivation).

213. I replied on 24th June 1987 (LOTH0000010_053) in which I commented on a draft 'advisory document' Dr Ludlam was preparing for candidate patients receiving trial materials, and I also raised concerns about the design of a consent form and asked him if he thought that commercially derived concentrates would be superior to Z8?

c. In a letter to Dr Ludlam, you expressed your hope that he would "not feel it necessary to go over to the purchase of commercial Factor VIII". Please explain why you held this view at the time.

214. I felt that buying commercial f VIII, even virus inactivated, would be a retrograde step, not least because virus inactivation processes are not fool-proof especially with higher virus loads which might feasibly be the case with commercial starting plasma from the USA.

215. I also commented that I had personally witnessed the reaction and had come to the conclusion that it differed little from similar reactions he had experienced with other infusions of other F VIII concentrates, and that 5 other patients receiving Z8 had not had any adverse reactions. I also commented that I understood that a variation on the Product Licence had been applied for.

d. How often, if at all, would product licensing issues require the purchase of commercial products to ensure that a suitably licensed product was available for use?

e. In your view, and based on your experience around this time, what were the ethical implications of issuing Z8 without a license and/or a clinical trials exemption? What was your view on the issuing of Z8 to patients in this manner?

216. I am no longer familiar with the details of licensing modifications of already licensed medications such as the various and progressive forms of heat-treated F VIII, so I cannot give a sensible answer to question d. For question e., I would say that although it seems that ethical issues would mandate not supplying 'unlicensed' Z8 or Z8 without a clinical trials exemption, I am not convinced that this episode used an unlicensed or non-exempt product.

217. At this distance in time (34 years) I have no other recollection of this episode, and no recollection of what procedure might have satisfied Dr Ludlam (or whether the 5 other patients were at the RIE or one of our outside collaborators). Dr Ludlam was clearly disturbed to find that in his absence one of his patients had been entered on the Z8 trial when the issue of compensation had not been resolved to his satisfaction. I do not know what form of reassurance Dr Ludlam was expecting or would accept. It seems that he thought that I had acted without proper procedure. Although at this stage I cannot recollect the precise order of events, I am sure that I did not mean to put Dr Ludlam in a difficult position, and that the medical staff in Dr Ludlam's team would not have gone ahead if they felt that I was acting inappropriately. I do not recollect undertaking the infusion myself or taking any follow-up samples of venous blood, and am sure that the procedure was conducted by competent medical staff with the patient's informed consent. It does seem, however, that Dr Parker – Dr Ludlam's colleague – was not aware of this particular episode, which is regrettable. I cannot recall how I was made aware that this patient was attending the haematology department that day (which has not been precisely dated) but assume that someone in the haematology department, or possibly in the blood issuing department of the EBTS (where the Z8 would have been stocked), informed me because they were aware of my interest in the Z8 trial.

218. I regret that Z8 was introduced without Dr Ludlam's knowledge. I think this was through miscommunication and my unjustifiable assumptions, and Dr Ludlam had the right to identify such problems and ask that they be addressed. It also seems that Dr Ludlam did not quite know who was responsible in the SNBTS for coordinating with him as on occasions he wrote directly to Dr McClelland or even to Dr Cash, thereby by-passing me possibly to the disadvantage of project management. I regret this and feel that I could have been more helpful; but as it is common for 'supplying colleagues' in the NHS (such as lab services) and 'using colleagues' (such as clinicians responsible for individual patient care) to have different approaches and even priorities, good, sensitive, thoughtful and diplomatic relations are always required. Although this patient suffered no long-term adverse effect, I still regret that my actions that day caused Dr Ludlam anxiety and disapproval, and accept that as the ultimate clinician in charge, he had the right to complain and that his complaint was justified. Fortunately, that episode did not affect our fundamental working relationship and we continued to work well together. In my opinion, the haemophiliacs in Edinburgh benefitted greatly from his care and dedication.

219. I do note that minutes (h) iii and (h) iv of doc PRSE0004163 (dated 3 March 1987) refer to the state within the SNBTS of product licences and of compensation, from which it seems that SHHD had not yet developed operational policies on these matters: I was not involved with these discussions and do not recall how much I was briefed on them at that time.

220. Note: Chapter 23, and Chapter 24 paragraphs 7 and 8 of The Penrose Report (PRSE0007002, pages 934-935 and 1015) includes dates when preparations of 'Z8' were released (Apr1987 "The SNBTS begins routine issue of FVIII (Z8) dry heat treated at 75- 80°C/72hr"; page 66 goes on to say -

221. 24.7 Within the UK, the Plasma Fractionation Laboratory and the Blood Products Laboratory (PFL/BPL) were able to supply Factor VIII concentrate (8Y) to England, Wales and Northern Ireland from September 1985. Over time, the product was found to be safe from transmission of NANB Hepatitis/HCV. It can be seen from the above tables that, with the exception of the Behringwerke pasteurised product (which resulted in low product yields and was not generally available in the UK), the PFL/BPL were the first fractionators able to produce a Factor VIII product that events were to show did not transmit NANB Hepatitis/HCV (albeit, as discussed at 24.22 below, they were not able to produce sufficient product to meet the needs of all haemophilia patients in England and Wales).

222. 24.8 In Scotland, the PFC was able to make available for clinical trial in December 1986 a Factor VIII concentrate (Z8) which, over time, was found not to transmit NANB Hepatitis/HCV. That product was available for use from April 1987. That date compares favourably with the achievements of commercial manufacturers in providing safe products, as shown in Table 24.1. In addition, unlike the position in England, PFC were able to supply a sufficient quantity of product to meet the identified needs of all Haemophilia A patients in Scotland.

Section 7: Production of cryoprecipitate

91. Did either the EBTS or the WRTC produce cryoprecipitate? If not, where was this produced for both the Edinburgh and South East Scotland region and the Wessex region, and what were the arrangements in place?

223. Both centres produced cryoprecipitate.

92. If the EBTS or the WRTC did produce cryoprecipitate, please describe:

a. where the production of cryoprecipitate took place;

224. EBTS – on centre premises which at the time of my arrival were in Archibald Place, Edinburgh then transferred to better adapted accommodation at Livingstone House, Cowgate, Edinburgh around, I believe, 1983.

225. WBTS – on the premises of the Centre in Coxford Road, Southampton.

b. broadly, the process that was undertaken, the capacity of the EBTS/WRTC to manufacture cryoprecipitate and whether this changed during your tenure and why;

226. EBTS Archibald Place. Donated blood was collected into 'Tuta' packs with two 'pigtail' lines capped with male luer-locks suitable for connection to separate packs. Donations selected for cryoprecipitate production were hard-centrifuged and the separated plasma transferred via a freshly connected pigtail line to an empty receiving pack, which was then snap-frozen by immersion into a bath of methanol and dry-ice to cooler than minus 60 deg. The frozen plasma was thawed overnight at about 4 deg C which left a cloudy precipitate: this was separated after another hard centrifugation, the supernatant plasma being transferred via another pigtail to a receiving pack. The retained cryoprecipitate was snap frozen – sometimes three or four cryoprecipitates were pooled prior to re-freezing as this forestalled some aspects of the 'bedside' thawing and preparation of the final product to be infused. When required for a patient, cryoprecipitates were thawed, pooled into more packs if indicated, and administered to the patient by one of the clinical (ward) staff. As far as I remember, the usual ultimate dosage for older boys and men was a pool from six donations.

227. This process was ingenious but criticized because of susceptibility to inadvertent introduction of environmental microorganisms. My recollection

is that when the facilities were transferred to Livingstone House, Cowgate, where the facilities were much improved, the pigtail system was abandoned for a more conventional closed-pack and environmentally safer system at less risk of contaminating the cryoprecipitate product. This produced single-donor packs of cryoprecipitate for clinical use, this system remaining for the rest of my appointment at ESEBTS.

228. Most donations at Edinburgh were collected at outside sessions: the capacity for collecting standard whole blood donations in the Centre of the former RIE were very limited, although the Centre's main facility did have an apheresis unit which was used mostly for clinical use.

229. The method of cryoprecipitate production at WRTC while I was accountable was similar to that used at EBTS, the snap-freezing process using methanol and dry ice; the cryoprecipitate being supplied unpooled and from single donors.

c. what proportion of blood collections were allocated to this process and were sent to PFC/BPL, how this decision was made, and whether this changed over time;

230. EBTS – my recollection is that for most of my time, about 60,000 – 70,000 donations of whole blood were collected each year, from which initially about half were retained as whole blood, the remainder being available as red cell concentrates for clinical use. Plasma from the bulk of the processed blood was sent to PFC at Liberton for fractionation, usually pooled from about 20 donations into a 5 litre capacity plastic pack and snap frozen, but a substantial portion was retained in single packs as Fresh Frozen Plasma from which a further proportion was the source of the cryoprecipitate. When 'Optimal Additive Solutions' (OAS) became available for preparing red cell concentrates, the yield of plasma per donation increased to about 300 ml which therefore increased the yield of

FVIII per donation, whether for cryoprecipitate production or fractionation. Many surgeons – particularly in the cardiac surgical unit – preferred unprocessed whole blood which therefore limited the amount of plasma available for FFP, Cryo or fractionation: it was my job to persuade the surgeons of the advantages to the heart patients of using red cells in OAS, which was achieved with some success by the use of surgical audits. Concentrates of platelets for clinical use were also prepared from platelet-rich plasma separated from fresh whole blood after low-speed centrifugation and separated into empty packs using the pigtail system from which platelet-poor plasma was also derived, pooled and sent for fractionation. The flexibility of the pigtail system improved plasma yield for fractionation. I cannot recall the exact proportion of donations each year from which cryoprecipitate was prepared but it would have been a few thousand each year.

231. WBTS. About 100,000 donations were collected each year during my time. Although the OAS system also came into use, the pigtail system was not used, as far as I recollect.

d. how much funding was provided by the SNBTS/Wessex Regional Health Authority for the production of cryoprecipitate; and

232. As far as I am aware, the funding for cryoprecipitate production at either Centre was not identified separately from the overall costs of blood collection and processing.

e. how quickly the EBTS could have increased its manufacture of cryoprecipitate, had it wished to, during the early 1980 s.

233. Please also see my response to Q 66 d.

234. EBTS output of cryo increased after the move to Livingstone House partly because of the availability of 'Optimal Additive Solutions' in the blood collection packs which enabled more plasma to be recovered from each donation of whole blood. In order to increase output further, more equipment, more staff, longer working hours and more plasma would have been required. Plasma collection alone would have increased costs. Given the resources and donor consent, any centre could have increased its output of cryoprecipitate.

235. Ways of boosting the F VIII content of donated plasma were considered, especially by donor inhalation of DDAVP snuff as a way of temporarily boosting F VIII concentrations in donor plasma; but such procedures would be fraught with consensual and ethical considerations. It is intriguing to consider the effects of such practices, but overall opinion was that the practical effects were unpredictable, so the possibility of adverse effects, if not actual harm, led to the abandonment of such proposals. Donor interests must always be considered as well as the interests of patients.

236. A pool of specific plasma donors donating more frequently by apheresis, analogous to the current practice of platelet concentrate donation by apheresis might also have boosted output but would also have required ethical consideration, especially if 'boosted'.

93. Please explain what consideration the EBTS gave to increasing the production and use of cryoprecipitate in response to the growing awareness of the risks associated with Factor VIII concentrate products in the 1980s.

94. Please describe the steps taken by the EBTS to increase the production of cryoprecipitate during this time. If no steps were taken, please explain why.

237. Q 93 and 94. I note from PRSE0001081 that the 'total; 'use' of F VIII concentrates (in 1986) was highest at the Edinburgh Centre at 2.3 m.i.u

per million population – which implies that about 2.6 million units were used annually at the time by the Edinburgh HC. I have no figures for the use of cryo by the RIE HC at that time but it was probably less than 1 million units which would have come from no more than 13,000 cryo units. As far as EBTS was concerned, it seemed that the low numbers of individual cryo units in each pool would minimise the risks of virus transmission although if a patient received, say, 12 units for each bleeding episode occurring, say, 12 times a year they would be exposed to 144 different donors. The introduction by 1986 of excluding all donors with an identifiable higher risk lifestyle and all donations testing positively for HIV and hep B minimised as much as possible the risk of TTI (transfusion-transmitted infection) by cryoprecipitate.

95. Please describe the arrangements for supplying cryoprecipitate to hospitals and haemophilia centres within the region covered by the EBTS and WRTC.

238. EBTS. The main hospitals were the RIE and Royal Hospital for Sick Children. The RIE haematology department was next door to the Blood Supplying department of the EBTS, but the cryo thawing and pooling was probably conducted in the EBTS Blood Bank and supplied directly by porterage to the wards. I cannot remember the precise system. The RHSC was less than half a mile away. Occasionally, haemophiliacs attended other hospitals such as Peel Hospital (Melrose) or St John's Hospital, Livingston: but I cannot recall specific incidences.

239. For WRTC, the main haemophilia centre was in the haematology Department at Southampton General Hospital (Haemophilia Director Dr Morag Chisholm). The haemophilia Centre at Lord Mayor Treloar was also supplied with cryoprecipitate from WRTC. As the WRTC was sited in the grounds of the SGH (although it was the 'property' of the Wessex RHA) and very close to the SGH delivery port for goods, delivering

consignments of blood, blood products, FFP and cryoprecipitate to the SGH was conveniently rapid and occurred routinely daily. Deliveries to Treloar was by road transport using the WRTC fleet of refrigerated vans.

240. Orders from both sites would have been received, logged and dispensed. I have no record of the scale of the average dispatch.

Freeze-dried cryoprecipitate

96. A memo you received in May 1980 stated that the EBTS did not have "adequate freeze drying facilities" to allow for the production of freeze-dried thaw-siphon cryoprecipitate (PRSE0003444). What was your view on this issue at the time? How else, if at all, was the production of freeze-dried cryoprecipitate limited by the facilities at the EBTS?

241. May 1980 was more than 41 years ago. Yet I do recognise the memo. However, I was still quite new in my job and was learning all the time about possible ways of increasing the yield of F VIII in cryoprecipitate. Many factors needed to be considered in these early studies, including reliability of assay methods needed to compare the yields of different modes of thaw-syphoning and, the 'contaminating' effect of other plasma proteins such as Factor VIII RAg ('related Antigen' - which turned out to be more related to von Willebrand factor), fibronectin and fibrinogen.

242. Freeze-drying is a specialised technique requiring carefully designed equipment, which had to accommodate different modes of presenting the material to be designed (bottle shape, content volume, etc) and had to meet GMP standards, including sterility. (I believe that in the end the equipment at West of Scotland Centre at Law Hospital was deemed not to meet GMP standards, even though FD Cryo from WoS BTS had been available for several years). It should be realised that the Glasgow Haemophilia Centre was about 20 miles away from the WoS BTS and the

relationship of the physicians/haematologists at the GRI and the WoS BTS staff not so close as in Edinburgh. This difference bore significantly on the experience and practices in the two cities.

243. The subtleties within this prolonged study of the uses of FD cryo (prepared at WoS BTS) for Scotland were quite profound and barely represented in the documents supplied. I don't think we in Edinburgh were in any position to decide which of the various options for preparing Freeze-dried cryoprecipitate could be put into practice. EBTS had no Freeze Drying facilities at this time. Earlier equipment had been used by the PFC when sited in the RIE and transported and replaced when PFC moved to Liberton for preparing fractionated plasma products.

97. On 28 January 1982, you attended a meeting of the Factor VIII Study Group at which members from West Scotland intended to expand the use of freeze-dried cryoprecipitate to patients on home therapy (PRSE0001020). As to this meeting:

a. Why did the meeting reach this conclusion?

244. I think that there was no 'conclusion' that West Scotland patients on home therapy would receive more freeze-dried cryoprecipitate: although this was an intention, as far as I can recall it was not achieved.

b. Please set out your view as to whether freeze-dried cryoprecipitate was suitable for home therapy, including any factors which you took into account in forming your view.

245. Clearly, WoS had been producing FD Cryo for some years with some success, whereas in Edinburgh that concept had been further developed in the PFC as FD fractionated concentrate. As far as I can recall, I was not

convinced that any advantages for Edinburgh patients on home therapy would result from the manufacture of FD cryoprecipitate at EBTS.

98. On 11 January 1983, you wrote to Dr Cash and Mr J. Watt regarding freeze-dried cryoprecipitate (SBTS0000269_002), commenting on an earlier letter from Mr Watt to Dr Cash (SBTS0000269_003).

a. Did you agree with Mr Watt that the higher yield of freeze-dried cryoprecipitate was "no longer relevant"?

246. I believe that you misunderstand Mr Watt's statement that "the argument that we need freeze-dried cryo because of higher yield is no longer relevant."

247. What John Watt was saying was that if the SNBTS Centres supplied good quality donated plasma to the PFC with 800 iu / Kg, and PFC produced a 'suitably pasteurised and purer' product from which 250 iu of F VIII was produced per Kg of that donated plasma, the amount of F VIII available for patients would be similar to that coming from cryoprecipitate. Furthermore, it would be better than cryo because it would be purer and more easily infused to patients in need. Hence, even high-yielding Freeze Dried Cryo would be no longer relevant. The 'suitable pasteurisation' may even make the PFC product virologically safer.

b. Why did you state that the case for small pool material would be less strong with the onset of a "properly pasteurised product?"

248. It may be noted that Mr Watt in his earlier letter also referred to 'properly pasteurised product' as well as 'suitably pasteurised'.

249. I actually wrote that 'with the onset of a properly pasteurised product, some of the cases for small pool or single donor material, such as

cryoprecipitate, will be less strong.' (For 'cases' read 'arguments.) As my letter also pointed out, cryoprecipitate can benefit non-haemophiliacs: such people included complications of major surgery and children with DIC.

250. 'Properly pasteurised' products would have meant the neutralisation of any and all infectious contaminants.

251. The main virtue of small pool or single donor materials (bearing in mind that at that time individual packs of EBTS cryoprecipitate for clinical use contained material from 3 donors), is that with a low incidence of "healthy" asymptomatic donors who were infected with a transfusion transmissible microorganism (of an order thought then to be of a magnitude of one in a few thousand), small pool materials, which would still have a small risk of transmitting infections, would nevertheless have a safety no better than that of 'properly pasteurised' products from larger pools (of a thousand or so donations).

c. Were you aware of any statistical evidence which showed that single donor products reduced the risk of infection?

252. Mr Watt had a tendency for rhetorical statements. He knew very well that no detailed study of the statistical probabilities of transfusion transmitted infections from individual donors, a handful of donors or thousands of donors had yet been conducted, nor was likely to be conducted. By the 1980's there were many reports of serum hepatitis in association with exposure to blood, serum or other blood products had been described. (See my response 418 to Q 168 which refers to early work by Dame Janet Vaughan in the late 1940's.)

99. Do you think that cryoprecipitate should have been used more widely? Please explain your view.

253. See my response to Q 66 d.

254. Making cryoprecipitate with high F VIII content is an art as much as a science and is difficult to standardise. Consequently, the F VIII content of cryoprecipitate produced by each UK RTC was highly variable in time and in place. Careful freeze drying might even-out some of these variables and indeed make it more suitable for home therapy, but I believe that this opinion was not held widely throughout the UK.

255. In spite of recognising that large-scale pooling plasma for fractionation was associated with an increased risk of transfusion-transmitted infection, in the very early 1980's some Haemophilia Directors may have been reluctant for the UK blood transfusion services to revert to cryoprecipitate production only. What follows in this paragraph is highly speculative, and also touched on by my responses to the next few questions, but had the Directors been restricted to using NHS-only source materials they may well have preferred, on convenience grounds, concentrates of F VIII fractionated from plasma donated by volunteer unremunerated UK blood donors. (This would have been my position as a Haemophilia Centre Director in the late 1970's.) Although fewer people with haemophilia may have been infected with HIV/AIDS from UK-BTS source materials, if in the early 1980's the policy had switched to universal cryo-only treatment there would nevertheless not have been enough materials to support the increasing number of young men with haemophilia, especially those who wanted to be physically more active. I believe that this would have been the case even if funds and facilities had been provided to increase cryoprecipitate production. Hence, demand for the UK-licensed commercial overseas F VIII concentrates from remunerated donors would have become irresistible. This would have negated any safety from TTI provided by a "UK-cryo-only" policy unless the haemophilia community had become convinced that banning commercial concentrates was in their long-term interest. It was extremely difficult at this time to balance the

short-term advantage of rapid and effective treatment of bleeding episodes by concentrates against the long-term advantage of preventing TTI-associated morbidity and mortality potentially offered by a UK-cryo-only policy.

256. Venous access. In my experience, haemophiliacs everywhere (and their mothers) used to dread the possibility of running out of veins. During my time at Liverpool, all access to veins for delivering F VIII and for blood sampling was conducted through single-use disposable needles. In the early 1980's, surgical techniques for inserting indwelling catheters to facilitate short courses of delivering chemotherapeutic agents intravenously were being developed for patients with malignant diseases. Such techniques were not considered for haemophiliacs (whose need was for life) until later and I had no experience of them. Although long-term indwelling catheters are now much more commonplace for people with haemophilia, I am not sure how well-suited they would have been for administering cryoprecipitate had that become the UK's main source of F VIII in the 1980's.

100. Please explain what consideration the WRTC gave to increasing the production and use of cryoprecipitate in response to the risks associated with Factor VIII concentrate products.

101. Please describe the steps taken by the WRTC to increase the production of cryoprecipitate. If no steps were taken, please explain why.

257. 100 and 101. As far as I am aware, the WRTC was not approached by the Southampton HC to increase the production of cryoprecipitate in spite of the known risks of TTI and of HIV/AIDS in the community (which included blood donors). Treloar HC put considerable pressure on the WRTC in the mid 1970's (before my arrival) who, I understand, worked very hard to meet their demands.

Section 8: Self-sufficiency

102. During your time at the EBTS and the WRTC, what did you understand the term 'self-sufficiency' to mean? Did this change over time?

258. The concept of 'self-sufficiency' for civilian societies is that all the needs of that society be met from internal sources. For specific activities such as State health care, which by their nature rely on international trade and private pharmaceutical enterprises, self-sufficiency has obvious limitations – as seen in the current pandemic: but within certain sectors such as the supply of human materials like blood, limiting sources from outside the State can be epidemiologically beneficial. Further limitations are posed by human biology: for example, the development of immune intolerance to non-self proteins, such as clotting factors, by persons born without those factors (or with non-functional deficient factors) who are treated with normally functioning factors sourced from other people or from recombinant technology. Whereas it is possible to limit the effects on people with haemophilia A of exogenous F VIII derived from human blood donors (by limiting exposure and viral inactivation), the demands and complexities of human biology complicate such aspirations, even were pasteurised and recombinant F VIII available 'freely'.

259. Given that UK demands for F VIII began to exceed endogenous supply from the early 1970's, it was inevitable that commercially manufactured F VIII sourced from blood donated overseas would supplement endogenous sources. The introduction of home therapy added to that challenge.

260. So the factors that changed 'self-sufficiency' of the supply of blood products over my time include increasing demand, the development of home therapy, the discovery of more TTIs, the increasing stringencies of

donor selection, the limited availability of UK-derived F VIII concentrates as demand rose – in Scotland as well as in the rest of the UK – and the availability of foreign commercial F VIII concentrates licensed for use in the UK.

261. It may be interesting to note that in 1976, John Cash predicted that a severe haemophilic on unlimited on-demand home treatment would require about 500 i.u per kg body weight per year, and that the UK would need about 50 million i.u F VIII per year. (John Cash and Mary Spensely, 1976. Haemophilia A and the Blood Transfusion Service: A Scottish Study. BMJ, 1976, 2, 682 – 684). Although these figures seemed daring at the time, the 50 million is short, probably by almost one order of magnitude, although the calculated individual demand is somewhat closer (but still short).

103. In your experience at the EBTS and WRTC, to what extent was 'self-sufficiency' a concept that informed the following:

a. plasma procurement;

262. The concept of self-sufficiency led to methods of increasing plasma procurement being developed across the UK: they included

- maximising plasma yields from individual standard donations (helped by the development of optimal additive solutions – OAS – but initially hindered by surgical reluctance to forego the use of 'whole blood'),
- better (more selective) clinical use of blood and blood products, such as FFP and platelets,
- and the (limited) development of plasmapheresis donor panels.

b. decisions with regard to cryoprecipitate production;

263. The production of cryo increased during my time at Liverpool. I have no data on the volumes of cryo produced from EBTS or WRTC but believe that it was fairly steady until recombinant F VIII and F IX products became available (which was beginning before the end of my time) in spite of successful efforts to neutralise viruses and improve the purity of F VIII and F IX products derived from UK blood donors. The arrival of vCJD had a profoundly diminishing effect on the use of blood derived F VIII and F IX although limited amounts of cryo were maintained for non-haemophilic use.

c. purchases of commercial blood products;

264. The purchase of commercial blood products was universally regarded as a 'necessary evil', given the demand and supply situation in the UK.

d. funding received from the SNBTS/ Wessex Regional Health Authority.

265. The supply of donor-derived F VIII in Scotland during my time was affected by funding limitations. In common with many medical 'advances', the costs of new developments (for example for heat treatment of F VIII concentrates) were a constant challenge before the arrival of vCJD forced the eventual closure of the PFC facility. The SNBTS continues to fund a well-organised Blood Transfusion Service.

266. The WRHA funded a major (c £2 million) development in the mid-1990s (before the reorganisation of the NBTS in England and Wales and the formation of the NBS in 1995) to upgrade to GMP requirements the Blood Products facility at the Southampton Centre, thereby allowing the expansion and improvement of the quality of plasma, cryoprecipitate and platelets, as well as red cell products.

104. What was your view on the prospect of the UK achieving self-sufficiency?

267. That this was a laudable but fundamentally unachievable aim which nevertheless inspired staff in the UK RTCs to maximise efficiency and quality of blood, blood products and plasma fractions. For reasons stated above, I never regarded that complete self-sufficiency in plasma-derived F VIII would be achieved, but efforts to minimise dependence on sources outside the UK (and this included from the EU, although we accepted EU standards and regulations) should be maximised. The development of recombinant technology has had a clear effect in replacing plasma-derived products in the UK.

105. As far as you are aware, did your views on self-sufficiency accord with the views of your peers and the Blood Transfusion Services?

268. I think so.

Section 9: Knowledge of risk of infection

HIV/AIDS

106. During your time at the EBTS, what was your knowledge and understanding of HIV (HTLV-III) and AIDS and, in particular, of the risks of transmission from blood and blood products? How did your knowledge and understanding develop over time? You may find PRSE0003481, PRSE0003244, PRSE0001638 and PRSE0003709 of assistance.

269. During this time the medical staff at EBTS read successive CDC reports starting with MMWR weekly July 16, 1982 / 31(27);365-7 and became aware of peculiar cases on Pneumocystis carinii emerging in the US and

affecting haemophiliacs with an epidemiology strikingly similar to that of hepatitis B. This condition – initially labelled by some as 'GRIDS' – was labelled 'AIDS' in late 1982.

270. We at EBTS became increasingly concerned that the Edinburgh Festival of 1983 might attract folk at risk of AIDS and it was known that visitors at previous Festivals had donated blood. We were concerned about how best to deal with such donors if they could be identified as visitors, especially from the USA but as far as I remember were unable to come up with specific policies about how to identify visiting donors who may have originated from high-risk populations.

271. From 1982 onwards the epidemiology and significance of HIV/AIDS became more apparent, especially the association with parenteral drug users (which was highlighted by a GP in Edinburgh, Dr Robertson) who was in frequent discussion with Dr McClelland. Our policy of not taking blood from identified drug users was reinforced. Discussions with the Terence Higgins Trust about collecting blood from MSMs (men having sex with other men, as they were called later) were helpful as they tried to educate their members about the dangers to recipients of blood donated by MSMs.

272. We became aware in early 1985 of a report published in the Lancet in 1984 (Melbye et al.) of HTLV III seropositivity in European haemophiliacs exposed to factor VIII concentrates imported from the USA. Lancet 22/29 December 1984, pp1444 to 1446) which although showing a lower percentage incidence in Scottish haemophiliacs receiving concentrates solely of PFC FVIII than among Danes who mostly received commercial F VIII, was nevertheless of concern to us as showing 12 of 77 Scots haemophiliacs as having anti-HTLVIII so who must have been exposed to an infected donation (donor). Colleagues from Glasgow Royal Infirmary

were co-authors of this report, which was referred to in our report of March 1985 (PRSE0003481).

107. How did your knowledge and understanding of HIV (HTLV-III) and AIDS change during your tenure at the WRTC?

273. When I took up my post at the WRTC I was very aware of the significance of HIV, to the extent that outwith my professional duties and because of my concern with the care of the HIV sufferers I made personal contact with the HIV-support community in Southampton.

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

274. Probably in 1982 – by the July 1982 MMWR weekly report referred to above which was the first clear-cut evidence that haemophiliacs were affected although there was a growing suspicion, based on epidemiological comparisons with hepatitis, that haemophiliacs and other recipients of blood might be affected.

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

275. EBTS. I was a co-author, with Dr McClelland and Dr Ludlam, of the paper in document PRSE0003481, which was a detailed enquiry into the illness of a patient attending and investigated by the RIE Haemophilia Centre.

276. WRTC. By 1990, investigations on TTI with HIV in blood donors were based on the results of the established screening tests and the risks to recipients were well known. The problem of 'false negative' results (and of 'false positives') were recognised and the NBS screening tests became

more sensitive with the introduction of HIV antigen testing as a marker of infection. Nevertheless, we knew that a 'window period' of infectivity between exposure and test-positivity remained in which non-detectable infection still rendered transfusion of blood from such individual could transmit HIV to recipients. It seemed that this window period lasted for only a few days (probably less than a week). I was not an active researcher at this stage.

110. Professor A L Bloom wrote to you on 23 May 1983 on the issue of AIDS and the importation of blood products (HSOC0001272), in response to your letter with suggestions about AIDS.

a. What suggestions did you make to Professor Bloom about AIDS?

277. I do not remember the details of my suggestions. No copy of my letter has been located.

b. What was your view on Professor Bloom's statement that it would be "counter-productive to ban the importation of blood products at this moment"?

278. Prof Bloom also expressed this view at the 14th meeting of the UKHCDs in October 1983 (doc PRSE0003244 – which is a copy of my rather detailed notes of that meeting and should be checked with the official minutes); and he was supported by Dr Peter Jones and 'several people' who – according to my account – agreed that patients should be encouraged not to refuse imported factor VIII. Dr Jones 'quoted the resumption of the use of such materials on the Western Seaboard of the USA'.

279. I cannot remember precisely what my view at that time was, but at some stage I did become concerned about the continued use of commercial concentrate in England but had no easy answer. I was probably influenced

by what I thought was a relatively safe concentrate from PFC Scotland although later this proved to be over-optimistic (Melbye et al Lancet 1984 22/29 December; pp1444-1446 (ref 1 in PRSE0003481).

c. What was your view on the deferral of home treatment for new patients?

280. I cannot recollect but probably sympathised with those who wanted to introduce HT for new patients, many of whom would have been young boys.

d. What was your view on the use of cryoprecipitate versus NHS concentrate at the time? What was your view on Professor Bloom's statement that he was not differentiating between the two for severely affected patients?

281. This was 1983. I cannot be sure without confirmation of my letter (which would put this correspondence into context). I may have concurred. More information may come from examining what the HCDOs decided on 'most of my recommendations'.

e. What was your view on the Haemophilia Society's concerns that the home treatment programmes were not being expanded with sufficient "vigour"?

282. They probably were understandably impatient to expand the home treatment programme at the time, but whether they appreciated the degree of the associated risks of still wanting home treatment may be doubted.

111. A letter from you to Mr R Perry of PFC dated 15 January 1985 describes the "implications of the AIDS situation" on a "possibly implicated batch

(0090) of Factor VIII concentrate" which had been given to "virtually all the haemophiliacs who were on our donor panel" (PRSE0000107).

a. **Was this batch implicated in the transmission of HIV? If yes, how did you come to know?**

b. **What further steps, if any, were taken in relation to the implicated batch?**

283. The batch of PFC F VIII concentrate 0090 was discussed by Dr McClelland in his evidence report to the Penrose Inquiry (PRSE0002760) which also identifies that in November 1984 I was aware of the strong implication that this batch was contaminated and infectious for HIV from a donation given in Scotland earlier in 1984. The first notification of a possible contamination of a batch of PFC F VIII was made by Dr Ludlam who reported it to Dr McClelland who then told Dr Cash and myself. About 16 haemophiliacs in Edinburgh were affected including most of those who donated their plasma (collected by apheresis) as a reagent for assaying the F VIII activity of samples of various blood products - including some sent by PFC - and also patient plasma for F VIII activity. The identification of this specific batch and the further steps taken are described in Dr McClelland's report.

284. Just to clarify, PSRE0000107 is also referred to in Q 75 and refers to a letter from me to Dr Perry about the need to supply factor VIII deficient plasma in order to assay F VIII activity in any clinical material relating to treating haemophiliacs. The easiest way to obtain this at that time was to use plasma collected from a severely affected but otherwise healthy haemophiliac with good veins, and to collect blood by plasmapheresis, thereby getting up to 500ml of suitable plasma – the red cells would be reinfused, and nothing given to patients.

285. As a result of this finding, it was decided that alternative sources of reagent plasma with no F VIII were required from materials prepared (not 'repaired') artificially by Dr Chris Prowse. This was for the safety of staff across the region performing F VIII assays on plasma from patients or on blood donation products and fractions.

Hepatitis

112. What was your knowledge and understanding of hepatitis (including hepatitis B and Non A Non B hepatitis ("NANB")/hepatitis C) and, in particular, of the risks of transmission from blood and blood products during your time at the EBTS? How did your knowledge and understanding develop over time?

286. I understood that there were risks of transmitting viral 'serum' hepatitis from my clinical medical student days (early 1960 s) probably when taught about vaccines. During my registrar training in the early 1970s - at the London Hospital and Brentwood RTC - I learnt about the significance of the 'Australia Antigen' and the adoption of immunological techniques for screening people (donors) for hep B infection.

113. How and when did you first become aware that there might be an association between hepatitis (including hepatitis B and NANB/hepatitis C) and the use of blood and blood products?

287. I observed at least one patient at the London Hospital in 1972 who suffered two bouts of hepatitis after receiving treatment with a single batch of commercial F VIII concentrate – thereby being advised by Dr Craske who emphasised that there were more serum hepatitis viruses than hep B and introducing me to the concept of NANB hepatitis.

114. How did your knowledge and understanding of hepatitis change during your tenure at the WRTC?

288. The main developments were the preparation of hep B vaccines which were thought to protect susceptible populations from hepatocellular carcinoma; and also the identification of the hepatitis C virus as the main (but not the sole) agent associated with NANB hepatitis.

115. What, if any, further enquiries and/or investigations were carried out at the EBTS and at the WRTC in respect of the risks of the transmission of hepatitis? What was your involvement? What information was obtained as a result?

289. We were of course concerned with the risk of TTI hepatitis and would have tried to follow up any cases of post-transfusion hepatitis, but the delay between being infected and the frequent subclinical presentation of any viral hepatitis made this difficult without close post-transfusion surveillance. I was not involved in any detailed surveillance programme either at EBTS or at WRTC.

116. In a scientific paper dated October 1986, Dr Gunson stated that the best estimate of the incidence of transfusion-associated NANB hepatitis in the UK from published data at the time was 3% (SBTS0001120). He further noted that 'if one assumes that the 2.3 million donations in the U.K are transfused to 750,000 recipients annually...then one would expect 22,5000 icteric or (bold font FEB; the quotation should have been 22,500) anicteric cases of NANB hepatitis each year.' Please answer the following questions

a. Were you aware of this paper and these findings during your time at the EBTS? If yes, when and in what circumstances did you become aware of the findings of this paper? If no, when did you become aware of it and/or the conclusions set out within it?

290. I believe that the annotations on SBTS0001120 are in Dr McClelland's handwriting and he would have discussed these findings with me but I do not remember the details of the circumstances whereby I became aware of this paper. To the left of the paragraph quoting the figure of 22,500 (sic – not 22,5000), Dr McClelland appears to have made an almost illegible note referring to 'FB' possibly suggesting that I check on the accuracy of this statement. He also underlined specific statements indicating that he thought they were significant. I find it difficult to justify the statement that 'the best estimate of incidence from published data is 3%' as this seems to include many people with non-specific indicators of liver malfunction after transfusion. The 3% claim is used to calculate the figure of 22,500 cases of icteric or anicteric NANB hepatitis each year and seems very high. However, this was a contentious issue until the specific HCV could be readily detected and identified in healthy people and those who were ill and revealed that the risk was more like 0.6 to 1%.

b. Were these figures regarding the prevalence of NANB post-transfusion hepatitis ever discussed within the EBTS or, more broadly, within the SNBTS? If yes, please describe the general response to these figures.

291. The response to these figures would have acknowledged that they supported the growing awareness that NANB hepatitis caused significant and prolonged damage to the livers of many infected people, and emphasised the need to develop better ways of screening out donors with NANB hepatitis. The trouble at this time was that no screening test was available and indeed the virus had not yet been visualised, so it was difficult to get a more reliable estimate of the true incidence.

117. Please provide details of any other information that informed your understanding of the severity and prevalence of HCV in the UK donor population.

292. I cannot recall the details of any other information but by 1979 we were already aware of Dr Preston's work published in 1978 which revealed the impact of NANB on the livers of haemophiliacs who received blood products .

General

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

293. EBTS. There was active participation in the HCDO meetings and a sharing of information. I also met with Dr Ludlam to discuss the management of TTI risks especially from clotting factor concentrates on an occasional basis - often rather informally. I also participated in cardiac surgical audit meetings which occasionally referred to TTI risks, especially in the context of increasing surgical blood salvage procedures (designed to reduce the number of transfused blood packs).

294. WRTC. I was aware of the developments concerning HCV detection and testing in the UK, but no members of the WRTC staff, including myself, were invited to HCDO meetings, or received any report, which may have been unfortunate. There were occasional meetings of the Wessex haematologists at which such issues could be discussed but there were not many detailed discussions. Visiting trainee haematologists were instructed on TTI, and Foundation-year doctors received a detailed training session within a week of their appointment which would have included TTI.

119. What, if any, role did each RTC have in advising those hospitals and haemophilia centres that it provided blood and blood products to, as to the risks associated with blood and blood products? Please give details of any steps taken in this regard.

295. EBTS had good working relationships with the Edinburgh Haemophilia Centre and the major surgical users and oncologists which included the risks associated with the transfusion of blood products.

296. WRTC. This was less well developed at Wessex at first, but in the last years of my appointment with the NBA, regular meetings were held with the haematology consultants and also with the staff and senior nurse in charge of the Southampton General Hospital Blood Bank. I was also well-known to the neonatologists (who practised intrauterine blood transfusion) and to the oncologists, especially the paediatric oncologists with whom I had occasional meetings to discuss the problems associated with the use of blood and blood products.

Section 10: Reduction of risk of infection

Donor selection

120. What donor selection policies and processes were in place during your tenure at both the EBTS and the WRTC, and how did these change following the emergence of:

a. AIDS/HIV;

b. NANB/HCV; and

c. HBV?

297. The donor selection policies at EBTS and WRTC were based on national standards which became applied universally across the UK. Donors were required to be healthy and, at the time of donation, be free of symptoms of short-term illnesses such as colds. They had to be adults, although in the early 1990's people over 17 years old were accepted. First-time donors had to be younger than 60 although regular donors could continue donating until 65 years old: these ages were later increased to 65 and 70 respectively. They had to weigh at least 50 Kg or 8 stone. They were asked questions about their medical history and general health – with time these became more sophisticated, tabulated, and lifestyles (including recent overseas travel) were more closely scrutinised, but in the early 1980s responses to lifestyle questions may have lacked detail. To exclude anaemia, before donation they all had to pass a test of fingerstick blood haemoglobin concentrations. Blood samples were taken from the donor line at the end of donation for testing for blood group and microbiology for TTI. Until 1985, the only routine TTI tests were for syphilis and HBV.

298. HBV. By 1980, all UK blood donations were tested for HBV, initially for the HbSAg by immunodiffusion then by ELISA. As methods improved the false negative rates declined but to this day, HBV remains the most common TTI – in UK about 1 in 500,000 donations were estimated to be infectious for Hep B.

299. AIDS/HIV. Initial attempts to screen out donations at risk of transmitting HIV were based on lifestyle questions aimed to identify donors who, for example, were men having or who ever had sex with another man, and/or parenteral users of addictive drugs. During personal visits to donation sessions and conversations with staff, I witnessed that some voluntary leaders of community sessions who knew many of the individuals attending 'their' sessions were often judgemental about apparent life-style preferences and would exclude donors based just on the leader's assumptions: this practice barred, quite inappropriately, many donors

judged by such arbitrary standards but as donor management became more professional and non-judgemental (in that sense), such exclusions declined. Nevertheless, strenuous efforts were made to make contact with the MSM community, especially through organisations such as the Terry Higgins Trust, to educate MSMs and persuade them not to attend blood donor sessions.

300. This approach was only partially successful – a study in 1984 (Melbye et al, The Lancet, December 22/29, 1984 pp 1444-1446; "HTLVIII seropositivity in Haemophiliacs exposed to factor VIII concentrate imported from the USA", https://www.sciencedirect.com/science/article/abs/pii/S0140673684916325 showed that of 77 Scots who mainly had SNBTS F VIII, 12 became seropositive for 'anti-HTLVIII', while of 22 Danes who had USA-made F VIII, 13 became seropositive. This indicates that SNBTS F VIII preparations were relatively safer than USA-made F VIII, but there was still an unsatisfactorily high number of Scottish haemophiliacs who got infected with HIV after receiving SNBTS F VIII

301. UK universal donation testing for HIV antibody was introduced on 15 October 1985: on the same day a system was introduced nationally whereby members of the general public could get themselves tested anonymously if they thought that they were at risk. In Edinburgh, on the previous Monday, the EBTS was advised by officials at the Scottish Office that there might not be enough reagents to introduce both facilities (i.e., to blood donors and to the general public) at the same time, so they proposed supplying just the blood transfusion services. We advised them that such a system could put the recipients of blood at extra risk as persons wanting to get tested anonymously would be attracted to donor sessions just to get a test: even if their donation had tested negative, people who had been exposed to HIV within the past few days could well be HIV negative but still be infectious due to what was called the 'window

period'. In time, more sensitive tests became available and the window period shortened.

302. NANB/HCV. In 1989 the genetic material of the long sought-for HCV was detected and used to make marker proteins of HCV which reacted with antibodies in the serum of people either with, or having a history of hepatitis C. This has been the basis of screening tests for HCV infectivity in blood donors. This technique has been highly successful in protecting people from HCV transmitted by HCV-screen-negative non-pooled plasma which has not been virus-inactivated but is not absolute as about 1 in 3 million donations in the UK may transmit HCV.

121. How were decisions made as to which donors were high risk and should be excluded from donating? What was your role in this process at both the EBTS and the WRTC? Were these decisions reviewed and, if so, how often?

303. While at the EBTS and particularly at WRTC much of the evidence of high-risk donation was focussed on the epidemiology of HIV/AIDS. It was felt that the similar epidemiology of HBV and HIV/AIDS, and probably of HCV, would protect blood recipients from all three TTIs. This focussed mainly on MSMs which, however, was contentious among citizens advocating non-discriminating human rights, who felt that MSM status alone should not cause donors to be excluded.

304. We therefore relied on epidemiological studies conducted by Dr Kate Soldan, who showed consistently year by year that a very significant proportion of all new diagnoses of HIV/AIDS (about 2000 out of 6000 or 32% each year between 2000 and 2005) were in MSMs (37.8% were heterosexual women, 2.2% were injecting drug users and 0.4% were blood recipients). The policy during my time was to exclude any man who was ever an MSM. I reported an analysis of complaints to the UK blood services on the policy barring homosexual men from donating blood to the

ISBT in 2006. During this period, in the UK 1396 complaints were received which included 781 about the exclusion of MSM as donors. A pdf version of the slides I presented is available [WITN3456003]. I conducted this review while I chaired the Standing UK Advisory Committee on the Care and Selection of Blood Donors. (These policies are now radically changed.)

122. Were there any difficulties in implementing the exclusion of high-risk donors, either at the EBTS or the WRTC?

305. A careful detailed explanation based on the epidemiology was nearly always accepted – only two of my responses to the 781 complaints were completely rejected by the complainant. I believe that the donor teams from both Centres managed to exclude high-risk donors well, but it would not have been possible for them to achieve a 100% exclusion rate.

123. You were critical of Dr Peter Jones' reluctance to ask donors about their sex lives and reject male donors who had had sex with other men, describing his attitude as "somewhat less than cautious" in 1983 (PRSE0003709). Please explain your view. Why did you disagree with this approach? What approach did you think should have been taken? Has your view changed over time?

306. Dr Jones (who I knew well) felt that asking donors about their sex lives verbally at public sessions was unacceptable and information should be restricted to printed leaflets. I doubt if he understood the conditions for staff at donation sessions but restricting information on the printed word and having no conversation was not practical. My view has not changed, although printed information is still needed. In 1983, of course, there was no internet and conversations at sessions were needed in order to get better donor understanding and compliance. Furthermore, the public attitudes to

sexual diversity are nowadays much more liberal although unfortunately there is still much prejudice and sensitivity.

124. In respect of leaflets given to donors (for instance PRSE0004850 and NHBT0000190_063, page 1), were such leaflets nationally agreed by the SNBTS and NBTS respectively, or did each RTC produce their own? How often were these leaflets updated, and how was their content decided?

307. I believe that the initial leaflets from EBTS were composed locally – they were the responsibility of Dr McClelland. They were updated from time to time, but I cannot recall how often. I believe that leaflets were produced nationally from September 1983.

125. What, if any, additional information was given to donors about the risk of them transmitting infection via their blood besides that contained in donor leaflets? When and how was such information provided?

308. Any extra information given to donors would have come from the experienced health professionals at the sessions – at the time, these were usually medical doctors trained by the excellent medical Associate Specialists at the Centre.

126. How effective, in your view, were leaflets and other communications at reducing the risk of donations from high-risk individuals?

309. I think that the combined approach of leaflets, conversations and verbal explanations was quite successful in reducing the number of contaminated transfusions, but sadly, plasma pools were occasionally contaminated with TTIs.

Introduction of virally inactivated products

310. This is only an incomplete record and I may not have been privy to certain aspects and events occurring during the trials. Note; there were several trials of products under development during this period in BPL/Oxford and in Scotland.

127. What role did you consider the EBTS had (or should have had) in pushing for factor concentrates to be virally inactivated in the late 1970s and early 1980s? In particular:

a. Was the need for safe products raised by you or anyone else at the EBTS with the PFC and/or pharmaceutical companies (or anyone else) during this period? If so, please give details. If not, why not?

311. When I arrived at EBTS in January 1980, I came with my Liverpool HC experience, which had been that most HC Directors held that post-transfusion hepatitis in haemophiliacs was an inevitable consequence of clotting factor replacement therapy: this was of concern, but secondary to reducing the morbidity and mortality ensuing from inadequate replacement therapy.

312. Also when I arrived at EBTS, I was not familiar with how the concept of inactivating viruses in donor blood or plasma was developing in general or in SNBTS, but shortly after my arrival, Dr Cash emphasised that hepatitis in transfused haemophiliacs could be a serious problem and that even though the factor concentrates prepared by SNBTS/PFC were from plasma donated by voluntary unremunerated selected local donors and tested for hepatitis B (and syphilis), research on how to reduce the hepatitis risk further was being undertaken in SNBTS: in 1980 this issue was being addressed mainly through donor selection criteria and testing for Hep B and syphilis. In time, methods of virus inactivation came to the fore. (Commercial companies were, for example, using chimpanzees and

other animals which were thought to be susceptible to NANB hepatitis as well as hep B which might not be detected by routine tests.)

313. Although I appreciated that virus hepatitis was a significant public health problem, Dr Cash's emphasis on hepatitis as a Transfusion Transmissible Infection (TTI) was salutary. So, I was quite excited about the prospects of viral inactivation while preserving clotting activity of plasma F VIII, and there was no need for me to raise the case for safe products with the PFC. I participated enthusiastically with such developments in SNBTS when they became feasible and there was no need for me to be 'pushing for' virus inactivation. I realised that safety trials would, self-evidently, be necessary while such products were being developed.

314. Apart from the possibilities of failure to reduce TTI incidence and unexpected adverse effects, another concern was the possibility of 'neo-antigens' in virus inactivated products and the spectre of inducing therapeutic resistance due to inhibitory antibodies after in-vivo infusions, but these were risks that would have had to be taken so long as the human participants gave appropriate informed consent. It may be noted that a pasteurised F VIII product from human plasma (Factor VIII CPS-P from the Netherlands) was associated with a significant increased incidence of inhibitors among Dutch and Belgian multi-transfused haemophiliacs in the early 1990's, which was after the period covered by the Question.

128. In late 1980, the German company Behringwerke published a paper on a Factor VIII concentrate which it claimed did not transmit hepatitis as a result of being heated in solution at 60° celsius for 10 hours. You were of the view that this paper was incorrect (PRSE0004926). Please explain your views. In particular:

a. What was your understanding of the effectiveness of heat treated products? In your opinion, what merit, if any, was there in their development?

b. Did your views on heat treated products change? If so, when and for what reasons?

315. I was very much on the periphery of the technical discussions but as F VIII activity (but not the antigen) was lost in plasma within hours when standing at room temperature, and even more quickly at body temperatures (37° C), it seemed unlikely that it could survive at higher temperatures.

316. Chapter 23 of the Penrose Report, paras 31 to 43, covers the discussions within SNBTS/PFC concerning Behringwerke's claim. It can be seen that the initial SNBTS response was severely sceptical and I was not the only person to express doubt. Dr Foster of PFC thought that it was literally inconceivable, and Professor Mannucci was unimpressed by the experimental protocols ("the clinical evidence was meagre and the design of the study retrospective and poor"). Behringwerke's low recovery of F VIII (8%) was also unimpressive and patent restrictions made it impossible to duplicate Behring's work with confirmatory studies although it was known that Behring had treated the product for 10 hours at 60°C in the presence of glycine and sucrose. But with Dr Cash's encouragement further studies at PFC did establish that under certain circumstances, sucrose could protect F VIII activity during heat treatment which killed viruses, so our initial scepticism became replaced with enthusiasm.

317. Other areas which were explored soon after and had an impact on the F VIII activities of various SNBTS F VIII products were procedures which slowed the thawing process, and the stabilising effect of adding calcium and/or heparin, as well as adjusting the conditions accompanying the

inactivation processes (temperature, time, the freeze-drying process, chemicals etc.).

129. Please describe your involvement in Dr Ludlam's 1983 trial of heat treated Factor VIII material NY 761. You may find MACK0001333 and PRSE0002568 of assistance.

318. Document MACK0001333 refers to a letter dated 13 June 1983 from Dr Cash to Dr Ludlam, copied to me, Mr Watt and Dr Foster: it outlines a protocol for clinical studies of the first virus inactivated product produced by PFC – NY761 and asks Dr Ludlam to trial a batch of that even though batches of non-inactivated F VIII from PFC would not be available. On 4th July 1985 [PSRE0002568], I wrote to Dr Perry including the results of 5 patients trialled with 'HT F VIII' (heat-treated F VIII) by Dr Bloom in Cardiff; one patient was known to have had inhibitors which caused him to have no response to infused F VIII, so it was not surprising that there was no discernible recovery of F VIII activity in his plasma although he had no adverse clinical effects. The other four had satisfactory recoveries of F VIII and no adverse clinical effects. This letter also reported results gathered by Dr Prowse, EBTS' senior clinical scientist, on three further patients from (presumably) the RIE and under Dr Ludlam's care. These seven patients (excluding the one at Cardiff who had inhibitors) gave 'excellent' validation of the efficacy of this product.

In particular:

a. What did coordinating the trial involve?

319. Coordinating the trial involved getting agreement for the clinical protocols from all clinicians involved, ensuring the availability of materials when needed – noting that this depended on patients presenting for emergency treatment of a significant bleeding episode – which inherently was unpredictable, collating the results and ensuring that as many of the

scheduled test results were documented, and producing an initial report for each participating clinical unit.

b. What comparisons were made between heat treated Factor VIII with cryoprecipitate and intermediate Factor VIII in terms of the product's performance?

320. Comparisons would be made with the results (recoveries, half-lives, clinical signs, etc.,) expected from long clinical experience with cryoprecipitate and intermediate F VIII.

c. How was the efficacy of the product assessed? In particular, was the product's prevention of the transmission of infection part of this assessment?

321. The only mention of TTI in the protocol of MACK0001333 was the optional identification of rising titres of anti-HBs in persons already positive. I am not aware if this was investigated or if other tests such as surrogate tests were conducted.

d. How were patients selected to participate in the trial of a new heat treated product?

322. Patients selected for the trial at RIE would normally have been selected by Dr Ludlam or, in his absence, a colleague in the haematology Department

e. In March 1985, Dr Ludlam wrote to you regarding the issue of compensation for patients who had an adverse reaction to heat treated Factor VIII during clinical evaluation (PRSE0001819). What did you understand these adverse reactions to be, and what was your view on this issue? What effect, if any, did adverse reactions have on the speed with which the trial progressed?

323. Document PRSE0001819 is a letter dated 19 March 1985 from Dr Ludlam to me explaining that he needed to be assured that the SHHD would compensate patients experiencing an adverse event, otherwise he would need to seek ethical approval of the study – which otherwise he wouldn't need. The sort of adverse reactions about which Dr Ludlam was, I believe, concerned would probably have included failure to inactivate viruses, immune disruption such as unexpected development of F VIII antibodies/inhibitors or even general intolerance to heat treated products such as prolonged 'flu-like symptoms induced by 'pyrogens' in the HT (heat-treated) products (pyrogens are well-recognised contaminants in many natural products and release factors such as interferons into the circulation), and other severely disabling events which affect the patient's normal life/livelihood. As far as I am aware, the only adverse reaction which occurred (this is addressed in my answer to Q90) was a short febrile episode in a patient who had previously experienced such symptoms after receiving infusions of other F VIII preparations. I think that otherwise there were no disruptions due to adverse reactions, and that if Dr Ludlam's concerns about compensation and product licenses delayed the trials, they still went ahead.

324. My view on this issue is that I respected Dr Ludlam's concerns and that he had every right to express them. Dr Ludlam was not responsible for the apparent reluctance of the SHHD to ensure compensation. On the other hand, systems of product licence 'variations' for modifications of F VIII production were in hand by the PFC and licensing authorities and it could be argued that Dr Ludlam should have had more confidence in the production and licensing procedures for supplying the various concentrates. Dr Ludlam clearly approved of the trialling in principle, but had reservations concerning patients' rights and safety. It may be noted that other participants, Professor Bloom and Dr Mayne of Belfast, were happy to proceed with the trials.

130. Please describe your involvement in the continued trials of heat treated Factor VIII during 1985 and 1986. In particular:

a. What, if any, time frame was put in place for the conclusion of these trials?

325. I cannot recall if a specific time frame was put in place, but I believe that it was not intended to be longer than a year or so.

b. At a meeting of the Factor VIII study group in November 1985, the differences between the heat treated products made at PFC and BPL were discussed (PRSE0003428). PFC was experiencing an average loss of 20% yield on heating, as opposed to BPL's 5-10% loss in yield. What was your view on this issue at the time?

326. Document PRSE0003428 dated 21 Nov 1985 presents the minutes of the SNBTS F VIII study group of that day and includes a reference to me reporting on three patients receiving HT F VIII with good recovery and half-life.

327. On the question of the different degrees of yield losses between PFC's product - 20% at PFC on the intermediate concentrate with 2% sucrose and heated to 68°C for 24 hours, versus 5 to 10% losses for BPL 8Y F VIII with sucrose and heated at 80°C for 72 hours, and the implication that PFC should have switched production to a BPL 8Y-like product, it must be recognised that there were many investigations of ways to inactivate viruses without damaging the delicate F VIII molecules from the time blood (or plasma) was collected to final product. These were compounded by impurities in the starting plasma such as fibrinogen, fibronectin and (if one wanted really high purity materials) von Willebrand factor; and also proteins of the prothrombin complex. Stability of F VIII during fractionation,

virus inactivation and purification is affected among other things by time, temperature, pH, citrate/calcium content, freeze-thawing conditions, precipitation inducers (such as heparin), chemicals (polyethylene glycol, sugars such as sucrose), the freeze-drying process itself, etc; so it is not surprising that different approaches – sometimes developed with the help of serendipity – resulted in different recoveries. Furthermore, PFC decided not to emulate BPL because the heparin content of BPL's product interfered with SNBTS' assay systems and replacing the SNBTS assay system with BPL's would take time, uncertainty about the effect of apparently minor variations on F VIII stability, and the need to purchase and be trained in using large scale size exclusion chromatography equipment (p 44 of PRSE0002291). The difference between losses of 20% and 5 to 10% may be more apparent than real anyway (assay performances are notoriously fickle). All manufacturers want to improve quality and stability in the most economic ways possible and PFC were well on the way to developing a high purity and virally inactive product, 'Z8'.

c. How was the product to be implemented across the service at the conclusion of the trials? What was your involvement in this process? You may find PRSE0004152, PRSE0002611, SBTS0000332_089 and SBTS0000324_073 of assistance.

328. These records show that I was involved in collating the results of the trials and reporting them. I do not remember being directly involved in devising how the use of the product was to be implemented upon trial completion.

329. Document SBTS0000324_073, dated 22 Jan 1985, is a letter from Dr Perry as 'Acting Director' (who succeeded Mr Watt) to me about the system of 'batch dedication' which Dr Ludlam and I desired in order to minimise further any TTI risk, and that because a new product was due to be launched later that year, the number of patients studied on this 'old'

product had to be reduced to minimise patient disruption if unexpected problems arose, and facilitate the transition of all patients to the new product.

330. Document PRSE0004152, dated 4 March 1985, is a letter from Dr Perry informing me that the first two batches of HT F VIII 68° 24hrs would be available in 2 weeks and asking that the trials be completed quickly so that the bulk of their current lots could be subjected to the new more extensive heat treatment. Document SBTS0000332_089 dated 21 Jan 1986 is a report from me to Dr Perry, copied to Dr McClelland and Dr Cash, detailing the responses of four patients with haemophilia A. The results forms were designed by myself and, as requested, returned to me when completed. In retrospect I would criticise the design of these forms for not giving the date of the procedures, and not specifying what type of HT concentrate was used although the batch number was recorded and therefore information on the nature of the product was retrievable.

131. Please describe your involvement in the trial of heat treated Factor IX product. In particular:

a. Were comparison studies on the same patients carried out with non-heat treated Factor IX products? If so, what was the benefit of these studies?

You may find PRSE0000732 and SBTS0000155_054 of assistance.

331. PRSE0000732, dated 23 June 1986 represents the minutes of a wide-ranging meeting of the Coagulation Factor Study Group: this part of the Q131 refers to minute 'k/i' which is cryptic and, unfortunately, remains cryptic to me to this day. I do not remember the 'elderly patient with marked liver failure who subsequent (to treatment with F IX) died….' although not from bleeding or thrombosis; but it should be noted that F IX

treatment at this time was not restricted to people with haemophilia B. Therapeutic F IX concentrates were derived from plasma proteins in the 'prothrombin complex' and contained traces of other factors (prothrombin, F VII and F X). The prothrombin-complex of factors (II, VII, IX and X) are synthesised, with the help of biochemical cofactors such as vitamin K, from healthy livers. Patients with liver failure are often deficient in the normal prothrombin complex factors although traces of activated factors could be present in their blood. This situation could lead paradoxically to a mixed clinical presentation of bleeding and thrombosis. It is possible that the 'elderly' and obviously very ill patient was not suffering from haemophilia B but from an acquired disturbance of haemostasis associated with liver failure and that the F IX product was given in an attempt to ameliorate this situation – in which it failed.

332. The second paragraph of this minute refers to 'inhibitor patients': These would have been people with haemophilia A (F VIII deficiency) who had become resistant to treatment with F VIII concentrates because of the immune development of antibodies which inactivated normal F VIII. F IX concentrates, especially those which would not be used for people with haemophilia B on the grounds of potential thrombogenicity, were sometimes used successfully to stop the bleeding of people with haemophilia A and inhibitors. As such, SNBTS F IX concentrates were of interest to HC doctors with haemophilia A patients with inhibitors, and therefore of potential trial materials.

333. Document SBTS0000155_054 represents a letter, dated 11 Sept 1985 from Dr Ludlam to Dr Cash, about a trial in the RIE of HT factor IX on three patients with haemophilia B (F IX deficiency). I have no clear recollection of this trial but was clearly involved as Dr Ludlam referred to advice from myself about comparing the results of the trialled HT F IX concentrate from PFC with batches of untreated PFC F IX concentrate with which the patients had previously been treated (and therefore not exposed to any

more TTI risks than previously). I cannot recollect whether such extra untreated concentrates were administered. One feature of F IX concentrates which differs from F VIII concentrates is the greater thrombogenicity potential of F IX materials, and particularly active traces of thrombin and of activated molecules of the prothrombin complex (F VIIa, F IXa and F Xa). Concentrates of F IX are screened for signs of clotting activation but even if screening shows no in vitro signs, clinical thrombosis may still occur. It is possible that heat treatment may increase thrombogenicity so a comparison of the effects of heat-treated F IX concentrates with non-heat treated might have been informative.

132. Please describe your involvement in the trial of 8Y product in 'virgin haemophiliacs' in 1986. PRSE0001641 and PRSE0004097 might be of assistance. In particular:

a. What constituted a 'virgin haemophiliac' for the purposes of the trial?

b. What was the benefit in carrying out a trial on these specific patients?

334. PRSE0001641, dated 1st July 1986, is a letter from Dr Cash to me explaining that the 'awesome task' of a NANB study on 'virgin' haemophiliacs i.e., previously untreated patients with haemophilia ('PUPs') receiving PFC F VIII concentrates for the first time. This 'awesome task' would not be undertaken until a definitive product (which would not be available for at least 5 years) became available. The reason for conducting trials of new therapeutic materials on PUPs is that their clinical and haemostatic responses would not be affected by previous treatments which might have affected these responses and particularly that they had not yet experienced a Transfusion Transmitted Infection (TTI). Therefore, any sign of an infection would be clearly linked to the product used for treatment. It is ethically essential that the treatment be clinically justified -

the trial of a new product which was not clinically indicated by, for example, an uncontrollable bleeding episode would not be ethical. The 'awesomeness' probably related to the random and rare availability of PUPs needing treatment and the difficulties in detecting NANB infection before the virus(es) had been isolated. Surrogate testing such as liver enzyme activity in patients can also be of variable value – for example, many patients would be young boys whose liver function parameters may normally differ from those of healthy adults.

335. With the availability of treatment with concentrates of specific factors, 'Virgin' haemophiliacs – 'PUPs' – had become rare. About 85% of haemophiliacs in the UK have haemophilia A (deficient in F VIII) and 15% have haemophilia B (deficient in F IX). The UK incidence of haemophilia A is about 100 – i.e., about 100 boys are born each year with haemophilia A. About half of these are severely affected and have no detectable F VIII activity; they are likely to present with their first bleeding episode within a year or two of birth. Hence, each major haemophilia centre in the UK can expect less than a handful of severely affected 'PUPs' a year. More mildly affected patients (with detectable F VIII activity even if untreated) may present when somewhat older, but also less frequently. A similar proportion of the rarer patients with haemophilia B are also severely affected but 'PUPs' present even more rarely. The value of 'PUPs' to researchers is that when first infused with a blood product, any development of markers of a transfusion transmitted infection (TTI) is most likely to have come from that infusion. The clinical responses and detection in their blood of the otherwise absent factor can also be solely attributed to the infusion. In order to increase the number of suitable patients (who are unlikely to have acquired a transfusion transmitted infection – TTI), individuals who have been infrequently exposed to low-risk blood or blood products, such as a few doses of very small pool or single donor units of cryoprecipitate, have been accepted by some researchers. I cannot recall if any such low-exposed patients were used in

any of the trials of UK NHS F VIII or IX. (It may be noted that in general, F IX products may be TTI less risky than F VIII products due to differences in fractionation methods which may lose viruses in materials discarded during fractionation.)

336. PRSE0004097 (7 July 1986) is a letter from me to Dr Perry passing on a request from Dr Ludlam to Dr McClelland explaining that Dr Ludlam was worried about the availability of SNBTS virus-inactivated F VIII for as yet untreated haemophilic patients presenting to his Haemophilia Centre. Dr Ludlam was asking if 500 vials of BPL 'products' for untreated patients' could be available, although as yet the Centre had no untreated patients on its list. This was not unreasonable in principle as PFC's supplies were apparently somewhat compromised by efforts to produce a superior quality F VIII product (eventually successful and known as 'Z8'). In the event, BPL supplied PFC with my suggestion of 50 vials of their product (8Y) for Dr Ludlam's patients if needed (PRSE0003143, 24th July 1986).

337. My letter (PRSE0001641) crossed with a letter (PRSE0003814) from Dr Perry to me which explained a) that the 'phase IV product' (i.e., 'Z8') would start being produced in January 1987 and be ready for distribution in September 1987: and b), as in the immediate future (i.e., July to September 1986) there would be no virus inactivated PFC product comparable to BPL's 8Y, supplies of 8Y will be made available for as yet untreated haemophiliacs . Dr Perry anticipated that after September 1986, PFC's 'phase III' product (in which virus inactivation was comparable to BPL's 8Y) would be available and then supplanted by 'Z8'. Meanwhile, on 24th July, Dr Perry wrote to me (PRSE0003143) that BPL were happy to supply PFC with the 50 vials of 8Y which would cover Dr Ludlam's request.

c. Why was the 8Y product used in a trial conducted at the EBTS developed by BPL (PRSE0002643)? Why was the PFC unable to

produce a virucidally comparable product to 8Y until September 1986 (PRSE0003814)? What, if any, effect did this have on clinical trials conducted at the EBTS?

338. Some aspects of this issue were addressed above. The history of the relationship between the Fractionation Centres in England and the one in Scotland is interesting and I would characterise them as a 'friendly rivalry' which, however, did not preclude cooperation. It would be quite wrong to attribute elements of competition between them as methodology and administrative experiences were frequently shared, and this was beneficial overall. Nevertheless, each side was proud of its achievements and shared comparable elements of frustrations, for example over funding. As England (with Wales) is almost ten times more populous than Scotland (with N Ireland), it would be reasonable to assume that BPL plus Oxford PFL could expect ten times the funding for Scotland's PFC (which, of course, was not the case), but Scotland was closer to achieving self-sufficiency and less dependent on imported commercial clotting factor concentrates. The swings and roundabouts of fractionation technology in developing high-purity low-TTI-risk products meant that at times there were imbalances of supply in each country: a good sharing relationship between the two organisations helped to improve the supply of safer materials.

339. The developments of virus-inactivated products by BPL and the Scottish PFC occasionally had phases when one Centre was a step behind but caught up through developments which put them one step ahead. As demonstrated above, the EBTS benefitted from the occasional availability of BPL products.

133. In December 1986, you wrote to Dr Cash regarding the use of patients for half-life and recovery trials of Z8. You stated that, due to the removal of Crown Immunity from BPL (and presumably PFC), Dr Ludlam was

"concerned about the situation as far as indemnity to patients who suffer as a result of being infused with the trial material" and that, as a result, you had a "strong feeling he would be unwilling to agree to such trials unless there is a specific commitment by the SHHD that any patients who suffer adverse effects as a result of the infusion will be given appropriate compensation"(PRSE0003951). What was your view on Dr Ludlam's concerns? What effect, if any, did the removal of Crown Immunity have on the trials of heat treated products more generally?

340. Document PRSE0003951, dated 6 December 1986 is as described in the question and is a repeat of the issue raised in Q129 e. Doc PRSE0001819, 19 March 1985. Whereas I respected Dr Ludlam's concerns, I was somewhat taken aback by this as I had rather assumed that by participating in the exercises in late 1985 and reported by me in January 1986 (Q 130c. Doc SBTS0000332_089 dated 21 Jan 1986), Dr Ludlam had agreed to such trials.

341. I do recall the justifiable interest and indeed excitement among the fractionators at PFC Scotland and the two at PFL/BPL England about the prospect of therapeutic-quality freeze dried virus-safe factor VIII concentrate suitable for previously untreated patients ('PUPs'). A case report in the Lancet (doc PRSE0003481; Tucker et al, Lancet, March 9, 1985 p585) led by Christopher Ludlam and of which Brian McClelland and I were co-authors, describes a haemophilic requiring surgery followed by a stormy course complicated by the acquisition of HIV. We later found that this patient had received some of a batch of the then standard Scottish PFC FVIII concentrate which became associated with transmitting HIV to a 'further 14 haemophiliacs (unpublished)'. The publication does not identify the number of the implicated batch but it was probably the 0090 batch implicated in Q 111. This degree of transmission was deeply upsetting for us all (the patient, clinicians and the Scots fractionators); we had to face the reality that HIV must have been present in the Scots blood

donor pool in spite of the SNBTS's best efforts at donor selection in the pre HIV-testing era. But also in that report is a reference to the poor purity of the SNBTS preparation being associated with persistent bleeding: although not directly commented in the report, the distinct possibility was that the persistent bleeding was associated with denatured fibrinogen in the fractionated product. In other words, a perception that the product might not only transmit HIV but also paradoxically interfere with this patient's post-operative recoveries. Hence, the value not only of a virus-safe product but also a purer product.

342. Nevertheless, I do appreciate Dr Ludlam's anxieties. He was directly responsible for the welfare of the patients attending the Edinburgh Haemophilia Centre, and this included minimising the risks of acquiring a TTI. It was therefore entirely reasonable for him to express dissatisfaction if there was a possibility that an as-yet not safety-proven product was offered without due consideration of a patient's interests.

343. As far as the removal of Crown Immunity was concerned, SNBTS were anticipating this (with approval) and were happy for its sites to be inspected by the Medicines Inspectorate whose advice was always appreciated in the interests of Good Manufacturing Practice.

Recall of unheated product

134. PFC recalled all of its unheated Factor VIII product in January 1985 for heating (see, for example, PRSE0001885). In 1990, Dr Lane commented that BPL was unable to do the same owing partly to safety concerns (see CBLA0000029, p. 136-137): "BPL could not take back, for reissue, unused unheated concentrate. The reason for this was quality control. We had no idea of the products which had been issued some time before and how they had been handled during transportation and storage. In these

circumstances we would not be willing to heat treat products which had been out of our control for a period and then reissue them…" Please answer the following questions as far as you are able:

a. **Were the Scottish blood services concerned with these aspects of quality control?**

344. I believe that the SNBTS regions were satisfied that they could recall unused products that were still fit for use.

b. **How, and by whom, was the decision made to effect the recall of unheated products? Why was PFC's approach different in this respect?**

345. I do not know.

c. **Are you aware of any other entities (e.g. pharmaceutical companies) which recalled, heated, and reissued products in this way?**

346. No.

d. **What was your opinion at the time on recalling unheated product?**

347. That it was a sensible approach and saved wastage.

Recall of Factor VIII Batch 0231100090

135. In 1984, a decision was taken to recall a specific batch of Factor VIII from Scotland and Northern Ireland (SBTS0002206). Please answer the following questions about the recall as far as you are able:

a. **Why was the decision not made to recall Batch 0231100090 prior to 3 November 1984 (in particular, on the 29 or 30 October 1984)?**

b. **What can you recall, if anything, about your conversations with Dr Cash and Dr McClelland on 29 or 30 October 1984?**

c. **Was the possibility of quarantining Batch 0231100090 raised? If not, why not?**

d. **In your view, how does this incident reflect upon the practice of recall more broadly? Were delays for 'confirmatory testing' typical?**

348. This is the batch implicated in Q111 and Q 133. I think that document PRSE0000828 gives a clear account, and is the basis of Dr McClelland's evidence to the Penrose Inquiry referred to in Q 111, but I cannot recall my conversations with Dr McClelland or comment on the delays identified although it may have led to Dr Ludlam's later concerns and influenced his attitude to the trials of heat-treated F VIII and of Z8. The delays were undoubtedly unfortunate as a quicker and more broad response was indicated; this was the first occasion of a recall for such a reason and was therefore a learning experience. Delays for confirmatory testing in such circumstances would seem to not be good practice if alternative materials are readily available

Recall practice and procedure at EBTS and WRTC

136. Please give an overview of product recall practice at EBTS/WRTC, and how this changed during your tenure.

137. What do you remember about any formal recall/notification procedures in place?

138. In your opinion, were such practices and procedures effective? From your experience, did clinicians generally comply with recall requests and if not, do you recall why not?

349. Apart from the episode identified in Q 135, I don't think that I was involved in any other recall/notification procedure, and cannot comment specifically on the efficacy of or compliance of clinicians with the practices and procedures apart from the observations above about the 'undoubtedly unfortunate delays'. This episode supports the case for suppliers and clinicians responsible for supplying patients with clinical products to undergo 'recall training'.

HBV testing

139. Prior to the roll out of BPL's RIA test for HBsAg to RTCs in 1981, the EBTS was using a modified, diluted form of Abbott's Ausria II RIA test. This modified test was sometimes known as MOD-RIA.

a. How would you characterise the relationship between the EBTS and Abbott during the time you were involved with the EBTS?

350. This was not part of my routine responsibilities in the Centre and I cannot recall anything about the nature of any relationship with Abbott over AusriaII RIA or MOD-RIA, although I do remember the terms.

b. Please tell us what you recall about whether Abbott were informed about MOD-RIA and how they responded. Was this before the publication of EBTS's paper on the subject in 1980 (see RLIT0000565)?

351. I have no recollection.

c. **Please describe what you recall about Abbott's response to being informed by the EBTS that they were switching to the BPL RIA test.**

352. I have no recollection.

140. In 1982, it was agreed that BPL would hand over the manufacture of their RIA test, which was supplied to SNBTS, to Wellcome.

a. **At a meeting of the Eastern Division of Consultants in the Blood Transfusion Service, lack of confidence in Wellcome is noted throughout (NHBT0092845_026). Were you aware of this lack of confidence? If so, please explain the factors you believe led to it.**

b. **What was your view about handing over the manufacture of the RIA test to Wellcome? Did you have any concerns, and if so, did you raise these with anyone?**

c. **Do you know when this handover was fully effected?**

353. I have no recollection of this episode and was not party to any decision-making. I did not attend the meeting of which NHBT0092845_026 is the minutes, and would not have expected to be present as this was a meeting of the English Eastern Division. The date of this meeting is 1982: I started at WRTC in 1990.

141. When, and for what reasons, did the WRTC stop using BPL RIA as its HBsAg test? As far as you can recall, when was an end to the use of BPL RIA first discussed? Please provide details.

142. When and for what reasons did the WRTC transition to using an ELISA test? If possible, please describe the steps that were involved in this

transition. Please tell us what you remember about the conversations that led to the transition at this time. When was a transition to ELISA first discussed?

143. Please describe any other tests for Hepatitis B used during your tenure at the WRTC, when, and why they were implemented.

354. I have no recollection of the circumstances of any transition at WRTC from BPL RIA to ELISA.

HIV testing

144. The Inquiry is aware of the introduction of HTLV III antibody screening of blood donations throughout the UK from 14 October 1985 (CBLA0002277). Please describe the implementation of HIV screening at the EBTS during this period. In particular:

a. What was the process for screening donors and/or blood donations? What confirmatory testing process was used?

355. From day 1 (Monday 14 October), all blood donations collected by EBTS were tested for HIV antibodies. I cannot recall what confirmatory tests were used.

b. What impact did the introduction of HIV screening have on the EBTS at the time? What additional resources were required? How was the introduction of HIV screening funded?

356. As far as I recall, donations continued to be collected to the same degree and there was no immediate shortage of blood.

c. What happened to all the unscreened blood that had been collected prior to HIV screening being implemented?

357. As far as I recall, all previously collected blood which was in date was tested for HIV, retained and made available for transfusion to patients.

d. What happened when a donation was found to be infected with HIV? Please set out the steps that had to be taken, with respect to the donor, the donation, and in terms of passing on information to third parties and/or identifying recipients of previous donations from that donor.

358. All donors were advised before donation that their blood would be screened for HIV (and hepatitis B and syphilis). A positive screening result by HIV ELISA on a donation was always interpreted as being capable of transmitting HIV to any recipient of that blood or blood product and plasma fractions derived from it. It would also hold significance for the donor's own health as well as the health of BTS staff processing and testing that donation. The donation did not enter stocks but it, or samples of it, would have been retained for further testing. This would have effectively prevented patients from being exposed to those donations. Samples from the donation would have been sent for confirmatory tests and if confirmed positive the donor would have been recalled and advised by an experienced senior member of the medical staff (Consultant or Associate Specialist) of the result and its social consequences, and another sample taken for confirmation. Sometimes, the confirmatory test was negative so further investigations were indicated on why the screening result was 'falsely positive'. Sometimes, further samples from the donor would also test positive to the screening test and negative to the confirmatory tests which would indicate a non-specific 'marker' cross-reacting with the reagents of the screening test, which was not picked up by the confirmatory tests, so the donor would have been advised that they were probably not infected; but they would also have been advised that this non-specific marker prevented their blood from being acceptable for

transfusion. I believe that this phenomenon was the subject of considerable discussion among all UK Directors of Regional BTSs and plasma fractionation centres.

Surrogate testing

145. Whilst you were employed at the EBTS and the WRTC, what was your opinion of surrogate testing as a potential method of donor screening, and how did this change over time? Please comment for each infection:

a. HIV; and,

359. EBTS. I have no clear memory of how much consideration was being given to surrogate testing before the introduction of specific tests in October 1985. We recognised that at that time, tests, such as for CD4 lymphocytes or for CD4:CD8 lymphocyte ratios, were being developed and used for diagnosis; but the practicability of introducing them may have been difficult and the significance of the results (sensitivity, specificity and clinical relevance) less than straightforward. But I cannot recall any definitive discussions.

360. WRTC. I felt that there was no need for surrogate testing in my time there as specific immunological testing for HIV had been used since 1985.

b. NANB/HCV.

361. EBTS. I recall considerable discussions although Drs Gillon and McClelland were leading these investigations at EBTS (and SNBTS and UK-wide) and I deferred to their opinions. As the documents show, there was considerable enthusiasm in the SNBTS to use tests such as ALT and testing for antibodies to Hep B core antigen, not least because it was thought that their use by commercial operators overseas (especially in the

USA) might enable them to claim a marketing advantage. I shared my colleagues' disappointment in the ultimate decision not to introduce them to UK BTSs but felt that my opinion was unlikely to have carried any extra weight.

146. In 1986, Dr D. B. McClelland wrote to you and others at the EBTS about the agreed points from the November meeting of the UK Directors Working Party, which discussed the possibility of introducing screening to reduce PTH NANB (SBTS0000370_068). What was your view on the American Red Cross's introduction of surrogate testing at that time? Do you recall your opinion on this decision to implement the limited study and its findings?

362. I cannot accurately recall my opinion on the ARC's introduction at that time. Throughout the 1980's discussions on transfusion-transmitted (TT) hepatitis among the world's transfusionists evolved from NANB hepatitis being a rare disease with minor clinical consequences to being a serious and sometimes fatal TTI. Because the first cases of TT NANB were described in the USA and seemed less common in Europe it was, for a time, thought to be an 'American problem', but this soon proved not to be so. However, the onset of TT HIV/AIDS attracted far more attention in the early 1980's, not least because there seemed to be an associated incidence between NANB and HIV especially among injecting drug abusers. With the advent of specific screening of UK blood donors for HIV in October 1985 (April 1985 in the US) attention returned to NANB although concerns about NANB had never 'gone away'. By late 1986 attention returned with some force, so I was happy for the EBTS to participate in a UK study.

147. At an SNBTS Directors meeting on 3 March 1987, the Directors agreed to "recommend to the SHHD that surrogate testing for NANB should be implemented with effect from 1 April 1988 as a national development requiring strictly new funding. Each Director should let Dr Cash know what

funds would be required in his/her region, assuming that both core testing and ALT would be undertaken in the Transfusion Centres" (PRSE0004163). Please expand on the following:

a. Whether surrogate testing (namely ALT or anti-HBc testing) was introduced at the EBTS during your tenure;

363. I believe that routine testing was not introduced although there was participation in preparative studies which were published (Gillon et al, Vox Sang 1988, PRSE0002655).

b. If so, whether this had any impact on the EBTS;

364. The above study showed that there would be a significant impact if routine testing were introduced. Gillon et al 1988 (above, PRSE0002655) concluded that combined screening with ALT and AntiHepBCore would lose 4.4% in their donor population and therefore screening this way was unjustified, and 'further studies are required'.

c. How the surrogate testing was performed;

365. They included testing for ALT and for anti-Hep B core antigen.

d. What the process was for screening donors and/or blood donations;

e. What, if anything, happened to the unscreened blood that had been collected prior to surrogate testing being implemented; and

f. What happened when a donation tested positive. Please set out the steps that had to be taken, both with respect to the donor, and

in terms of passing on information to third parties and/or identifying recipients of previous donations from that donor.

366. 'Reactive donations' in the prospective studies were probably withdrawn but I have no recollection of what their donors were told. As no routine systems were introduced, there would have been no impact on the numbers of donations collected or the routine workload.

148. In July 1987, many SNBTS Directors wrote to the Lancet to state that surrogate testing was "inescapable." They stated that "no large study to answer this critical question has yet been presented, and we agree that the size of the benefit to be gained from surrogate testing cannot be accurately established without such a study. However, the time for this study has already passed" (PRSE0001444). Did you agree with the reasoning provided in this article?

367. I did agree. The SNBTS directors were justified in their comments as the conduct and analysis of such a study would take several years by which time it was likely that more specific tests would become available. That did not mean that surrogate testing need not be introduced.

149. A report prepared by Dr Gunson in August 1987 set out the conclusions of a Working Group established by the Council of Europe Committee of Experts on Blood Transfusion and Immunohematology to consider the introduction of routine surrogate testing ('the Working Group report') (NHBT0008816_002). The Working Group concluded it could not provide a recommendation on the introduction of surrogate testing in light of the following considerations:

a. the use of surrogate tests to reduce the incidence of transfusion associated non-A non-B Hepatitis (NANBH) and its possible value as a public health measure remained controversial;

b. there was no guarantee, in a given country, that there would be a significant reduction of NANBH; That's what was hoped would be revealed by a large study.

c. the introduction of surrogate testing in some countries could lead to a severe depletion of donors which could compromise the blood supply;

d. This would have been a distinct possibility and if surrogate testing was introduced, provision would have to be made for interviewing, counselling, medical examination and treatment of anti-HBc positive donors and donors with raised ALT. which would be the responsible thing to do having taken on the scheme.

Please advise whether you were aware of the Working Group's report. If you were, did you agree with the conclusions reached by the Working Group? If not, why not?

368. I cannot remember how much I was aware of the report's details at the time but I recollect being disappointed with these conclusions. Point c. above indicates that in those European countries with a relatively high incidence of hepatitis, the discovery of any markers for NANB hepatitis in a donor could reduce the amount of blood collected for standard transfusions to embarrassingly low levels and compromise care. However, Transfusionists in countries thought to have a lower incidence might too easily be critical of such concerns. Inevitably, when specific markers became available (which was within 4 years) concerns about finding more people with TTI hepatitis would have to be addressed. Note that many people with high serum ALT activity would not have been infectious: however, it would have been reasonable to conclude that those with anti

HB core antibodies might be infectious with HBV even if they were HBsAg negative.

150. The Working Group's report from 1987 commented: "If a stance is taken that blood should have maximum safety then the tests would be introduced" (NHBT0008816_002). Please explain your views on this statement. In your view, did the decision not to introduce routine surrogate testing indicate a decision not to provide "maximum safety"?

369. Using the word 'maximum' was always going to be a hostage to fortune because 'maximum' was never going to be possible. I think a better choice of word would have been 'optimal'. Although the costs of 'optimising' safety might still have been substantial, there was a case for applying for the necessary funding, although the report's conclusions may have reduced the chances of successful applications.

151. In October 1989, Dr Gunson, the Chairman of the Advisory Committee on Transfusion Transmitted Diseases ('ACTTD'), recommended: "The routine introduction of non-specific tests should be deferred, unless this is necessary for the acquisition of product licences in the UK for fractionated plasma products" (NHBT0000188_072, paragraph 7.5). Then, in November 1989, the ACVSB concluded that there was no case for using surrogate testing for non-A non-B Hepatitis (NHBT0005043). Please advise whether you were aware of the decisions made by ACTTD and ACVSB. If you were, did you agree with the decisions made by ACTTD and ACVSB? If not, why not?

370. I do not recall precisely when I was made aware of the decisions made by the ACVSB which, it appears, were meant to be confidential (and sharing information with Consultants such as myself not encouraged), nor of the circumstances, but did become aware probably through discussions among the EBTS consultants. The minutes in NHBT0005043 show the

mixed feelings and controversy which I do recall. Although the late Jeremy Metters was an experienced and highly respected deputy chief medical officer, he may not have appreciated the epidemiological implications surrounding the screening of TTI as much as transfusionists experienced in virus screening. His comment that 'the Department must bear in mind the possible litigation that could arise from a prolonged delay in the introduction of general screening' is revealing (although that would probably not have occurred to me at the time), as is Dr Metters' following statement that the NHS Management Executive would want to know more facts and figures. (He would presumably have been familiar with NHS ME thinking.)

152. In 1990, Dr Gunson wrote to you to express his concern that testing apheresis plasma donations for ALT would "lead to a double standard of platelet standards viz a viz those prepared from whole blood donations" (NHBT0000077_090).

a. If possible, could you explain what is meant by a 'double standard' and why it would be problematic?

b. In the same document, Dr Gunson also states "I only hope that once we have sorted out anti-HIV testing some relative approach to ALT can be made." Can you please provide further information regarding the rollout (or lack thereof) of anti-HIV and ALT testing?

371. This letter is dated 24 July 1990 while I was still in EBTS where apheresis was used to collect plasma for anti-D immunoglobulin to be prepared at PFC which (if it was the same as BPL) required the surrogate testing as the RIBA tests for hepatitis C had not yet been introduced. Apheresis was also being used to collect single-donor platelet concentrates which would not have been subjected to surrogate testing for NANB: hence the 'double standard', although I believe that the anti-D plasma would have been

pooled and therefore potentially put more patients at risk from a falsely negative donation if the IgG fractionation process did not remove or neutralise TT NANB viruses.

372. HIV testing began in October 1985, as mentioned above. Actually, I believe that Dr Gunson's reference to 'HIV' in this letter was a typographical error as it would make much more sense had 'HCV' been typed rather than 'HIV'.

373. I believe that routine ALT testing was never rolled-out for routine testing of blood donors.

c. What impact did anti-HIV testing have on the failure to implement ALT testing?

374. Although, as mentioned above, I think that the reference to HIV was a typographical error for 'HCV', the development and introduction of HIV testing did have a considerable impact on the development of screening tests for NANB including the surrogate tests. HIV appeared on the scene when interests and concerns about NANB were beginning to accelerate. By 1980, Eric Preston's finding of cirrhosis in the livers of multi-transfused haemophiliacs, and thus the spectre of NANB, were beginning to sink home – at least in me – but took more of a back seat when HIV appeared on the scene as the run-up to HIV testing required considerable effort, time and money. This (understandably) distracted attention away from the work in developing NANB screening, including assessing the value of ALT testing until 1986 or so, after the implementation of HIV screening tests.

153. In 1991, you responded to Dr Gunson to note that anti-HBc tests and ALT tests were not performed at the WRTC and that AST tests would be performed in certain circumstances instead (NHBT0000077_079).

a. Can you please elaborate on the objective of AST testing mentioned in this document?

375. This letter was written in October 1991, a year after I took up my appointment at WRTC and was a response to questions asked by Dr Gunson. As far as I can recollect it was in the context of a 'lookback' process of tracing patients who, prior to the introduction of specific screening tests for HCV in September 1991, had been transfused with blood from a donor found to be reacting positively to the RIBA-2 test, but I would need to see a copy of Dr Gunson's letter of 25 September 1991.

376. Many enzymes get released into the blood when the liver is damaged by cirrhosis. Cirrhosis is a complication of chronic hepatitis, especially from HCV but also from other infections including HBV, and by non-infectious causes such as alcohol, obesity and diabetes. These enzymes include the similar but distinct AST (ASpartate transaminase) and ALT (ALanine transaminase) which transfer NH2 (amino) groups from aspartate and alanine respectively to ketoglutarate to form the vital, very versatile and multifunctional glutamic acid. Increased concentrations of AST and ALT in serum indicate the possibility of cirrhosis but cannot specify the cause. Although raised concentrations of ALT are more specific for liver damage than AST, the concentrations of either enzyme are increased by other causes such as damage to other tissues, and also of red cells (haemolysis) which can be damaged during sampling if the patient had 'difficult veins'. However, ALT had always been preferred in the published studies and maybe should have been by Wessex; but given the decreasing emphasis of the value of ALT as a marker of NANB, and the unavailability of ALT testing from the clinical chemistry laboratories at Southampton General Hospital where AST testing was preferred as an indicator of liver dysfunction, I accepted AST testing as an alternative to ALT.

b. In the same document, you also note that "ALT tests are not conducted routinely in a local laboratory and we have, therefore, to rely on the AST". Please explain your views, including the relative utility of ALT and AST tests in this context.

377. ALT tests were preferred, and there was more experience of ALT testing of blood donors, so I would have preferred testing WRTC donors for ALT; but I judged that as the chemical pathology service at Southampton General Hospital did not test routinely for ALT but did for AST and was unwilling to test WRTC blood donors for ALT, we should accept AST as the best enzyme surrogate tests available for us until the RIBA test for hepatitis C was introduced. I probably felt that it didn't make much difference to the local (Wessex) management of such donors/patients if the liver function tests used AST rather than ALT.

c. Would you have used ALT testing if it had been conducted routinely in a local laboratory?

378. Yes if it were conducted at SGH; less likely from a laboratory outside Southampton due to logistics. Approval for using outside labs (including any funding implications) might have been necessary from the WRHA. I do not recall being charged by the SGH laboratory service for any AST testing.

Introduction of anti-HCV screening

154. In February 1990, you wrote to Professor Cash to say that you had "developed a very strong feeling that the screening of donors for HCV antibodies should be introduced at the earliest possible opportunity" (PRSE0001562). You went on to state that your view was "actually one based on the risk of future litigation".

a. How did your view on this issue develop over the preceding years? How, if at all, did your view change through the remainder of 1990 and 1991?

379. This letter was accompanied by a report by me of a meeting organised by Ortho on 8 February 1990 and referred to in the Penrose report (Ch 31.187, PRSE0007002 p. 1419) (in fact, I made two reports – a very brief one which seemed to underplay the value of surrogate testing and a more detailed account prepared a few days later)

380. The few years before 1990 were characterised by deep concerns in the UK BTSs about TTI (transfusion transmitted infection) not only from HIV/AIDS but also NANB hepatitis. With specific tests for the former but none for the latter, while patients were contracting TT NANB hepatitis, the operational challenges of screening donors for NANB were greater. By February 1990, the prospects of an acceptably sensitive, specific and direct diagnostic test were increasing (in the form of RIBA – recombinant immunoblot assay) but improvements were being made constantly by several manufacturers making it difficult to set a target date for implementing donor screening.

381. Although my reports don't emphasise the risk of not screening, listening to the 'between the lines' messages and considering afterwards made me feel that even though the technology in early 1990 may not have been good enough to be used for screening, it was developing quickly and feasible methods could soon arise, so I felt that it was important to consider the possibilities of litigation if a patient contracted TT Hep C when a test which was available was not being used. Although not mentioned in my letter, I recalled then that there had been some concerns that the UK introduced routine screening donors for HIV antibody in October 1985 while in the USA screening programmes had started in the Spring of 1985, and some colleagues were concerned that UK BTSs might be susceptible

to litigation by UK patients contracting TT HIV between March and October 1985.

382. For these examples, 'litigation' should be viewed as a sort of surrogacy for 'responsible practices': in other words, the risks of litigation against a practitioner would be reduced not by fear of litigation itself but by the adoption of 'improved' practices. In considering what such improved practices might involve, it is important to consider patient rights and expectations in the wider context of societal responsibilities – such as balancing the degree of disruption in collecting enough blood to secure clinical supplies against the possible reduction of supplies by introducing more excluding testing regimes of uncertain provenance. Such balancing – which could have medico-legal consequences – needs a sophisticated sharing of expert opinions way beyond those of a specialist 'transfusion doctor' like myself; but at that time (February 1990) my perhaps naïve feeling was that HCV screening even by an 'imperfect' method needed to be introduced soon after those two meetings.

383. I doubt if I was aware at that time of Dr Metters' comments referred to in my response to Q 151 ("the Department must bear in mind the possible litigation that could arise from a prolonged delay in the introduction of general screening").

b. What was the basis for your concern about the risk of future litigation at the time?

384. As patient (recipient) welfare and minimisation of risk was our main concern, I thought that Transfusion practitioners could be at particular risk of being held responsible for 'avoidable' TTI events, and it was looking increasingly like TT NANB hepatitis could largely be avoidable. My move to Southampton in October 1990 did not fundamentally change my views

but I was still concerned about the delay in introducing HCV screening tests in the UK during 1990.

c. What other factors, if any, contributed to your view that screening for HCV antibodies should be introduced?

385. The main factor was safety for patients receiving transfusion of blood or blood product.

386. It should be noted that the profound but understandable professional differences of opinion within medical and administrative expertise began to feature largely at this time, complicated by the very peculiar biology (as we thought then and even more so now) of HCV.

387. Here was a virus that

- could not easily be detected by conventional means (microscopically, cell cultures, etc)
- had a rather vague epidemiology
- mostly associated with needle stick injuries but such risks were very recent in terms of human behaviour (so how did it evolve? – insect bites?)
- low but not absent risk of sexual transmission
- low rate of transfer at birth
- to which the immunological reaction of infected patients varied widely
- from no apparent effect and symptomless spontaneous resolution, to
- long delays (many months) in the appearance of symptoms and/or signs after exposure, to
- being without symptoms but experiencing up and down waves of detectable/undetectable antibody, to
- high antibody levels
- whose clinical effects were so subtle and variable that infected people might

- not know for decades that they were caused to be ill, or
- have an acute phase jaundice after which apparent complete resolution, or
- die of cirrhosis and/or hepatocellular carcinoma years later, or
- die of fulminant disease

388. The different professional concerns were between:

a. academic virologists
b. transfusionists focussed on donor care (counselling, etc)
c. clinicians responsible for patient care
d. professionals in public health
e. budget holders

389. Academic virologists tended to prioritise unlocking the secrets of viral biology including how to identify their peculiar characteristics (which could help develop curative medication):

390. Transfusionists look for optimal ways of detection (diagnosis) which tolerated certain degrees of uncertainty but did not risk too many false results (positive and negative):

391. Clinicians caring for individual patients who want to minimise therapeutic mishaps:

392. Public Health professionals have an epidemiological interest in minimising spread

393. Budget holders encouraging 'value for money'.

394. Note: an important but somewhat neglected expertise seemed to have been missed in such deliberations – the views of an experienced medical ethicist.

395. The 'best' (or optimal') solutions can only come about when all parties listen to each other's open analyses with respect and willingness to adjust their own viewpoints toward practicality. Good communications are vital. Meetings with limited specialist expertise held 'in confidence' from which certain parties are excluded are likely to fail and end in acrimony. Failures in these areas characterise many of the difficulties we experienced in the attempts to optimise patient care and minimise TT infections.

d. As far as you know, did other consultants and directors within the SNBTS and NBTS agree or disagree with your view at the time?

396. I think most agreed, but I do not recall specific discussions although I was aware of concerns about the impact on donation collection, staffing and the need to develop counselling services for HCV positive donors and recipients.

155. Dr Gunson wrote a letter to all RTC directors suggesting a delay in commencing anti-HCV screening from July to September 1991 so that "'second-round' comparative evaluation" of the testing kits could take place (NHBT0000073_065). Did you agree or disagree with Dr Gunson's suggestion to delay testing to undertake this comparative evaluation? Please explain the basis for your answer.

397. I agreed with Dr Gunson that undertaking a comparative evaluation would take time and commitment which would make a July start date difficult and that it was too hasty to make a full evaluation in those earlier computer days.

156. In response to Dr Gunson's letter, some RTC directors suggested a staggered start date for the implementation of testing (i.e. different start dates for different RTCs) while others supported a uniform start date. Which view did you take? Why?

398. I was uneasy about staggering implementation dates as I felt that patients across the country deserved to be treated alike, and that 'post-code lottery' (although that term was probably not around then) was not in the British tradition of fairness.

157. Despite Dr Gunson's suggestion to delay the introduction of screening, the Northern RTC led by Dr Lloyd introduced routine testing in April 1991, becoming the first centre to do so. Dr Lloyd's view, in contrast to that of Dr Gunson's, was that, the "Second Generation HCV tests were acceptable tests for donor screening" by June 1991 (NHBT0000076_009), and that deciding not to implement testing despite having the capability "would be indefensible under the current Product Liability Legislation" (NHBT0000074_014). You wrote to Dr Lloyd regarding his decision in May 1991 (NHBT0000074_021). As to this letter:

a. Why did you disagree with Dr Lloyd's decision to implement testing?

399. At the time, and because communications were inadequate and often secret, I was not convinced that Dr Lloyd's definition of 'second generation tests' covered the possibility that the further improvements to the RIBA design which were on the horizon would be significantly better than the tests he introduced at Newcastle. If new tests showed a marked superiority in sensitivity and specificity, users of the old tests might be missing infected donations (false negatives) and alarming donors who tested falsely positive. This would clearly be an undesirable situation.

b. Have your views changed since then? If so, why?

400. At the time, I didn't realise quite how far these technological developments had progressed. Furthermore – as I realise now and in Dr Lloyd's defence

– it would probably not have been so difficult for tests using 'first generation' kits to be supplanted by 'second generation' kits as they became available given local support (i.e., financing arrangements). I do not remember precisely how and when such kits were made available to WRTC.

401. As it turned out, there was probably not that much difference in performance, although I have not seen any data to that effect, so Dr Lloyd's decision may in retrospect be seen as justified.

402. My current feeling is that the UKBTSs should have introduced HCV screening in 1990 using the then-available technology, and should have been fully funded centrally to cover the extra expenditure involved in donor counselling and the recruitment of new donors.

c. Why did you consider the "image of a coordinated service" to be more important than each RTC beginning testing at the earliest possible time?

403. There was quite a lot of emphasis on 'image' at that time which in retrospect may not have been justified. However, a service which is coordinated and dedicated to delivering high quality products to all its beneficiaries (to which all the UK BTSs aspired) would be inherently fairer. A 'staggered service' providing a qualitative miscellany of its products would be much more susceptible to justified criticism. I think my use of the term 'image' was perhaps somewhat unfortunate – it's not so much the 'image' which counts but the quality of the service. Nevertheless, I felt that the desire of Dr Gunson and of Dr Cash to have UK uniformity for an official start date was justified.

d. In what sense did you consider the action of the Newcastle RTC to have an impact on potential liability under the CPA and Product Liability?

404. It would have been difficult to predict the outcome of individual liability in the event of litigation against one Regional Centre which for various reasons – not least Regional funding which could vary – had been slower than others in introducing an improved testing regime. This is one situation where a National organisation with one budget might be better than having Regions with different demographics and budgetary priorities. However, the delay (to 1st September) was difficult to justify and inconsistent with my earlier concerns about litigation.

e. What effect, if any, did the points raised in Dr Lloyd's reply (NHBT0000192_044) have on your view? You may find NHBT0000076_009 and PRSE0001183 of assistance.

405. I do not remember being at the 'recent' meeting in York referred to in PRSE0001183 (4 July 1991) and NHBT0000076_009 (of 24 June 1991) but clearly it influenced Dr Lloyd in taking his action. I don't know what I wrote in my letter which prompted the reply from Dr Lloyd on 14 May 1991 but clearly it seems that Dr Lloyd did not object to national uniformity had the date of July 1991 been adhered to. In July 1991 I still felt that adherence to a national start date was desirable even if it had to be deferred to 1st September. I did not really know why deferral to 1st September was necessary or if WRTC could have been ready before then had WRTC been given adequate notice and funds.

158. What issues did the WRTC encounter with the procurement of anti-HCV screening kits? You may find NHBT0000075_049 of assistance.

159. How was the anti-HCV screening programme funded? Did the WRTC experience any issues with funding? If so, how did this impact the roll out of anti-HCV screening? You may find NHBT0000193_092 and NHBT0000075_076 of assistance.

406. NHBT0000075_049 (dated 20 Aug 1991) indicates, regrettably in retrospect, that WRTC was one of the Centres which had difficulties in procuring funds for the HCV screening of donors as the RHA Treasurer wanted the 'users' of our service – i.e., the hospitals where blood transfusions were administered – to pay rather than the RHA. This clearly caused difficulties for some hospitals which had already set their budgets for 1991/2. (I think the 'internal market' whereby user hospitals paid the WRTC for every unit of red cells and platelet concentrate had not yet been established, so user hospitals were unfamiliar with this form of payment within the NHS). Nevertheless, the timescale of three weeks' notice from the National Procurement Directorate to Regions to negotiate prices for the test kits from the manufacturers does seem to have been brief and put some Regions at a disadvantage.

407. NHBT0000075_076 (16th December 1991) shows that the funding was expected to come from the 'User' hospitals paying the RHA per item of 'wet' blood used (I cannot remember how freeze-dried NHS clotting factors for patients attending the haemophilia centre were procured). User reaction was variable – some willing to be compliant and others complaining of 'extreme difficulty'; and that the RHA will 'top slice' those who don't pay.

408. NHBT0000193_092 (19th December 1991) described this as 'optimistic'. Nevertheless, WRTC began routine donation testing for HCV using the 'Abbott ELISA' kit and any repeat reactives would be subject to supplementary testing by RIBA 2.

160. What impact did HCV testing have on the WRTC? In particular:

a. What was the process for screening donors and/or blood donations?

409. Donors attending the session would have been told that their donation would be tested for HCV and that they would be notified if the result was positive.

b. What happened to all the unscreened blood that had been collected prior to the HCV testing being implemented?

410. In order for all blood issued after 31st August 1991 to be negative for HCV, all the blood in stock from the 1st September would have been tested – which is why early stocking of test kits was needed so that donations issued to hospitals during August 1991 would be HCV negative. I cannot be confident that that was the case given that Centres had at the most, 3 weeks (before 1st September) in which to introduce the systems. Hence, some untested blood may well have been issued during the first week or two after the tests were implemented. Although usually most blood was issued to hospitals within three weeks of donation, the expiry time of four or five weeks would indicate that a few HCV untested units may have been issued. I have no data on how many untested units were issued or even transfused after August 31st.

c. What happened when a donation tested positive? You may find NHBT0000077_079 of assistance. Please set out the steps that had to be taken, both with respect to the donor, and in terms of passing on information to third parties and/or identifying recipients of previous donations from that donor.

411. NHBT0000077_079 indicates that the donor of any donation testing positively or equivocally in the supplementary RIBA2 'confirmatory' test

was called to see one of the consultants (either Dr Herborn or myself), the significance of the test explained and a further blood sample taken for extra testing for HCV (RIBA 2) and liver function enzyme markers in our local laboratory (which – as explained above – was for the AST activity). Donors testing negatively by RIBA2 were not counselled any further. As far as I recall, in very few if any donors whose donation reacted positively by RIBA2 did the second blood sample taken at this visit test negative.

Provision of diagnostic screening kits

161. Please describe the arrangements in place at the EBTS and the WRTC with regards to the provision of diagnostic testing kits for donation screening ("screening kits").

412. EBTS – I cannot recall: this was not in my area of responsibility

413. WRTC – see above. Screening kits would have been delivered by their manufacturer directly to the Donation Microbiology Testing laboratory at WRTC, invoiced and paid for by the RHA.

162. Did you, or anyone else at the EBTS or the WRTC, contract directly with any pharmaceutical company involved in the manufacture and/or importation and/or sale of screening kits, or were contracts negotiated on a national basis?

414. WRTC only. The purchasing arrangements were as described above. I believe that the earlier attempts to recover costs from the user hospitals was not so successful as the RHA Treasurer had hoped.

163. What were the key factors influencing choice of screening kit and/or pharmaceutical provider?

415. Our laboratory staff preferred the Abbott because they were familiar with it.

164. What, if any, influence did pharmaceutical companies retain after supplying imported blood products and/or screening kits to the UK? For example, can you recall whether pharmaceutical companies provided advice on the implementation or use of the products?

416. Abbott would have offered an after-sales service. Ortho would have done also but I suspect that WRTC staff were more used to the Abbott service.

Risk of infection from cryoprecipitate

165. During your time at the EBTS, please set out how, in your view, the risk of infection from cryoprecipitate differed to the risk of infection from factor concentrates.

417. Because the number of donors each patient was exposed to was substantially lower (usually 12 per transfused dose) than it was from factor concentrates pooled from a few thousand donors from PFC.

166. In your letter to Mr J Watt of PFC from December 1982, you described Dr Ludlam as using "less of the PFC material in favour of cryoprecipitate" and stated this was an "encouraging trend" (PRSE0001487). Please explain your views. In particular:

a. What was the "PFC material" to which you referred? PFC intermediate factor VIII concentrates
b. Why did you consider a greater use of cryoprecipitate to be encouraging?

418. This letter (PRSE0001487) was written ahead of the Christmas break in 1982 at a time when EBTS stocks of PFC intermediate factor VIII

concentrates were running low; so EBTS stocks were supplemented from WSBTS and Inverness. The switch to cryoprecipitate by Dr Ludlam – which was mostly for inpatients – was, I believe, to reduce exposure to pooled concentrates from commercial suppliers: the 'encouraging trend' was a comment in favour of low-donor exposure from cryoprecipitate and away from commercial factor concentrate.

167. In your evidence to the Penrose Inquiry, you stated that cryoprecipitate "was felt on good grounds but not on established grounds, to be a safer product" (PRSE0006024, page 16). Please explain your views, in particular the reasons you considered that cryoprecipitate was not established as a safer product.

419. The 'safety' aspect I was referring to did not relate just to the risk of transmitting viral infections from cryoprecipitate (which would have been lower than from a fractionated product) but a more general application of the concept of safety when using a thawed but still viscous liquid, pooled under clean but not sterile conditions, and infused under some pressure through a narrow needle. We were also concerned at the time that the plastic packs could have 'pinholes' which would compromise their sterility from other microorganisms such as bacteria and fungi in the water bath into which cryo packs were inserted for thawing. I believe that at that time there was no epidemiological report comparing the incidences of adverse events during and after infusion of cryo with infusion of fractionated product. But infusing cryo was a much 'messier' procedure than infusing a fractionated product – and the commercial manufacturers did develop fractionated products which dissolved readily in low volumes of water; so infusing them was much easier for the infuser and more comfortable for the patient whose exposure to extraneous bacterial or fungal infection due to contamination of cryoprecipitate during its preparation would be avoided.

168. In your evidence to the Penrose Inquiry (PRSE0006024), you referred to Richard Titmuss's book 'The Gift Relationship', first published in 1970, which states "the larger the pool the greater is the risk of infecting patients with hepatitis" (HSOC0019917, page 22). Were you aware of this general hypothesis as to the risk of large pool products? If so, please provide details. Please describe any evidence of which you were aware which supported this hypothesis and any evidence which contradicted it.

420. I think every transfusionist was familiar with the description of increased incidences of jaundice in patients receiving pooled plasma. An early and well-authenticated description was given by the eminent wartime haematologist Janet Vaughan in the BMJ in 1946 (Sept 21, pp409-413; RLIT0000052). As a life-saving measure, 2,040 civilian air-raid casualties received pooled serum or plasma (400 pools in all, varying in size from 30 to 200 litres; i.e. approximately 100 to 600 donors), of whom 1,054 survived and 77 got infectious jaundice. They were compared with 1,284 patients receiving single units of blood (average 2.75 bottles each) of whom 891 survived to be traced and none of whom got infectious jaundice. This was an extraordinarily well conducted and detailed study. (Dame Janet, as she became, was well known to my mentor at the London Hospital as she had worked with his father, so I was aware of her 'legend' from when I was a trainee there.) No well conducted study has contradicted this concept.

Autologous Transfusion

169. An audit report of the WRTC from March 1992 stated that Centre medical staff supported the concept of autologous transfusion in appropriate cases (NHBT0009786_001).

a. Were any steps taken to develop an autologous transfusion programme at the WRTC?

421. Yes. They culminated in a student project under my supervision which was conducted in 1999.

b. What was your opinion of autologous transfusion? You may wish to refer to NHBT0111550, in which you imply your support for autologous transfusion.

422. This letter, dated June 1991, was addressed to Dr Roath, a consultant haematologist at Southampton Hospitals and not in the BTS. (Chichester is in the Regions served by BBC Radio Solent but not by WRTC). I do not recall receiving a reply from Dr Roath who might have been the doctor misheard by the prospective patient referred to at the beginning of my letter. In the letter I used the phrase 'cautiously encouraging it, although pointing out various drawbacks' which just about sums up my feelings at the time. In the December 1987 issue of the Journal of the Royal College of Surgeons of Edinburgh, I co-wrote – with Dr Gillon – a commentary on an article in favour of autologous transfusion; our commentary referred to a pilot study being conducted at Edinburgh. Consensus conferences on autologous transfusion were held at the Royal College of Physicians in Edinburgh in 1995 and 1998.

423. By 1999, after reading several published reviews and with the experience gained from our student project, we concluded that there was little, if any, overall benefit from a planned pre-deposit autologous transfusion programme. Most of the potentially benefiting patients, such as those requiring joint replacement surgery were older and often in chronic pain (so found movement, including walking, painful or at least uncomfortable) and found it not convenient to travel to the BTS donor unit every week for 3 or 4 weeks. Also, the blood loss at surgery was often less than one unit so they would not have needed transfusion anyway. Furthermore, several patients experienced mild adverse symptoms even though they received

their own blood – whereas red blood cells store well, other components do not.

424. As Chair of the British Committee on Standards in Haematology Transfusion Task Force, I authored, with Dr V James, the "Guidelines for policies on alternatives to allogeneic blood transfusion. 1. Predeposit autologous blood donation and transfusion" (British Journal of Haematology 2007) (WITN3456004).

General

170. Please describe all other steps or actions taken at the EBTS and the WRTC to ensure blood safety and to reduce the risk to recipients of blood or blood products of being infected with a transfusion transmitted infection.

425. At both centres, donation collection staff were meticulously trained by the each centre's senior nursing officer and medical staff in donor selection and examination, particularly in the pre-donation questionnaires which became more complicated over time and as more TTIs were identified – syphilis and other sexually contracted diseases, hepatitis B, HIV/AIDS, HCV, HTLV I / II, the later discovered such as West Nile Virus: also awareness of other infections associated with travel such as malaria, trypanosomes, etc,.

171. Was blood safety ever subject to cost, time, staffing or any other constraints? If you felt a particular course of action needed to be taken to ensure blood safety, were you free to take it?

426. Screening for TTI's requires dedicated staff equipment and reagents. These were costed and budgeted for each year. The finance departments at CSA/SNBTS/EBTS and, at Wessex RHA until the establishment of the

NBA in 1994, had to approve of the budgeting and any new purchases. The introduction of screening tests for HCV were, however, affected by 'Users' (i.e., hospitals usually expressed by their Blood Bank administrators) who had not budgeted for them adequately. In effect, those hospital users in Wessex which could not or did not pay for the service were bailed out by the Wessex RHA

172. How, if at all, did the desire for consensus across the SNBTS during your time at the EBTS, and the NBTS during your time at the WRTC, impact efforts to achieve blood safety at a local level?

427. SNBTS/EBTS: although there were differences in approach and practices among the Scottish Regions – the WSBTS (Glasgow) system being more like the English in having a separate site (around 20 miles from central Glasgow) and not engaging in any routine clinical service although providing a specialist diagnostic service for blood transfusion serology – the SNBTS, which included a well-developed plasma fractionation centre (PFC) was well coordinated under a National Medical Director. This allowed a good interchange of developments in the practice of blood transfusion and harboured a research centre funded by the Medical Research Council. The WSBTS covered approximately half the country; the EBTS approximately one quarter, the remaining quarter being covered by Dundee, Aberdeen and Inverness.

428. WRTC: In England and Wales, although there was a National BTS Medical Director (Dr Gunson with offices in Manchester), when I took up my post at WRTC the service was provided by 15 distinct Regional Centres, of which Wessex, based at Southampton, was the last to be established in 1970 – coinciding more or less with the establishment of a Medical School in the University of Southampton based mostly at a re-built Southampton General Hospital within the grounds of which the WRTC was sited. Ironically, the WRTC was equipped with a washing plant for glass bottles

used for collecting blood donations and was among the last to switch completely to plastic sometime in the late 1970's. Nevertheless, the practices at WRTC conformed broadly to those at the established Regions, particularly from the Bristol and SW Thames out of which 'territories' the area covered by the WRTC was created - Wessex hospitals to the east of Southampton from SW Thames; those to the west from Bristol. The total population served for collection and supply was about 2.5 million and the number of donations collected about 100,000 per year.

429. Dr Gunson provided a welcome system allowing improved coordination and standardisation of practices at the crucial time covered by this Inquiry, including and especially for protecting recipients from TTI. There were, inevitably, differences in practices across the Regions – largely influenced by demographics but also by varying degrees of academic work associated with the local universities and teaching hospitals.

173. In March 1991, you expressed concern at how BPL's proposed reduction in the quarantine period of plasma to four weeks would impact the safety of blood (NHBT0001343). In your general view, how did decisions taken at BPL impact blood safety? What influence did you as the Medical Director of an RTC have over these decisions? What happened if your own opinion conflicted with the decision or advice of BPL?

430. My concern – as shown by the doc NHBT0001343 – was that by reducing the 'quarantine' for holding plasma donated for fractionation to four weeks when, as far as I was aware, the incubation period for several viruses including HBV and – for all we knew HCV – might be much longer and therefore prejudice the safety of products fractionated from pools of plasma released after four weeks. I am not sure how much practical effect reducing the quarantine period to 4 weeks would have had but at the time I felt that this was an imposition which required further discussion. I do not recall what, if any, outcome there was to the reduced quarantine period.

There were not many occasions when my opinion conflicted with those from BPL although there were occasions when BPL thought that the Wessex input of plasmapheresis donations could have been enhanced.

431. At this time, the UK Blood Services were engaged in providing support for the UK Armed Forces engaged in 'Desert Storm' – the invasion of Iraq by US Allied forces following the occupation of Kuwait by Iraqi forces. This had a significant effect on decision-making processes including the introduction of HCV testing.

174. To what extent were you and other RTDs reliant on the decisions of other bodies (advisory committees, directorates, SNBTS/NBTS, DoH) to achieve blood safety? Who or what was responsible for defining what constituted safe blood? What happened if your own opinion conflicted with the decision or advice of that person or body?

432. We were all heavily reliant on the advisory committees – EAGA, JPAC, SACTTI, ACTTD, ACVSB etc., and in England on the advice from Dr Gunson who seemed to be influential in both committees although RTC Directors were a bit confused as to why there were two committees (ACTTD, ACVSB) with what appeared to be similar purposes in defining what constituted 'safe blood'. The definition of 'safety' is always open to contention as the concept of 'absolute safety' is unrealistic; but at the pragmatic level, I think most RTC Directors were united on the principles of the safety of blood which begins with the selection of 'safe' donors and the methods of collecting their blood donations. I recall no occasion when I felt sufficiently strongly against a particular recommendation to feel the desire for independent action.

175. In January 1992, Dr Marcela Contreras wrote, ahead of an ACTTD meeting, that "the attitude towards transfusion safety has veered away from the concept of 'maximum benefit at minimal cost' towards the notion

that if a procedure shown to prevent transfusion-transmitted infection and disease is available, it should be introduced" (NHBT0000044_095). Do you agree that this was a shift that the BTS made? Please explain the reasons for your answer, including any relevant references to discussions with colleagues and official policy within the BTS.

433. I did agree that there was a shift but this was not just by the BTS. John Barbara was highly respected by Dr Contreras and myself as a virologist with a realistic sense of the application of virology to transfusion practice. The letter's reference to 'maximum benefit' needs to be seen in the context of removal of Crown Immunity etc., (which I accepted as desirable) and deciding just how far a BTS could go in pursuing the most cost-effective policies. Donations in which the only marker for hepatitis was antibody to the HB core antigen with no HBsAg or HBsAb would be a challenge as their clinical significance was not yet established (i.e., how many recipients of such blood would get infected with Hep B), so there was a case for the ACTTD to consider. I believe – but this needs confirmation – that the 'look-back' scheme may have been designed at least partly to address such issues. As a non-specialist in the detailed serology of hepatitis B at the time, I was prepared to advocate any advice from the ACTTD but do not recall what the specific advice was. The issue of the sensitivity and specificity of the anti-HBc test when there is no HBsAg or HBsAb was clearly a matter of great interest at the time as shown by articles in 'Transfusion' but I do not recall the outcome of these discussions.

176. If you do agree:

a. When, in your view, was this shift made?

434. I think that the cost-implications of introducing a screening test for NANB / HCV in blood donations and how such costs would be met was all part of the growing awareness of the challenge. In England, where blood for

transfusion had been supplied without cost to the user hospitals/clinicians/patients etc, awareness of these cost-implications emerged among the clinicians very slowly – it 'wasn't their problem'. The shift away from 'maximum benefit at minimal cost' occurred more rapidly among the BTS community (especially among the senior staff responsible who had to apply for funding for the testing) than among the hospital clinicians and budget holders.

b. Who was responsible for the original policy and who for the change in policy?

435. I assume that it would be the ACTTD and the ACVSB but do not recall who I held responsible at the time.

c. What caused the change to occur?

436. I do not recall in detail but suspect that a growing sense of professionalism among BTS staff (in the wake of loss of 'Crown Immunity' and the need for visits by the Medicines Inspectorate to RTCs) encouraged an enhanced sense of responsibility.

d. What is your opinion of the merits of cost-benefit approach to blood safety as against the latter approach?

437. The phrase 'value for money' began to be added to the phrase 'cost-benefits'. 'VfM' began to be used in the NHS from about this time and matured in the 1990's and early 2000's into the concept of 'Quality Adjusted Life Years'. To practitioners on the ground, these concepts seemed somewhat arcane and indeed distasteful to some who felt that clinical services justified a 'free rein' and who instinctively opposed the 'Internal Market' approach which, in England, resulted in clearly defined monetary charges between RBTSs and hospitals. Nevertheless, more

realistic assessment recognised that the unmentionable word 'rationing' in relation to health care had somehow to be accepted. Although 'blood safety' could never be absolute, it was professionally necessary, responsible and meritorious for BTS staff to help to balance minimising the risk of TTI against rising costs.

e. Was the introduction of anti-HCV testing affected by this prior approach? What about other transfusion transmitted infections?

438. The delay in introducing the screening test for HCV was undoubtedly affected by the practical implications of the English RTCs getting funds from their RHAs and hospitals. Cost implications for selecting and testing donors for other infections such as malaria, T cruzi, West Nile Virus, etc had also to be considered as international travel was increasing and could have affected the blood supply

Section 11: Services for donors

177. What counselling was offered to donors prior to (i) HIV testing (ii) HCV testing and (iii) HBV testing taking place? Please describe the process.

439. At each donation session, every donor was told that their blood would be tested for hepatitis and, after October 1985, for HIV. With the introduction of HCV testing from September 1991, the testing for hepatitis would have been reinforced but the term 'HCV' may not have been used specifically but a more general description along the lines of a 'new test for people for whether they'd ever had jaundice'. I believe that such information was available in leaflets at the session and also accompanied postal invitations to donate. Furthermore, the questions about lifestyle and travel used to help identify 'risky' donors may also have elicited elements of advice from session staff, if not actual counselling, to prospective donors. Session staff

were trained to call to the attention of the Session leader or doctor any prospective donor for whom advice following their answers to the questionnaire was deemed necessary.

178. What counselling and psychological services were available for donors who tested positive for hepatitis or HIV? Were such services delivered by the EBTS or were referrals to other agencies made?

440. EBTS: the establishment of counselling and advisory services for such donors was established by my predecessor, Dr Gillon, as 'donor consultant' in 1985 and would have involved hepatologists and psychiatric services as indicated. I cannot recall the details as I cannot remember if any donors were referred to me at that time. We had two excellent Associated Specialists who would have handled such situations and referred any problems to me: although I cannot recall any such referrals, there may well have been some.

179. Were such services delivered by WRTC or were referrals to other agencies made? Please describe the process. You may find NHBT0009786_001 from paragraph 2.7 of assistance in answering this question.

441. I have nothing to add to the information in paragraphs 2.7, 2.8 and 2.9 except that the consultant haematologists would have been only Dr Herborn and myself, and from 1992, Dr Brearley; and to add that if indicated, referral to a hepatologist did occur when donors had markers of HBV or HCV. Psychiatric referrals were available when needed but I do not recall any such services being required. Our GPs were generally co-operative and some donors preferred to see them rather than Dr Herborn or myself.

180. In a letter to Dr Andrew Herbourn in June 1990, you spoke of the need to be able to refer donors who tested positive for HCV to liver specialists in the region (NHBT0000189_175). Was this adopted when testing was introduced? Please provide details.

442. This letter was written in June 1990 after I had been appointed to WRTC but nearly 4 months before I took up the post. A system of referring HCV reactive donors to Southampton hepatologists was enacted after HCV screening of all donations was initiated in September 1991.

181. What counselling and psychological services were available for recipients of infected donations? Were such services delivered by the EBTS and the WRTC, or were referrals to other agencies made? Please describe the process.

443. Although I personally counselled some donors testing positive for HCV, at EBTS and at Wessex RTC, I cannot recall the details of the system at either Centre although the system at WRTC was established by Dr Herborn and, as far as I can recollect, the system operated satisfactorily. Few if any affected donors felt the need for psychological counselling but several were happy to be referred to the clinical hepatology service

182. Were these arrangements sufficient in your view? If not, why not?

444. As far as I can recall, the system worked sufficiently well

Section 12: Look back programmes

General

183. Please confirm whether you were involved in a look back process relating to any infection during your time at both the EBTS and the WRTC. If

so, please provide an overview of the relevant programmes and detail your involvement.

445. EBTS: I do not remember the degree of my participation in any lookback process.

446. WRTC: I was involved in the HCV lookback but arranged for Dr Herborn to lead the process. After HCV screening of donations was introduced in September 1991, any donation confirmed reactive to HCV (by Abbott ELISA and RIBA2 tests) alerted us to the possibility that previous donations from that donor, even though negative for HIV and HBsAg, could nevertheless have been infectious for HCV. We traced the hospitals to which any previous donations from the implicated donor had been sent and asked their blood bank to initiate a search for any recipients of such blood. When such recipients were traced, we tried to ascertain the medical history of any survivors (at that time about 50% of recipients of blood died within a year of transfusion from their underlying illness). As many survivors as possible were traced and tested for HCV following the transfusion. This required approval by the medical consultants in charge of the hospital blood bank, and close cooperation from their staff. Sadly, too often, this was not forthcoming in spite of repeated attempts to emphasise the case. I stress that this was not usually the fault of the laboratory scientists in the blood bank but from their budget holders and consultants, as there is no doubt that the extra workload put on the hospitals was high and in effect somewhat demotivating and unrewarding.

184. Did you consider there was an ethical obligation to inform patients who may have received transfusions from infected donations? If not, why not?

447. Yes

185. To what extent could an RTC implement its own local look back programme? Did either the EBTS or WRTC do this? If so please give details. If not, why not?

448. An RTC-only lookback programme could only be implemented if that RTC had direct access to recipient records: such conditions existed at EBTS which crossmatched liquid blood components for compatibility with identified recipients, and was 'onsite' at the main hospital (the RIE) where most of the transfusions were given; but not at Wessex RTC. Look back programmes require full cooperation of the clinicians and other health professionals (laboratory scientists, nurses, etc.,) who record the details of each donation/component administered and of each patient transfused, and of adequate access to all patient records. Even though the WRTC was situated in the grounds of the SGH, WRTC staff needed permission to enter hospital records and files. This need not have been difficult but in practice WRTC staff had to rely on the hospital staff.

HIV

186. Were you involved in setting up any national or local HIV look back programmes during your time at either the EBTS or the WRTC? If so, please describe this process and your role in it and how it was funded.

449. EBTS: no.

450. WRTC: no formal lookback but before my time at WRTC there was at least one possible recipient of blood from a donor later found to be HIV positive who was investigated during my time. The results were inconclusive because there seemed to be an error in the hospital's recording of the patient and donation identity details.

187. Were you involved in implementing an HIV look back programme during your time at either the EBTS or the WRTC? Please give details.

451. No

HCV

188. Were you involved in setting up any national or local HCV look back programmes during your time at the EBTS? If so, please describe this process and your role in it and how it was funded.

452. No

189. The Inquiry is aware of your involvement in a HCV look back programme at WRTC in 1995 (NHBT0088415). Please describe the process of the look back, including your role. You may find NHBT0088418_001, NHBT0022650, NHBT0020355, and NHBT0020468 of assistance.

453. As can be seen from the documents identified in this question, I was involved quite actively in the attempted look back programme at WRTC although Dr Andrew Herborn, medical consultant at WRTC, was of considerable assistance in leading the identification of the affected donations which also involved donor records and WRTC laboratory staff. Dr Robinson's letter (31 March 1995) gave clear advice and instructions about the procedure which was followed meticulously by the staff of the WRTC. As is clear from document NHBT0088415, by 11th April 1995 we had already identified 90 HCV positive donations of which 60 had been donated before 1991 and about 400 components had been distributed to hospitals from these 60 donors from the 'late 1970 s'. We had a clear plan of action [NHBT0088418_001] and wrote to the haematologists in all WRTC-supplied hospitals. I do remember presenting the scheme to one of the 'regular' meetings of the Regional haematologists around that time. I

do not recall any overt opposition, but it was not received with great enthusiasm.

454. I do not remember Dr Pollock or the Region he came from (it's not identified); but it seems likely that the two documents [NHBT0020355], 10th February; and NHBT0020468, 13th February) refer to the same donor, the second letter having some more details. That, and the 19 April 1995 letter from Dr Hewitt [NHBT0022650], indicate that WRTC staff were already actively working on the local lookback programme.

190. In a letter to Tim Wallington in September 1995, you stated that the performance of Wessex hospitals in look back exercises had been poor. You noted that the bigger hospitals had failed to send back forms, and that Southampton hospital had asked for extra funds to assist with the exercise (NHBT0087649). As to this:

a. Please describe the work involved for the hospitals in completing the look back programme;

b. What was the expectation of the WRTC as to how the additional work necessary by the hospital was to be resourced and funded? At the time, did you consider additional funding necessary to complete this task? Has your view changed? You may find NHBT0087657 of assistance.

455. The expected contribution from the Wessex hospitals was to locate the 'fate' of each component issued to them prior to September 1991 identified by the WRTC as coming from a donor found by our screening programme to be HCV positive. This was undoubtedly an onerous exercise, potentially going back 15 to 20 years, involving visiting the paper record in laboratory archives (to identify the patients for whom the implicated blood component had been prepared) and then visiting the archive holding the patents' notes in each hospital for a record of the actual transfusion. (I visited the

hospital archives of patient notes in the Southampton General Hospital (SGH), which were sited on SGH premises adjacent to the WRTC building: the archives were not in a good condition, the holding area being distinctly unkempt and notes somewhat scattered.)

456. I cannot recollect fully the events between my 20th July 1995 letter (NHBT0086757) to Dr Provan, at that time the haematology consultant in charge of the blood bank at SGH, explaining that the SGH would get no extra funding to cover the costs of their participation in the HCV lookback exercise, and my 25th September email exchange with Dr Wallington (NHBT0087649); but I do recollect my personal frustration at the lack of progress and my attempts to 'get things moving'. I did prepare a 'league table' of Wessex hospitals which complied, and by how much they'd managed to trace and report (NHBT0087650). I do not remember if this was sent to the Wessex hospitals, but I do remember that several discussions were held with hospital staff at SGH and other hospitals, including Portsmouth and Winchester, largely to no avail.

457. In December 1991 Dr Gunson wrote to all RTC Directors in England and Wales (NHBT0000079_021) asking how much financial support was received for the introduction of HCV screening. I replied in two letters (16 and 19 December 1991, pages 11-13 of NHBT000079_021) explaining that I had informed the hospitals that the RHA was not prepared to give any financial support other than the costs of the building works to accommodate the testing equipment (£40,000), and that I was expecting at least some users to start meeting the costs. I also wrote that the RHA would 'top-slice' users unable to pay the costs. In my letter of 19 December, I was less optimistic.

458. The early to mid-1990s was an unsettling period for the English Blood Services which until then had been administered through the Regional Health Authorities. The National Blood Authority came into force in April

1993 and took over the responsibilities from the RHAs of the RBTSs in April 1994. This diminished the role of the RHAs by removing their responsibilities, especially toward the Blood Transfusion Services, until the RHAs were abolished in 1996 following the Health Authorities Act of June 1995.

459. During the interim, the refurbishment of the WRTC facilities funded by the WRHA was completed in two phases – the computerisation of all donor and donation records, followed by the on-site construction of new facilities including a refurbishment of the donation collection suite and new laboratory facilities for microbiology testing, donation processing and blood component preparation. The output from the WRTC to the hospitals was never interrupted during the year or so of work. The Quality Assurance department was enhanced by upgrading staff appointments and the new computer system. This work was begun in 1995 under my watch but completed under the NBA which had been established in 1994 although the WRTC continued to be managed locally by myself and the senior staff until 1996.

460. I recollect that the Wessex hospitals' reactions to the reorganization and the establishment of the NBA, mainly expressed by the administrative and health professional staff in the haematology departments, were mixed but overall, rather indifferent. Regional BT Centres like Wessex seemed to lose status, not helped in some circles by the introduction of 'cross-charging' the hospitals' blood banks for the blood products supplied, although this system was eventually accepted – as it had to be.

461. In September 1994, the British Blood Transfusion Society (BBTS) held its Annual Meeting in Southampton. The BBTS caters for all grades of staff at hospitals as well as Blood Centres. The invitation to host the 1994 meeting was at the request of the Society and first received in 1990/1, with the promise (which was fulfilled) of considerable organization help from the Society but which required considerable input from local WRTC staff (who

regarded it as an honour). The staff of the Blood Bank at SGH were invited to participate in the organization but withdrew after a year of desultory participation. In 1992, at an emergency meeting of WRTC staff so far involved, a proposal to withdraw from the meeting was discussed but firmly rebutted. This episode shows admirable professional commitment from the WRTC staff but lack of engagement from the Wessex hospitals; although the staff of the Army Blood Supply Depot in Aldershot (in Wessex 'territory') contributed significant help. We were particularly disappointed by the lack of engagement by the SGH staff and haematology consultants.

462. I think this outline of events helps to explain the background of why the Wessex hospitals, except some of the smaller ones, failed to engage adequately with the HCV lookback exercise. They seemed to assume that as they were being charged for the blood and blood products, their contribution to the funding for the lookback was covered. On the other hand, while it had responsibility for managing the WRTC, the WRHA was supportive – bailing out, for example, the costs of introducing the screening tests for HCV when introduced in 1991 and funding the essential refurbishment of the WRTC facilities. This resulted in a good quality provision of blood and blood products until the incorporation of the core functions of the WRTC into the SW and Midlands Region at Filton shortly after my retirement.

c. Was the poor performance of hospitals in the region remedied? If so, how?

463. Sadly, no

Section 13: Relationship with pharmaceutical companies

191. What influence did pharmaceutical companies retain after supplying imported blood products and/or screening kits to the UK? For example, can

you recall whether pharmaceutical companies provided advice on the implementation or use of the products?

464. Imported blood products – any influence would be on the purchasers, not on RBTSs.

465. Screening kits. Microbiology testing in RBTS laboratories depended on commercial suppliers of the test kits and associated software for which training by the suppliers was given. Nevertheless, the laboratory staff were trained in the principles of transfusion microbiology as trainees in order to gain their professional qualifications, so the commercial and pharmaceutical companies were training people who were experts in their field.

192. Have you ever:

a. provided advice or consultancy services to any pharmaceutical company involved in the manufacture and/or importation and/or sale of blood products or screening kits?

466. No.

b. received any pecuniary gain in return for performing an advisory/consultancy role for a pharmaceutical company involved in the manufacture, sale and/or importation of blood products or screening kits?

467. No.

c. sat on any advisory panel, board, committee or similar body, of any pharmaceutical company involved in the manufacture, importation or sale of blood products or screening kits?

468. No.

d. received any financial incentives from pharmaceutical companies to use certain blood products or screening kits?

469. No.

e. received any non-financial incentives from pharmaceutical companies to use certain blood products or screening kits?

470. No.

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

471. No.

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

472. There was no need for me to get involved with any of these activities, so I was never familiar with the details of any regulations, nor needed to declare any interests.

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

473. No.

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

474. No.

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

475. Not relevant.

Section 14: Information handling and information sharing

197. Please describe the record keeping system in place for blood donations and blood donors at the time during your tenure at both the EBTS and the WRTC. In particular, please explain what records were kept, in what form, where and who had access to them.

476. EBTS: I cannot remember the details.

477. WRTC: The following text is an outline of relevant events recalled from memory and I cannot guarantee its chronological accuracy but is the best I can do at this stage. When I took up my post (October 1990), donor records were entirely on paper cards and filed in wooden box files which took up the whole of one corridor outside the donor suite. During the 1980's some donor records had been transferred – under RHA auspices – to facilities at Park Prewitt mental hospital near Basingstoke: unfortunately, the storage conditions were unsuitable (contaminated among other things by bird droppings), so conditions for retrieving them were difficult (a small number of records were lost irretrievably) but our staff persisted in retrieving them for purposes including the HCV lookback.

478. The laboratories were equipped with automated analysers: the equipment for determining donor blood groups was of advanced design and kept meticulously efficient by the lab staff. Their output was entered onto computer disks, the information from which was transcribed onto cards as a paper record. The equipment from the donor microbiology lab was also automated but less compact: its information was also transferred to paper.

479. Computerisation of the records was being considered by WRTC staff before my arrival but an attempt initiated by the WRTC General Manager (Mr Jim Smith) to adopt a system based on that at the Cardiff Centre was unsuccessful. In 1992/93, by which time Mr Smith had left the WRTC, I applied to the RHA for funding to install a new computer system based on the 'Digitus' system at Trent/Sheffield RTC and the WRTC was funded £200,000 by Wessex RHA to do so. With help from WRHA and staff from Trent RTC, the system was thoroughly tested, tweaked and improved to specifications drawn up by WRTC lab scientists and RHA computer experts. Over about a year, prior to each planned session to which known donors were invited, the records of those donors were entered onto the 'Digitus-plus' system. This system also recorded the components prepared from each donation. The medical information from each donor was also meticulously included from their paper card records by Dr Herborn.

480. These records were used for the HCV lookback programme from the WRTC. The staff were highly motivated by a sense of responsibility and led largely by Dr Herborn and the Principal Medical Laboratory Scientists responsible for generating the records and the quality control system. I was impressed and gratified when the system became fully and successfully functional in 1995.

481. In August 1997, the system was successfully incorporated into the 'Pulse' system from Savant adopted by the NBA: the transfer was relatively straightforward as the Digitus-plus system was largely compatible with

Pulse. I continued to use the system for my research into donor health in the mid-2000's.

198. Please set out how long these records were kept for.

482. I think there was no time limit.

199. Please set out what policy or practice was adopted by both the EBTS and the WRTC in relation to the destruction of these records.

483. Not known for either Centre.

200. As far as you are aware, did all RTCs follow the same record keeping practices, or did each centre implement its own system?

484. No; our computer system was derived from that used in Sheffield which seemed to be the best model available – and was ultimately and conveniently successful. The other English RTCs had developed their own systems: I believe that the final incorporation into 'Pulse' was in early 1998.

201. Do you consider that the record keeping measures in place at the EBTS and the WRTC were adequate to prevent donors who were suspected of carrying blood-borne infections from continuing to give blood donations at that centre?

485. EBTS – I cannot answer authoritatively but am confident that it would have been.

486. WRTC – although cumbersome, the paper record was maintained meticulously by the donor and laboratory staff and was used successfully as the basis for the lookback. The computerised records were more convenient to handle and were more than adequate to prevent known

suspects from donating further unless a donor was intentionally fraudulent, such as a change of identity at a different regular session; this phenomenon was not unknown but was very rare. I recall being told by my staff of an adult son of the same name as his father (and of the same blood group) being innocently sent to a donor session by the father as a substitute: fortunately, the donor staff noticed the son's youthfulness and the potential dangers of this innocent act were explained. This point illustrates the sociological need for vigilance by session staff for the unexpected.

202. Minutes of the NBTS / Central Blood Laboratories Authority ("CBLA") Liaison Committee suggest that electronic lists of donation numbers were being used to positively identify plasma received from RTCs. WRTC was listed as one of four RTCs where records in this area were "deficient" (NHBT0017208 at paragraph 3.3). As to this:

a. Do you agree with the assessment that electronic records at WRTC were deficient at the time? If yes, what was the cause of the deficiency in supplying electronic records of plasma packs?

487. Although the year of document NHBT0017208 is not recorded, it must have been 1992. This was before we had comprehensively and successfully computerised our records. I would not disagree with that assessment – the components paper recording system may have been regarded as particularly weak.

b. What steps, if any, were taken to improve the electronic recording of plasma packs from the WRTC?

488. See my answer to Qs 196 and 200. I do remember that the computerising team advised the staff in the components section to improve their performance following the introduction of computerisation.

203. In October 1992, you replied to a letter from Dr A Rejman who was requesting information regarding two patients infected with HIV through blood or tissue transfer (DHSC0004180_052). You stated that "difficulties have arisen through a desire to maintain confidentiality of records of the donors" and that "some of the documents which would have enabled us to provide the link have gone missing".

a. What impact, if any, did the need to maintain donor confidentiality have on record keeping practices?

489. These two patients received blood donated before I was appointed to WRTC: the incompleteness of the records for the first patient is regrettable. One of the difficulties I had in reporting to Dr Rejman was that although I had no clear evidence, I was under the impression that the putative donor – who could not be identified with certainty eight years after the transfusion – may not have been adequately identified or informed, and that 'confidentiality issues', which might have included checking with the donor about lifestyle risks, were mismanaged by inexperienced staff in 1984: but I cannot explain why some records were missing although the reasons may be quite innocuous: this was of course before HIV screening of donors was introduced.

490. The events surrounding the second patient seem even more nebulous although the dates are 1988, after HIV screening was introduced. It seems quite possible that the patient did not receive any HIV positive blood.

491. Confidentiality issues should not impact on making and maintaining accurate records, as it is necessary to link any adverse event experienced by recipients to the implicated donation and donor. This is true whether the adverse event is of an infectious nature or not. However, there are very few circumstances which justify a patient being told the identity of the

donor of any blood or blood product they receive, and I believe that donors assume that the anonymity of their donation is accepted practice.

b. How common were external requests to find archived records? How often would these records be successfully located?

492. Such requests were rare: I recollect very few in my time. It is quite possible that records originating from before computerisation might be difficult to trace – I have indicated some reasons in previous answers – location, condition, unconventional or idiosyncratic filing systems, accidental destruction (fire, water, decay, etc.), neglect.

c. What procedures were in place to prevent records going missing?

493. I was not directly responsible for devising the procedures for maintaining the integrity of records, whether computerised, microfiched, or on cards, so cannot comment. I did trust the staff at WRTC and cannot recall any event which justified any lack of trust.

204. The Inquiry is aware that the Communicable Disease Surveillance Centre (CDSC) maintained a database to keep track of reporting of blood donors who tested positive for HIV (NHBT0004742_001). The Inquiry understands that this database was in existence in 1989, although it is unclear for how long the CDSC operated it. Please answer the following questions regarding this database, as far as you are able:

a. Were you aware of the database, if so, when did you become so aware?

494. Yes, but I cannot remember when – probably soon after the screening of blood donations for HIV was introduced.

b. Who proposed the creation of the database?

495. I do not know.

c. Did the WRTC contribute data on HIV positive donors to the database? If not, why not?

496. I assume so. There were annual reports of all people in the UK found newly infected with HIV and assume that some of these were identified initially by blood donation, including any collected by WRTC.

d. Are you aware of whether other RTCs contributed data on HIV positive donors to the database?

497. I do not remember being made specifically aware but assume that they were.

e. Did centres within the SNBTS contribute to the CDSC database? If not, did the SNBTS have a comparable scheme for data collection?

498. I do not know.

f. Did the WRTC maintain a separate, or additional, database to track HIV positive blood donors?

499. Almost certainly yes.

205. A NBTS departmental memorandum dated 15 May 1989 notes that "it has been decided to re-introduce the original 'J' donor system" to identify donors involved in cases of post-transfusion hepatitis (NHBT0005388). Were you aware of the existence of this system? If so, please answer the following questions regarding this system, as far as you are able:

500. I was not aware of this system which appears to apply to the Manchester Centre.

a. The use of the word "re-introduce" implies that the J donor system had been operational at an earlier time. When was the J donor system first introduced, and why did it stop operating?

501. I do not know.

b. Who proposed the re-introduction of the J donor system?

502. I do not know.

c. What was the intended scope of the J donor system? Were all RTCs expected to contribute to it?

503. I do not know.

d. Did the SNBTS also operate the J donor system? If not, was a comparable system in place in Scotland?

504. I do not know.

e. Was the proposal for the re-introduction made to a committee or forum similar to the regional transfusion centre directors' meetings?

505. I do not know.

f. What was your view of the proposal for the re-introduction of the system? How was the proposal received by other RTC directors?

506. I had no view as it seems to have been local to Manchester.

g. What was the purpose of the system and what information was it intended to collect?

507. I do not know but assume that the 'J' refers to donors at risk of transmitting Jaundice.

h. Was the J donor system re-introduced? If so, when and how did it work?

508. I have no recollection.

i. Was the J donor system widely used after the "re-introduction"? If no, why not? If yes, who was responsible for overseeing the system?

509. I do not know.

j. As far as you are aware, does the system still exist?

510. I do not know.

206. In addition to the database(s) mentioned above, did the WRTC share information with other RTCs about excluded donors, donors that posed a risk to the safety of the blood supply, or infected blood donations? If yes, was this on a formal or informal basis? Please describe the mechanisms WRTC used to share this information, if any.

511. I do not remember receiving any reports of a registered WRTC donor who developed jaundice and stopped donating; so I do not know if any such donors were followed up. The WRTC was very willing to share information about excluded donors with other RTCs but this would probably have been

given just on an informal basis – if, for example, a donor new to Wessex and grounds for exclusion identified, had previously donated in another RTC.

207. In his statement in the A and Others litigation, Dr Gunson expressed the view that "there was no central organisation to ensure that...all RTCs operated in a uniform manner" (NHBT0000026_009). Do you agree? In your opinion, were the information sharing measures in place between RTCs adequate to prevent donors who were suspected of carrying blood-borne infections from continuing to give blood donations?

512. I would agree with this statement from Dr Gunson, and suspect that the measures for sharing information about donors suspected of putting recipients at risk of TTI could have been improved from the informal basis described above by a more centralised system.

Section 15: Meetings of various committees

208. The Inquiry understands that you served on various committees relating to blood transfusion and the blood services. Please set out, in broad terms:

a. the relationship between these committees and the Departments of Health in England and Scotland; and

b. the relationship between these committees and the NBTS/SNBTS.

513. The main national (UK) committee on which I served from 1996 until 2006 was the 'Standing Advisory Committee on the Selection of (Blood) Donors' (SACSD) which in 2000, because of the increasing responsibilities of the UK Blood Services for donor health and welfare, was renamed the Standing Advisory Committee on the Care and Selection of Donors (SACCSD). The SACSD/SACCSD was analogous to the Standing

Advisory Committee on Transfusion Transmitted Infection (SACTTI) which, in 1993, succeeded the ACTTD established by Dr Gunson in the 1980's: this was to give Dr Gunson, as National Director of the (English) NBS, expert professional advice. Both the SACCSD and SACTTI were answerable to the Joint Liaison Committee of the UKBTSs and the National Institute of Biological Standards and Control – NIBSC: this joint Committee was chaired by Dr Bill Wagstaff, Director of the Trent Regional Blood Transfusion Centre at Sheffield. As such, the SACCSD's remit was to advise Dr Wagstaff's Joint Committee of the issues surrounding donor selection and of the UKBTS's duty of care for the donors (such as minimising the hazards of donation to donor health, providing the immediate after-care of donation, and explaining the relevance of any clinical findings relating to the donation such as markers of potential infection).

514. It is important to note that the remit covered the whole of the UK and N Ireland and its membership was drawn from all four nations in the UK. The National Directors of the English and Scottish Transfusion Services were members of Dr Wagstaff's committee and in a good position to communicate the recommendations it received from its subcommittees such as the SACCSD. The SACCSD produced successive issues of the so-called 'Red Book' – a series of editions of a text giving guidelines which were used as a Quality Assurance controlled document applying to all the UK Transfusion Services: it was an essential tool to ensure that they met the requirements to obtain the legal licenses from the Medicines Control Agency.

515. I was Secretary of the SACCSD from 1996 to 2000 under the Chair of Dr Virge James; then Chair from 2000 to 2005. I was succeeded as Chair by Dr David Hutton. I attended my last meeting in May 2006.

516. As Chair of the SACCSD I attended other meetings concerned with specific aspects of donor selection such as that held at the Hospital for Tropical Diseases on 4 May 2001 (JPAC0000028_083) on the risk of T cruzi infection, and a Joint Meeting of SACs on 22 November 2000 (NHBT0001972) on the problems of vCJD. Document JPAC0000005_138 (my report of 13 May 2003) summarises these other meetings.

209. Given your role as Medical Director of WRTC whilst also chairing and serving on various committees, please describe:

a. the relationship between these committees and individual RTCs;

517. The RTCs received copies of the 'Red Book', and any other relevant materials such as leaflets for donors, and a regular 'A – Z' of donor exclusion criteria. It had a close working relationship with SACTTI, one of whose members was also a member of SACCSD. These principles applied to communications from other related committees and sub-committees.

b. how committee recommendations would be communicated to RTCs; and

518. By mail and email communications with senior personnel concerned with implementing the SACCSD recommendations and policies as set out in the 'Red Book' and other communications such as the 'A – Z'. The senior personnel included medical consultants and donor session managers

c. how committee recommendations were implemented at RTC level. Were there any common barriers to implementing committee recommendations? If yes, what were they?

519. On the whole, these recommendations and any training requirements were well received and managed by Centres' donor teams and medical staff. At the NBS Southampton Centre, where I was based after the NBA succeeded to its management, there were regular training sessions in which I was sometimes involved. These sessions were also useful to me as Chair of the SACCSD as I could communicate closely and easily with front line practitioners. I understood that such experiences were the normal at other Centres. (I occasionally worked as a member of a donation collection team thereby maintaining first-hand experience of the practices and challenges of a blood donation collection session.) Inevitably, occasional anomalies became revealed – such as confidentiality issues for hearing-impaired donors and the use of sign-language interpreters, or the use of blood from people with hereditary haemochromatosis – and required specific agenda items to be brought for discussion at future meetings.

520. One point to bear in mind is that the SACCSD was more than advisory: it also defined the principles of blood collection by the Transfusion Services and was the principal source of operational guidelines and practices,

Meetings of UK National Advisory Committee on the Care and Selection of Blood Donors ("SACCSD")

210. The Inquiry understands that you participated in this advisory committee, serving as both the Secretary and the Chair, attending your final meeting in May 2006 (NHBT0040547_001). The Inquiry holds minutes of meetings of this committee from 1991 to 2006. The meetings of minutes you attended are listed in the Schedule for your reference. What do you consider to have been the purpose(s) of those meetings?

211. Please explain, as far as you are able, the decision-making remit of the group.

212. Do you consider that these meetings were conducive to fulfilling the purpose(s) for which they were established?

521. See my responses to Q 208 above. The purpose of these meetings was principally to update the principles and practices of selecting donors from whom the safest possible blood could be collected consistent with the advice from our sister committee, the SACTTI, and subcommittees. Furthermore, the care of donors became more significant as collection procedures became more complicated and people with identifiable but clinically insignificant anomalies – such as the inherited condition 'Factor V Leiden', or even 'old age' – required extra consideration.

522. Several issues overlapped with the remit of SACTTI – an example is seen in my letter to Dr Chitra Bharucha (JPAC0000124_008) which referred to issues relating to T cruzi, syphilis and HIV in male donors with a history of MSM. Donors with a history of surgical repair using allogeneic dura mater posed a question which is addressed later in the section concerning Creutzfeldt-Jakob disease.

213. You stated in an email to Maria Evandrou that the committee set first-line guidelines on donor selection policies, and was answerable to the Chief Executives and Medical Directors of the BTS, as well as the Department of Health (JPAC0000014_133). Considering this detail:

a. How influential was the committee in setting national policy on donor selection?

523. My letter to Maria Evandrou was dated 8 April 2004 by which time Dr Wagstaff, chair of the UKBTS/NIBSC Liaison committee had been replaced by the four National Blood Transfusion Services' Chief Executives and Medical Directors who, in turn, were answerable to the

Minister of Health at the DHSS in Westminster. Nevertheless, the Liaison Committee and its subcommittees including the SACCSD and SACTTI remained influential in setting the quality standards of UK blood transfusion services for donors and recipients.

b. Did any conflicts of interest exist between the aims of the committee and those of the organisations it was answerable to? If yes, what effect, if any, did these have on the development of policy?

524. Not as far as I am aware. In my time and experience, the committees worked well together for a common purpose. However, a combined SACCSD/SACTTI meeting (JPAC0000137_019) was held in November 2004, also attended by representatives of other committees, and emphasised the need to avoid duplication. Inevitably, sometimes viewpoints differed according to individual experiences – such as criteria for testing for one disorder (HIV, HBV, HCV, etc) in a patient setting or in a setting of an apparently heathy community (such as donation sessions), but such differences became accommodated as bases for the published 'Red Book' guidelines.

c. What other organisations, if any, had influence on the committee's advice?

525. No other organisations within the Blood Services although specialist advice was often sought from individuals such as Dr Evandrou. The Terrence Higgins Trust was a valuable external source of advice concerning policies about donations from MSMs which helped counter some of the concerns about these policies expressed by members of the public or indeed from individual MSMs.

d. In March 2000 Professor Ian Franklin of the SNBTS wrote to you regarding a statement released by the committee related to HIV (NHBT0002656). As to this:

i. How were the committee's decisions communicated to the NBTS / SNBTS?

526. Dr Franklin was one of the four Medical Directors of the UK BTSs – in his case, of Scotland. I think his concern was justified, but the SACCSD was not alone in perhaps by-passing Professor Franklin and his colleagues who formed the 'Red Book Executive'. I believe that his diplomatic letter bore fruit at subsequent Joint Liaison Committee meetings (see minute 5 of the SACCSD meeting of 10 May 2001 – SBTS0000413_013). (Around this time, this committee was named 'JPAC' – the Joint Professional Advisory Committee of the UK Transfusion Services.)

527. The following is an extract from a letter I wrote in 2005 (to an enquirer about the exclusion of MSMs as donors – see the next section), explaining the consultative structure of the donor selection rules.

528. *Finally, I can assure you that all our donor selection rules, including the criteria regarding gay men, are examined regularly and updated according to the latest epidemiological information. The committee structure for these processes are accountable to the medical professions and to Government. The Joint Professional Advisory Committee (JPAC) is accountable to the Medical Directors and Chief Executives of each of the four UK national blood transfusion services. The committee on Microbiological Safety of Blood, Tissues and Organs for transplantation (MSBTO) – which is chaired by Professor Lindsey M Davies CBE, Special Professor of Public Health Medicine and Epidemiology – is directly accountable to the Department of Health. These structures provide a detailed system for the appraisal of all criteria which govern the safety of blood for recipients.*

ii. **What, if any, changes were made to these processes when dealing with issues with "political importance", such as HIV transmission?**

529. I think that there was no need to change the processes for dealing with issues such as HIV transmission. However, the NBTSs were frequently and understandably pressurised by correspondence from advocates of the LBGQ community to recruit MSMs as donors. The services agreed that I, as Chair of the SACCSD, should respond in person to each of these requests. A pdf copy of my correspondence in 2005 with one complainant (complainant's name redacted) is attached [WITN3456005]. I presented my experience of responding to all the complaints received between 2002 and 2006 to a meeting of the International Society of Blood Transfusion in Cape Town, South Africa in 2006 – pdf version attached [WITN3456003].

214. In a committee progress report dated May 2003 (JPAC0000005_138), you stated that: 'JPAC expressed a wish for the current criteria to be reviewed on a more "evidence" basis, particular [sic] in order to prepare better for anticipated periods of shortage. It was agreed that the principles of safe donor selection must not be compromised by a perception of adjusting the rules to maintain the supply.'

a. **What did you understand JPAC's suggestion to mean? How else were blood donor selection criteria established other than with reference to evidence?**

530. The quality of the evidence behind 'evidence-based clinical practice' has widely variable degrees of 'strength' and it is common, when publishing clinical guidelines, to cite the specific levels of strength of each piece of evidence quoted. These include for example whether the evidence is

anecdotal, or of low statistical power, to evidence which has been firmly established and up to evidence which has been repeatedly confirmed.

531. Requirements for evidence may also vary according to the circumstances. For example, what evidence might be needed to justify modifying the rules during a prolonged shortage of blood? In this example, evidence for the safety of collecting blood more frequently without increasing the risk of donation-induced iron deficiency might be needed; or, in the context of risks of TTI, shortening the temporary deferral time after returning from short-term travel in a 'high risk' geographical area from, say, one year to six months.

b. Was the principle of safe donor selection compromised by adjusting the rules to maintain supply?

532. I don't think so. That was why evidence was needed – to help avoid compromise to the safety of the blood supplied.

215. It appears the committee developed recommendations on the deferral periods of donors in particular categories, in particular, for donors who may pose a risk of HIV or hepatitis transmission (JPAC0000124_008).

a. How frequently were the deferral periods for donors reviewed?

533. All donor selection criteria, including deferral periods, were reviewed regularly, and committee members reported any relevant findings – by themselves or by expert consultations (literature searches, expert consultations etc) – to the SACCSD.

b. Please describe the process of reviewing whether a deferral period was appropriate, including the types and sources of evidence which were taken into account.

534. SACCSD committee members, including myself, were remitted to conduct literature searches in peer-reviewed journals or use their own research experiences on matters of interest. We were often assisted by members of the SACTTI and also by Dr Kate Soldan, at the time statistician at the PHLS at Colindale, who attended occasional SACCSD meetings

c. How were decisions ultimately taken on whether to revise an established deferral period?

535. Recommendations would be passed to JPAC who were ultimately responsible for any decisions on donor selection criteria.

216. A fax from Dr Galea to you in December 1998 describes the questioning of blood donors by the blood services in the Netherlands, Germany, Ireland and America (JPAC0000021_006).

a. How frequently, if at all, were international approaches to donor selection and donor questionnaires analysed? Who instigated this research?

b. What impact, if any, did the practices in other countries have on the development of donor selection policies?

536. I find it difficult to recall exactly what Dr Galea's somewhat cryptic fax of 11/12/98 (JPAC0000021_006) was about, but he seems to have been investigating donor selection practices in countries overseas. I note that minute 11 of the SACCSD meeting of 15/12/98 (JPAC0000008_180) at which Dr Galea presented his apology of absence and to which he seems to refer in his fax, refers in part to retrospective changes in donor selection criteria which could impact on his role in tissue banking. It seems, therefore, that Dr Galea in his role in SACTB (tissue banking) himself instigated or caused to be instigated an international enquiry about donor selection in the context of tissue banking (cornea, bones, fascia, etc.,) and

what retrospective factors might impinge on the selection of tissue donors. If this were the case, it had little relevance to blood donation. However, selection practices in the EU occasionally had profound impacts on UK practices because of the need to comply with EU Directives. Nevertheless, I believe that with JPAC approval, minor variations were allowed.

217. Please consider the Committee's role in respect of donor leaflets and blood safety leaflets aimed at excluding high-risk groups. In particular:

a. What role, if any, did the Committee play in determining the content of such leaflets?

537. By the mid-1990's the SACCSD had a major role in determining the content of blood safety leaflets. Doc JPAC0000001_014 which was written in 1995 by Dr Peter Flanagan, a former member of SACSD and at the time Clinical Director at NBS Leeds, describes the background of an updated leaflet for staff and for donors on the need for 'safe blood' for transfusion. This gives a full account of its advisors (from the SACSD and commissioned experts), and how its design was commissioned and field tested (by the DoH and the Central Office of Information). The information supplied by Dr Flanagan was intended to help staff training and to inform donors.

b. How often did the Committee consider the effectiveness of such leaflets? How often were they updated, and what did the review process entail? You may wish to refer to NHBT0008562_001 and NHBT0008562_002.

538. The next version in 2001 was the result of updating work and research conducted by members of the SACCSD. As this work was in effect continuous and upheld by the regular meetings of the SACCSD (four or five times a year, and with many communications by telephone, fax and emails), the task of coordinating the various updates fell largely to me as

Chair of the SACCSD. This indicated a clearer need to separate materials for staff training and for donor information.

c. In your view as a committee member, what role did donor leaflets and blood safety leaflets play when mandatory exclusion and selection criteria existed? How did both strategies work together to reduce the risk of infection?

539. The leaflets played an essential role in donor education and staff development. The 2002 version was followed by a clearer separation of the educational requirements for staff and for donors.

d. In 1995, the scope of the Blood Safety Leaflet was expanded to cover HBV and HCV. Why were these viruses not included earlier? In your view, what impact did their addition to the Leaflet have? You may wish to refer to JPAC0000001_014.

540. Previous printed guidance, especially for donors, had been limited to concerns about HIV. With the advent of screening for HCV (on top of the long-practised - since 1972 - screening for HBV), it became apparent that a clearer and more comprehensive guide to the selection of 'safe' donors was needed for BTS donation collecting staff and for donors. However, staff at donor sessions had long been trained to ask donors about any history of jaundice as well as in the exclusion criteria for life-style risks for acquiring HIV; but these were more 'ad hoc' and required more regulating. 'Jaundice' in particular was open to misunderstanding as some donors recalled that their mothers had told them they were jaundiced at birth. This phenomenon is not uncommon but is mostly due to the immaturity of the neonatal liver having to cope with an increased load of haemolysing red cells which happens around the time of birth. Neonatal jaundice is most apparent in babies of fair skin complexion and is of no significance regarding the safety of blood donated when they become adults.

541. As health professionals gained a better understanding of the significance of HCV infection, it became necessary for the general public, and particularly for blood donors, to share that awareness. The blood safety leaflets were a good potential source of such information and over time, the information leaflets for blood donors became designed more suitably.

Standing Advisory Committee on Transfusion Transmitted Infections

218. In 1989 the UK Advisory Committee on Transfusion Transmitted Diseases ("ACTTD") was set up by Dr Harold Gunson to consider the implications of transfusion-transmitted infections on the transfusion services in the UK and provide advice to the Department of Health. The Inquiry understands that ACTTD was replaced with the Standing Advisory Committee on Transfusion Transmitted Infections ("SACTTI") following the creation of the NBA in 1993 (DHSC0006906_013). The Inquiry understands that you attended meetings of SACTTI and provides the minutes of the meetings you attended in the attached schedule.

219. What was the function and remit of SACTTI? In particular:

a. Who did SACTTI report to, how frequently and by what means? DHSC0006906_013 refers to a letter from Dr Robinson to Dr Jeremy Metters in September 1985.

542. I have no reason to doubt the advice Dr Robinson gave – namely that the SACTTI was formed to advise the UKBTS/NIBSC Liaison organisation, the NBA and the SNBTS on all matters concerned with the possibility of TTIs and infections from banked tissues held in Transfusion Centres. (The Welsh and Northern Irish services are included in this definition). Also, the SACTTI could commission, conduct and coordinate trials of new technology for screening donors for TTI agents, consistent with the work of national research committees.

b. Did SACTTI have any powers or was it purely advisory? (You may find NHBT0008002 of assistance).

543. Dr Robinson's letter to Dr Ala (NHBT0008002) neatly described the frustration which resulted from a fundamentally advisory committee getting involved with the nitty-gritty of implementation. This may be partly because many of its members were very familiar with the challenges of implementation and from variations in, for example, demography across regions and nations, and wanting to anticipate some of these difficulties for implementers. I think it would be unwise to regard it, and also the SACCSD, as purely advisory: elements – actually rather more than elements – of pragmatism needed to be considered by both committees in order to facilitate implementation, even though implementation would be conducted by staff responsible to the National Executives.

544. This issue has a bearing on my answer to Q212 d i).

c. How did SACTTI's remit differ from its predecessor ACTTD?

545. As SACTTI arose out of the ACTTD, its remit seems to have been similar but I get the impression that SACTTI was somewhat closer to the implementers. I think ACTTD was too dominated by academic experts with less understanding of the design of screening generally healthy populations than of diagnostic testing of ill patients.

d. How frequently did SACTTI meet?

546. As I was not a member of SACTTI, I have no direct knowledge, but I think it was at about the same frequency as that of the SACCSD. However, SACTTI had rather more subcommittees than SACCSD – such as considering donors at risk of tropical diseases – especially malaria, and

also Leishmaniasis and Chaga's disease (T cruzi) which were of concern in the mid-1990's. It also – as addressed later, donations from donors at risk of contracting CJD, particularly vCJD as a consequence of the BSE crisis which affected UK donors from 1996 onwards.

220. Please explain the relationship between the SACTTI and the WRTC/NBTS, including but not limited to:

a. whether SACTTI made decisions that the WRTC/NBTS was required to implement; and

b. whether, and how frequently, you provided feedback on the recommendations made by the SACTTI. Please explain, to the best of your knowledge, the relationship between the SACTTI and other RTCs.

547. Even though I was no longer Director of the WRTC from 1996, with the Southampton Centre's accountability being transferred to the NBA, my office base remained at the WRTC site and many of my duties, and all the duties of my medical colleagues there, remained - including the essential medical advice for donor care, selection and interpretation of testing results, especially of results which were anomalous.

548. I was also conscious of the fact that my Chairmanship of the SACCSD and its close relationship to SACTTI should have been advantageous to staff whose work was affected by regulatory changes. In this regard, I endeavoured to help as much as was appropriate – for example, explaining at training sessions why any changes in procedure or documentary advice (as in the SACCSD's donor leaflets) were necessary.

549. I assume by 'feedback' you are referring to feeding back the local WRTC staff's reactions to SACTTI's recommendations. I recall no difficulties in feeding back staff reactions.

221. What was the impact of there being so many committees in place at around the same time? Was there overlap between them? If so, how did this impact their effectiveness?

550. Certainly, there was an increase in the number of committees and subcommittees and the potential for 'too many cooks' also increased. JPAC0000137_019 records the minutes of a rather packed joint meeting of the SACTTI and SACCSD (30 present although Kate Soldan was counted twice: and over 20 apologies for absence). This meeting resulted in a better understanding across the parties, especially on issues such as malaria – the exclusion rules being quite complicated and requiring further training for senior donor staff.

NBA Executive

222. The Inquiry understands that you attended certain meetings of the NBA Executive during 1993 and 1994. The minutes of the meetings you attended have been provided for your assistance in the attached schedule.

223. As far as you are able, please describe:

a. The remit and composition of this group; and
b. The frequency of these meetings.

551. I believe that I attended most, if not all of these meetings, but only six documents concerning these meetings have been listed in the emails sent to me. The 11th meeting was held on 8th August 1994; the first having

been held on 20th October 1993: this gives a frequency of these meetings during 1993/4 of once a month, which accords with my memory.

552. These meetings had been called by Mr John Adey, the first Chief Executive of the NBA in order to keep the then Directors of Regional Transfusion Centres informed about the impending unification of the management of the RTCs in England into the National Blood Authority

Western Division of NBTS Consultants

224. The Inquiry understands that you attended certain meetings of the Western Division of NBTS Consultants during 1991 and 1992. The minutes of the meetings you attended have been provided for your assistance in the attached schedule.

225. As far as you are able, please describe:

a. The remit and composition of this group;
b. The frequency of these meetings; and
c. The relationship between these meetings and those of the Regional Transfusion Centre Directors.

553. I attended two meetings – in March 1991 and in June 1992. At the first meeting I was able to meet some of my Regional BTS Medical Directors for the first time; one interesting point was raised by the Colonel in charge of the Army Blood Supply Depot in Aldershot about the problems experienced by Allied Forces in the then ongoing First Gulf War about the colour-coding of the blood group labels on blood packs. This resulted in the labels being printed only in monochrome permanently.

554. At the second I was able to announce my appointment by Wessex RHA as Chief Executive of the Wessex RTC.

555. These meetings were a useful forum for the exchanges of professional news and views about Blood Transfusion Practices and I learnt more about the Standing Advisory Committee frameworks, as well as the slow progress in developing the application of screening tests for HCV. I think the remit was to share information among the RTDs concerning the quality of the blood supply and national developments.

Section 16: Variant Creutzfeldt-Jakob disease (vCJD)

226. Following the BSE outbreak in 1985, and the first human death from vCJD in 1995, the risk of vCJD transmission by blood was confirmed in 2003. The Inquiry is interested to gain an understanding of your knowledge of risk, your involvement in discussions within the blood services, and any actions taken with regard to vCJD since 1985.

Knowledge of risk of vCJD in blood and blood products

227. When and in what circumstances did you first become aware of the risks of transmission of vCJD through blood and blood products?

556. BSE emerged as a threat to the health of cattle in the early 1980's and there was an immediate concern about the health of people eating beef products. In 1990 the then Minister of Health used his 4-year-old daughter in a publicity stunt to show that beef burgers were safe, an action which drew wide criticism in view of the increasing incidence of 'Mad Cow Disease' in the UK and its link with cattle-feed being bolstered by animal protein, including beef brain.

557. Later that year, the Phillips report on the origin and effects of BSE was published showing the clear link with cattle feed. Although by the mid-1990's the Mad Cow Disease epidemic was on the wane as a result of

increasingly stringent restrictions on the reinforcement of cattle feed, there was still great concern among some environmentalists and allied thinkers that humans might prove vulnerable so when in 1996 the first human cases of vCJD tragically and worryingly emerged, it was no great surprise to many, including myself.

558. I published an article- F Boulton (2003). The Impact of variant CJD on transfusion practices in the UK: Transfusion and Apheresis Science, 28, 107-116 (WITN3456006)

228. Please provide a summary of any discussions relating to the development of scientific understanding of the risks of both vCJD infection and of secondary transmission via blood and blood products.

559. I wrote the following passage in 2009 (Prevalence of variant CJD in the UK ***BMJ* 2009; 338 doi: [RLIT0000774 and RLIT0000775]**

'*For the last nine years or more, UK citizens and those visiting UK during the BSE years have been barred from donating blood in most developed nations overseas. Donors who were transfused in UK are completely barred, even in UK – losing a particularly well-motivated cohort of recruits. Millions of pounds sterling have been spent on leucocyte-depleting donated blood in attempt to reduce vCJD transmission risk, which is probably only partially effective (although other benefits, especially the improved quality of the stored blood are very welcome). Younger patients receive Fresh Frozen Plasma from donors residing in lower-vCJD endemic areas, principally the USA, resulting in a convoluted counter strategy to lower the risk of other transfusion-transmissable diseases, such as viral hepatitis: these counter strategies involve the introduction over and above the standard high-cost viral testing systems of extra means such as photo-chemical antisepsis. These decisions are justified, as such recipient patients' life expectancies extend well into the likely incubation period for*

clinical signs of vCJD infection even for PRNP 129-valine homozygotes. Prion-reducing filters for plasma have been under development for years and, when effective, will be welcome. Safe 'prionicidal' antisepsis – leaving plasma or blood proteins unaffected – is another theoretical possibility: but the inevitable consequences of all such strategies and developments include complicated control systems, increased opportunities for human error, prioritisation challenges, and further dramatically upward-spiralling costs'.

229. What was your understanding of the relative risks of vCJD infection from the use of commercial or imported blood and blood products, as compared with the use of domestically produced blood and blood products?

560. BSE and vCJD are principally problems for the UK with some effects in Ireland and about one-tenth of the UK effects in France. As such, imported blood products are likely to be at low risk of transmitting vCJD, but the impact on providing FFP for children required imported products of intrinsically high risk of viral TTI which had to be countered by chemical treatment – a somewhat convoluted way of managing this need.

230. Please provide an outline of any steps you are aware of which were taken to ensure that the UK Government, blood services, NHS bodies, medical profession and patients were informed and educated about the risks of vCJD transmission via blood and blood products.

561. Additional measures to prevent TT vCJD from non-red cell products were taken after I retired (2006). Leucocyte depletion of all UK red cell products has been accompanied by the absence of any further cases of TT vCJD

Role of Regional Transfusion Centres

231. The Inquiry seeks to understand what actions the UK Government, blood services and other organisations took in response to the risk of vCJD transmission via blood and blood products. We are particularly interested in the role of RTCs in responding to the risk. As to this:

a. How did the blood services communicate the emerging risk of vCJD to the RTCs?

b. We note from JPAC0000007_095 that a workshop was proposed by Elizabeth Love to discuss the issue of vCJD and the division of responsibility between various bodies and committees. Please can you comment on the outcome of these discussions, whether a framework document was prepared, and what role, if any, the RTCs were to play in this regard.

562. Dr Love's 'call for action' in December 2000 was timely and followed by meetings filed by the Inquiry as documents JPAC0000029_108; JPAC0000088_067; JPAC0000086_019; JPAC0000114_018; JPAC0000118_015; JPAC0000051_056; JPAC0000051_053. I cannot recall if a framework document was prepared. The main role of the RTCs was to provide universal leucodepletion of red cell, platelet and plasma products. The contribution of this strategy appears to have been successful in reducing the incidence of TT vCJD apparently to zero after the fourth case (and fatality) in 2007, but it will be difficult to determine the degree of such success although the possibility of a delayed 'wave' of new cases may be receding as time goes by.

Risk reduction measures

232. Please provide details of your involvement in, or knowledge of, any discussions or proposals, whether accepted or not, that were made in an effort to protect the blood supply from the risk of vCJD. To assist you we

have referenced below documents which indicate your presence at meetings where particular risk reduction measures were discussed. However, please provide details of your involvement in all discussions and proposals where they are not referenced within the same.

563. See below

233. The risk reduction measures include but are not limited to:

a. donor selection and exclusion policies (NHBT0001956_002; JPAC0000006_162; JPAC0000086_019, JPAC0000114_018; JPAC0000061_022; NHBT0004312);

564. NHBT0001956_002 – not located

565. JPAC0000006_162 – see minute 8 a) for my involvement, including the possible review of donor status of family members of people with vCJD

566. JPAC0000086_019 – no specific action by me recorded

567. JPAC0000114_018 – no specific action by me recorded

568. JPAC0000061_022 – SACCSD and others to discuss operational policy of deferring any recipients of blood as blood donors – This policy was adopted

569. NHBT0004312 – the exclusion of certain professions deemed possibly to be at increased risk of transmitting prion disease by transfusion of their donated blood: such a list might include neurosurgeons, veterinary surgeons dealing with cattle or sheep infected with BSE/Scrapie, carers of people with vCJD or other forms of CJD, abattoir workers, butchers, farmers – Not recommended by me

b. development of screening diagnostic tests (NHBT0001956_002, NHBT0042193_007,JPAC0000061_022,); JPAC0000088_067

570. NHBT0001956_002 – not located.

571. NHBT0042193_007 – My review of donor acceptance to compensate for donation losses on the introduction of a vCJD screening test: identified 8 possible criteria for re-reviewing: more frequent donations by each donor: encouraging more donations from people with genetic haemochromatosis: bleeding older people: shortening temporary deferral people returning from malaria risk areas: review of medications currently requiring deferral: review of piercings conducted by health care professionals other than acupuncturists: modifying the anaemia screen (not allowed under EU regulations): allowing donors cured of a previous malignancy. One more possibility – reviewing criteria for excluding MSMs was ruled out.

572. JPAC0000061_022 – SACTTI/vCJD working group. SACCSD again to look at deferring all transfused donors (17th June 2005).

573. JPAC0000088_067 – FEB; no support for family members of vCJD victim to be excluded from donation.

c. importation of product from the USA or elsewhere (BSHA0000066_002);

574. See my response to Q22.

575. Minute 8 ii) of BSHA00000066_002 refers to TT vCJD reduction by methylene blue treatment of FFP from foreign (vCJD-free) sources for neonates and children, which has been mandated by the DoH needs a source reference for which Dr Marc Turner was asked to supply.

d. surveillance;

576. No recollection of being involved.

e. product recall;

577. No recollection of being involved.

f. quarantine of batches;

578. I believe that this was more an issue for BPL and plasma.

g. filtration policy (JPAC0000061_022); and JPAC0000061_022 (June 2005) has a minute describing the difficulties in validating prion reduction filters.

579. I was not involved.

h. recombinant blood products.

580. No recollection of being involved.

234. In providing this outline, please state where possible:

a. when and by whom any proposals were made;

581. I have no recollection of such proposals and measures.

b. the factors considered when deciding whether to implement these proposals;

582. I have no recollection of such proposals and measures.

c. decisions made on such proposals, including the date on which they were made or rejected; and

583. I have no recollection of such proposals and measures.

d. how any such measures were implemented in practice, including efforts made to monitor their effectiveness.

584. I have no detailed recollection of such proposals and measures.

235. Please provide your opinion as to whether the risk of secondary transmission via blood and blood products was adequately mitigated in the UK in line with what was known about the potential risks of vCJD at that time.

585. Little was known about the risks of TT vCJD in the late 1990's and early 2000s but the absence of any further TT vCJD since the paper by Dr Hewitt et al was published: NHBT0095180 (P E Hewitt , C A Llewelyn, J Mackenzie, R G Will, 2006. Creutzfeldt-Jakob disease and blood transfusion: results of the UK Transfusion Medicine Epidemiological Review study. Vox Sang. 2006 Oct;91(3):221-30. doi: 10.1111/j.1423-0410.2006.00833.x.) indicated that the risk of secondary transmission via blood or blood products was adequately mitigated.

236. Please provide your view as to whether any decisions or actions of could and/or should have been made earlier and how this might have impacted the number of individuals considered to be at risk of developing vCJD.

586. The only feasible measure which might have introduced mitigation earlier would probably have been universal leucodepletion.

Section 17: Other matters

237. Please provide a list of any articles you have had published relevant to the terms of reference.

587. Attached.

238. Please provide details of any complaints made about you (insofar as relevant to the Inquiry's Terms of Reference) to your employer, to the General Medical Council, to the Health Service Ombudsman or to any other body or organisation which has a responsibility to investigate complaints.

588. No relevant complaints have been made about me.

239. Please explain, in as much detail as you are able to, any other issues that you believe may be of relevance to the Infected Blood Inquiry. To assist, we have provided a list of issues.

589. I have reviewed the List of Issues to consider what I can say that may be of relevance.

590. I start by acknowledging the courage and tenacity of the people in the UK with haemophilia, and their families, who were affected by the tragedy caused by the acquisition of infections transmitted by the transfusion of human blood products, whether the products originated in the UK or overseas. The same goes for those patients and their carers affected by the transfusion of single donor product (red cells, platelets, plasma, etc.,) which transmitted an infection to them with prolonged and very significant adverse effects on their lifestyles, livelihoods and life-expectancy.

591. Furthermore, the tragedy – which has resulted in thousands of premature deaths among UK citizens – has affected deeply many of those health professionals who specialised in the clinical management and laboratory support of people with inherited and acquired bleeding disorders. I

acknowledge the dedication and commitment displayed by these and their supportive volunteers who continued their work in spite of their exposure to the increasingly infectious hazards to which they were exposed by their occupation.

592. The last quarter of the 20th century was accompanied by a significant change in the expectations of people with haemophilia and their families. For the two decades or so prior to then, the best that UK haemophiliacs could expect was an efficient diagnosis of their clinical condition and advice on how best to avoid harm while also being advised positively that life-milestones such as schooling, teething, vaccinations, etc., could – with care – be negotiated successfully. Nevertheless, a life of recurrent pain and an increasingly 'crippled' physical state could also be anticipated, as well as a distinct possibility of an unexpected and rapidly fatal bleeding episode. With better understanding of the inherited cause, mothers frequently developed a 'guilt-complex' which also needed careful handling.

593. Although blood transfusions were recognized to have a role in alleviating acute haemophilic bleeds before the 20th century, and increasingly in the decade prior to WW1, the pathogenesis of haemophilia (i.e., lack of specific plasma proteins) became generally accepted only in the 1930's.

594. Nevertheless, although the clotting activity in the blood of affected people could be improved after transfusing whole blood straight from the donation (conveniently aided by taking the donor's blood into a pint-bottle where it was mixed with an anticoagulant such as citrate before being transfused), too often that improvement was not accompanied by the desired clinical improvement as the sudden increase in the volume of the patient's circulating blood could induce heart-failure. The advent, therefore, of the crude but effective concentrate from fresh plasma in the form of cryoprecipitate (1965) was a God-send to the haemophilia A (F VIII

deficiency) community as sufficient clotting activity could be transfused to control bleeding episodes without stressing the haemophiliac's heart.

595. Some practical knowledge and experience of crudely fractionated products had been gained by UK researchers in the years after WW2 and was subsequently applied for NHS patients, although at first in very insufficient quantities. Nevertheless, these pioneering experiences were applied successfully to the clinical management of people with haemophilia A although the transfusate was prepared from pools of plasma collected from several donors: the adverse icterogenic effects of transfusing pooled plasma which had already been recognized could have been acknowledged better by those responsible for the care of haemophiliacs. Part of this tragedy is the time it took to recognize the long-term effects of these adverse experiences; but by their nature it takes a long time to observe and interpret the significance of long-term effects. Nevertheless, the pathologists, microbiologists and epidemiologists who untangled the icterogenicity of transfused blood are among those to be commended.

596. People with haemophilia B (the form of haemophilia which had affected European Royalty) should not be forgotten, for even though the challenges they presented were different (far fewer people are born with deficiency of F IX than of F VIII, and F IX is more stable and easier to handle), their suffering prior to the availability and provision of specific factor concentrate was just as pronounced. Although F IX fractions from pooled normal plasma may be associated with fewer TTIs – the process can separate, at least partially, the F IX-rich end-product from infectious viruses – the issues of TTI remain and people with F IX deficiency merit just as close attention as those with F VIII deficiency.

597. Although beset by profound funding problems, those responsible for managing what funds were available – in many cases led by the Medical Research Council – deserve to be commended for their contribution to the advances in the physiological, biochemical and genetic understanding of

all aspects of transfusion including the development and provision of materials, technical equipment and reagents for providing therapeutic blood products, and for their organisational planning, operational and training skills: these saved many lives.

598. The 'World in Action' TV programme "Blood Money" was broadcast in December 1975. It began by showing the beneficial impact of infusing people (boys and men) with commercial (predominantly American-sourced) F VIII concentrate and how it improved their lives and that of their families. I have no doubt that this broadcast, although open to (unjustified) accusations of sensationalism and journalistic self-interest, should also be regarded as a beneficial landmark. Prior to 1973 people with haemophilia and their families led frustrating and shortened lives, and their occupational opportunities were limited. After 1973, when commercial American concentrates were licensed for use in the UK, their lives could be transformed. The relief experienced by haemophiliacs – and their mothers – was often very profound and demand for concentrates inevitably increased and continued after the broadcast.

599. The spectre of transfusion-transmitted infections (TTI) 'lurking' in the shadows was largely cast aside by the licensers, medical professionals and affected families who – in effect – acted together to balance the justification in favour of using clinically effective concentrates against the known but still (in spite of "Blood Money") under-appreciated risks of TTI. (I include myself among those who 'acted together' in this way.)

600. In July 1975 (six months before the broadcast) Dr (now Lord) David Owen, then Minister of State at the DHSS, announced that £500,000 would be awarded to help the NHS to achieve self-sufficiency in home-produced F VIII (by mid-1977) through expanding the collection of blood plasma and building new facilities. This was a well-intended decision which is still a landmark in the wider 'politics' behind the aim to achieve a 'safe' blood

supply for the UK. Lord Owen specifically emphasised the virtue of using UK volunteer donors.

601. I must also commend my teachers, mentors and colleagues from whom I learnt so much. They are too many to name and many have passed on, but special mention must be given to Professors Ilsley Ingram (whose undergraduate lectures were unforgettable), Roger Hardisty, Richard Huntsman, George Jenkins, Adam Turnbull, Alastair Bellingham, Arthur Bloom, John Cash and Ian Franklin, and also Dr Harold Gunson. I learnt my technical skills, such as they were, from Dennis Canning, Susan Greene, Jane Mears and Margaret Kenwright, whose professional skills I admire and to whom I am indebted.

602. I also learnt much from the haemophilia community, among whom are the late Mr. John Prothero (who I first met when he was a schoolboy and I a student at St Thomas' Hospital) and the Revd. Alan Tanner from the early days of the Haemophilia Society, and also Mr. Julian Lander who led the Society's Liverpool branch in the 1970s and became a member of the Society's Executive Committee until 1995.

240. Further Specific issues

a) The case for self-sufficiency (Q32 et sec in the List of Issues; Section 8 of the written Statement under Rule 9)

603. Unfortunately, UK 'Self-Sufficiency' for human-blood derived clotting factor VIII was never going to be realised. The main reason which has emerged is that the sheer quantity of qualitatively administrable blood-derived F VIII to meet the demand proved unachievable – see the calculations below. This is complicated by the fact that Factor VIII is an unstable protein and does not store well. When therapeutic-grade UK F VIII became available, there was never going to be enough material to satisfy every UK resident with severe haemophilia.

Calculations – demand

604. One millilitre (ml) of normal fresh plasma contains 1 international unit (iu) of activity. After leaving it in sterile conditions at room temperature for 12 hours, much of the activity is lost and irrecoverable.

605. An adult man has about 3,000 iu F VIII circulating in his blood. An adult haemophilic with no F VIII would need approximately 1000 iu to achieve a brief peak of, at best, about 30% of normal F VIII activity which nevertheless would very significantly help his blood to clot. Unfortunately, this activity would decline to less than 10% by the following day. To maintain a degree of activity which allows a 'normal' social lifestyle, he would need 'prophylactic' infusions at least three times a week.

606. This rate gives a total of about 150,000 iu each year per haemophilic. In 1975 there were about 3,000 severe haemophiliacs in the UK, although many were young boys with lower blood volumes and therefore better responses to doses of 1,000 iu F VIII. Nevertheless, recurrent bleeds into their skeletal joints and other tissues caused by their haemophilia could require higher relative doses to maintain effective prophylaxis. Under a (somewhat artificially modelled) 'steady' demand, the precise degree of which is difficult to guesstimate, this annual requirement for all UK haemophiliacs could add up to a mean of approximately 450,000,000 ranging between 300,000,000 and 600,000,000 iu F VIII.

607. On top of this, up to 10% – possibly 30% – of the treated haemophiliacs would develop inhibitors. The treatment options would include daily massive doses of fractionated F VIII to 'swamp' the patients' immune systems and produce immune tolerance so that more standard treatments might be reinstated. This strategy would increase the demand on F VIII supplies very significantly, possibly by an extra 30,000,000 iu each year.

608. Then there are the remaining 3,000 or so moderately or mildly affected haemophiliacs. The concept of 'mild' in this context is misleading, as when such people suffer traumatic haemorrhage, their blood losses can be life-threatening, but they respond well to standard treatment with F VIII concentrates. Hence another 30,000,000 iu or so of F VIII might be needed annually: although DDAVP therapy would probably alleviate the need in many of these patients, bleeding from severe trauma or major surgery (unplanned or planned) could only be met by F VIII concentrates.

Calculations – supply

609. The theoretical maximum F VIII yield from one 'SAGM' donation of blood (300ml) is about 300 iu. Hence, at least 1,000,000 donations would be needed: but as the final yield of fractionated heat-treated F VIII from fresh plasma averages no more than 25%, at least 4,000,000 donations of fresh plasma would be needed, if not more, which at best could just about supply the 300,000,000 iu needed. The UK BTSs received less than 2,000,000 blood donations each year, and a considerable portion of separated donor plasma was required for other clinical purposes, leaving a large annual shortfall of more than 200,000,000 iu which could not practically be filled by dedicated plasmapheresis donors without vastly more expense in equipment, staff and donor recruitment.

610. In Italy in 2011, the total demand for and supply of F VIII was nearly 400,000,000 iu, 76% of which was recombinant – Calizzani et al 2013. Blood Transfusion. 2013 Sep; 11 (Suppl 4): s64–s76. doi: 10.2450/2013.011s, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3853991/ (In 2011 the population of Italy was 59.62 million and that of the UK 63.02 million.)

611. These necessarily very approximate calculations indicate the order of magnitude of the challenge. It might have been difficult to make a

calculation of this sort when Dr Owen was advised in 1975, as the 'vision' of a full prophylactic supply now available was held by very few (and eccentric) people at that time. The inhibitor challenge was recognized, as was the impact of bleeds among mildly affected haemophiliacs, but the magnitude of the required responses not fully appreciated except by some German practitioners who were advocating very high doses for those with inhibitors. My own recollection of Dr Owen's announcement was that £500,000 would make a helpful but minor contribution to self- sufficiency (even though at today's prices this would equate to more like £10,000,000). Nevertheless, as the UK NHS plasma fractionation industry was poorly developed by 1975, this would at least have been a good start, and Lord Owen is to be commended for the attempt.

612. My calculations above would have astonished John Cash, who – as an advocate of Scottish self-sufficiency – felt that with enough support the Scottish PFC could supply all the FVIII needs for Scotland. Although this advocacy was very successful in ensuring a good quantity of F VIII, in practice it still left the Scottish haemophiliacs leading a more restricted life-style compared with that which they might have felt 'entitled' to, although their health prospects were – I believe – considerably enhanced. The Scottish consumption of F VIII peaked in 1988 at about 13,300,000 iu of which about 93% was from the PFC (Penrose Inquiry, chapter 21, PRSE0007002 from page 805,). In 1988 the Scottish population (5.44 million) was just less than one-tenth of that of the UK (56.68 million) so, adjusting for the population changes by 2011, the Scots could have expected in the order of at least 30,000,000 iu to achieve self-sufficiency, more than 2.5 times that supplied by PFC in 1988. (I never discussed these issues with John Cash in detail, accepting that his ambition at the time was meritorious and deserved support.)

613. One more point on self-sufficiency: clinical services depend on reliable laboratory support and research. Although UK laboratory scientists were

and remain among the world leaders and often led fundamental break-throughs such as the nature of blood groups, monoclonal antibodies and transfusion microbiology, and developing reagents and diagnostic techniques such as radio-assays and immune-assays, their work is international and collaborative as are the diagnostic techniques. Scaling up needs industrial-sized support. Blood Transfusion is a global activity, reliant on R & D and commercial pharmaceutical support from all over the world. Stringent attempts to apply self-sufficiency would be detrimental to any national blood transfusion service although good services would be sensitive to local sociology and demography and adjust to changing circumstances such as immigration and pandemics.

a. ***The changing attitudes and life-styles of people with haemophilia in the latter half of the 20th Century.***

614. The arrival of effective therapy in the form of factor concentrates had an electrifying effect on people with either form of haemophilia. Up to about 1970, men with severe haemophilia had usually grown up in life-restricting circumstances: timidity and anxiety had surrounded their childhood and career opportunities were restricted particularly for those from a more deprived background: for them, manual labour and direct military service were out of the question. Those whose lives had been saved by transfusion frequently expressed fulsome gratitude to their medical teams, regarding them with respect and admiration, as did the Haemophilia Society the establishment of which was supported by the medical community. Attitudes towards the provision of clinical care changed after 1970: the availability of 'curative' treatment understandably raised expectations and as they reached their teens boys entering the 'growth spurt' and adolescence became more demanding, sometimes beyond what was realistically achievable in the eyes of their care-providers. A partial answer was the development of 'home therapy' by which acute bleeding episodes could be controlled by the swift and timely intravenous

administration (by self or by parent – usually mother) of factor concentrate. It was in this context that the Lord Mayor Treloar School at Alton (which is within the WRTC region) began to accept boys with haemophilia and under the guidance of their medical director, Dr Aronstam, promoted the concept of prophylaxis – preventing bleeding episodes by frequent (thrice-weekly) iv infusions of F VIII / F IX. For F VIII this was initially as cryoprecipitate which was replaced by NHS and commercial concentrates as they became available.

615. But the small quantities of NHS-made concentrates available could not suffice – hence the licensing of commercial concentrates of F VIII and F IX in the early 1970s opened the 'taps' generally to meet the demand from the haemophilia centres promoting local home therapy programmes (which included Liverpool) and the Treloar School boarders, the effect of which was to increase the demand in Wessex in proportion to the amount of plasma collected from the local population.

616. The inevitable and predictable consequence was a rise in transfusion transmitted hepatitis nationally even though the virus responsible for the apparently dominant form of 'serum hepatitis' had been identified, thereby allowing donor-screening; but such 'safety measures' were woefully inadequate for protecting recipients of products made from plasma pooled to the degree operated by the manufacturers and carrying other as-yet unrecognized infections.

617. Lord Owen's well-meaning announcement in 1975 could not protect the haemophilic community to the degree desired. So, in spite of "Blood Money", the balance of opinion among patients and care-providers swung in favour of expanding home therapy programmes. The arrival of HIV/AIDS in the early 1980s led within a few years to the provision of 'heat treated' or 'pasteurised' concentrates later versions of which also neutralised hepatitis viruses; but by then the tragedy had unfolded, justifying the

demands for 'better care' and consideration from and for the haemophilia community.

618. I note that in 1983 the Haemophilia Society had sought advice from Prof Bloom about the possible impact of AIDS; I assume that this correspondence (DHSC0001228) will be of considerable interest to the Inquiry. The only point I would make here is that Alan Tanner accepted Prof Bloom's remark that 'we are no strangers to infectious diseases, such as hepatitis, which can be transmitted by factor concentrates', and that British concentrates are no safer than those from the United States. From this it can be suggested that the Haemophilia Society should have been aware before the onset of AIDS that UK blood products carried a hepatitis risk.

b. Informed consent.

619. The concept of informed, documented and signed consent – which is now a 'no-brainer' – was not well established when I took my first consultant post at Liverpool. Its elements were there – founded on trust by patients in the professional code for registered medical practitioners and, for those patients who took an interest, the (false) impression that on graduating all medical doctors took the 'Hippocratic Oath'. However, this historic Oath was based on the concept of medical benevolence accompanied by secrecy (the doctor knows more than the patient) for which reason several medical schools, including my own, abandoned oath-taking from the graduation ceremonials: today such oath-taking would seem anachronistic.

620. The way this worked up to the 1970's was that patients consulting medical practitioners were assumed by those practitioners to follow the advice given and undertake whatever course of treatment was prescribed (often written illegibly on official-looking printed paper – itself a source of mystic professionalism). By collecting medicines from dispensing High Street

chemists, the patient's consent was tacitly assumed. Similarly, consent was tacitly assumed from hospital in-patients about to undergo medical interventions including surgery. As all such interventions were assumed to be documented in the patients' record notes which were then archived, these forms of documentation were generally deemed to be adequate: specifically designed consent forms were thought not to be necessary. This was a form of 'doctor-centric' practice.

621. 'Patient-centric' practices began to emerge before 1980 and became more developed thereafter: in its best form, this may be summarised as holding 'pre-intervention discussions' with patients and the use of medical consent forms. Paper forms can be unreliable, and are being replaced by 'digital consent', the most advanced forms of which involve 'dynamic consent'. These facilities were unavailable for most of the time covered by the Inquiry, but the general lack of specifically documented patient involvement has proved an embarrassment – and worse.

622. Many haemophiliacs whose treatment with factor concentrates began when they were infants and who grew up with frequent IV injections as a 'way of life' do not recall when or even if their personal consent was ever sought. This should not be too surprising given the parental (and indeed genetic) role in planning the management of haemophilic infant boys, but nevertheless is regrettable.

623. However, I know how difficult it can be to explain the pathophysiology of the haemophiliac patient's condition to lay people – let alone the mother of a first born boy found to have haemophilia: but on reflection, this should not surprise us. Nevertheless, it should have been axiomatic that at whatever age a patient gains the capacity to understand 'cause and effect', their active consent be sought involving the parents when appropriate. This patient-centric consent should be reliably documented and is important for the protection of the health-care professional and the patient alike.

624. The frequent absence of any such document in the records of many haemophiliacs treated in this era – especially the early days – is a matter for regret. One of the reasons why I supported the establishment of a local group of the Haemophilia Society in Liverpool in about 1977 was to inform patients and their parents about the developments in haemophilia care. Although this was focused mainly on the (successful) expansion of the home-care programme by the time I left in January 1980, I did comment to members at meetings on the association with infectious jaundice. These comments would probably have understated the association with jaundice which – in common with many other HC Directors – I felt was usually followed, when clinical signs developed, by eventual remission and rarely by long-term complications. Professor Preston's findings in the late 1970's should have alerted us more strongly; but by then the expanding home therapy programmes being developed nation-wide took priority until the onset of the much more dramatic AIDS epidemic in the early 1980s.

d. Compensating the loss of established donors during prolonged supply shortages (Issues 60, 71; and section 4 and Q232 b of the written Statement under Rule 9)

625. Stanworth et al (2020 - DOI: https://doi.org/10.1016/S2352-3026(20)30186-1) addressed the problems of blood supplies in England quite early in the Covid-19 pandemic, as did Choudhury et al (2020 doi: 10.1111/voxs.12578) for the Asian Association of Transfusion Medicine.

626. My response to Q232 (doc NHBT0042193_007 'Possible Impact on the UK Blood Supply of Testing for v CJD') may be relevant as it refers to ways of compensating for lost donors by modifying certain selection criteria. On reflection the suggestion that donation input could increase by 500,000 a year seems optimistic and would depend on the way the

resources were deployed. Furthermore, many selection criteria have changed since 2002, so many of the various strategies suggested in NHBT0042193_007 may no longer be applicable.

627. I am aware, for example, that NHSBT have introduced a JPAC and government-approved "Assessment of Individualised Risk (FAIR)" scheme which emphasises a more individualised selection interview process designed to accommodate sexual lifestyles more liberally without prejudice to recipient safety. Thus, the selection criteria operating during my time regarding men who have sex with men has been completely revised without apparent detriment to blood safety. No doubt there will be further developments along such lines.

628. Criteria relating less directly to TTIs are nevertheless worth further consideration. This includes the inter-donation-interval and the threshold for Hb concentration in pre-donation blood and monitoring for donation-induced iron deficiency, which was an interest of mine before I retired. A more individualised approach may well be beneficial here too including medications, body weight, gender, recent donation history, past history of malignant disorders from which the donor has completely recovered, travel overseas, etc,.

e. The future (361 and 362 of the Issues)

629. The latter part of the List of Issues focusses on various schemes for improving the microbiological safety of transfused blood and blood products, ending with 'the future'. Although the Issues numbering 361 and 362 do not directly address the immediately preceding issues (schemes) identified, this seems an appropriate place to comment more generally on the future of the National Blood Transfusion Services.

630. The BSE/vCJD episode had a profound effect on the UK BTSs, so that in effect the only 'home-grown' products acceptable for treating patients were

red cell concentrates and platelets: immunoglobulins – including anti-D for the prevention of alloimmune haemolytic disease of UK newborns due to anti-D in maternal blood – are no longer prepared from UK donations. Universal leucodepletion, introduced to reduce the risk of TT prion-disease, had the secondary beneficial effect of almost eliminating leucocyte alloimmunization and the transmission of leucocyte-carried infectious microorganisms such as herpes viruses (CMV) and certain bacteria (Yersinia, etc.). Red cells suspended in crystalline solutions with small amounts of donor plasma and no working white cells or platelets have proved acceptable for UK patients although reinforcement with UK platelets and foreign-sourced clotting factors has occasionally been necessary*.

631. The year 2014 marked the 18th anniversary of the withdrawal of UK blood for overseas use (and of the acceptance by many overseas administrations of blood donation by visiting UK nationals). The documented UK cases of TT vCJD up to now is less than a handful. As dietary measures for UK residents excluded contamination from beef offal etc., in 1996, consideration could be given to donations from donors born since 1996 who are aged at least 17 years to using their plasma and plasma products for NHS patients such as FFP and specific immunoglobulins like anti-D for transfusion. Investigating if blood from such donors is more risky for transmitting vCJD than donations which preceded the BSE/vCJD crisis (from before 1980 or so) could be considered, especially as more specific tests for vCJD have been developed.*

632. Although the topics of 'artificial blood' and 'chemical oxygen carriers' have surfaced from time to time, and recombinant technology will make redundant the transfusion of many blood-derived plasma proteins such as albumin, immunoglobulins, haemostasis-related factors (f VIII, f IX, vWF, fibrinogen, fibronectin, antithrombin, plasminogen etc.,) red cells and

platelets will not become redundant in the foreseeable future so blood donors will continue to be needed in the UK, and donor selection criteria and TTI screening must conform to internationally agreed standards based on rigorous evidence.

633. * These statements should be confirmed with the latest UK recommendations from JPAC etc.

f. Concluding remark

634. The Inquiry's final report and conclusions should provide an ideal opportunity to improve public awareness and especially of the health-care providing communities – students and fully accredited professionals alike – concerning the relationships between professionals and patients. The subject of the report and its conclusions should be included in the curricula of all medical schools and allied educational institutions, and adopted by all the General Councils of the Health Professions, including and especially the General Medical Council.

635. Wherever possible, patient care should be individualized along principles very similar to those conceived by the NHSBT 'FAIR' programme for donors. I once had the privilege of advising Frances Delaney, the representative of the EU commission for Health and Consumer Protection, that 'everyone has the right to be considered for donating their blood, but not an automatic right to actually donate. If they are deferred or rejected from donation, they have a full right to a clear and true explanation for their rejection. They can disagree with those reasons but do not have the right to insist that a donation be collected from them.' Similarly, patients have the right to a clear and true explanation of any treatment planned for them as part of the process of consent.

Statement of Truth

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

GRO-C

Signed _____

Dated 26th October 2021

Table of exhibits:

Date	Notes/ Description	Exhibit number
2006	Analysis of complaints to the UK blood services on the policy barring homosexual men from donating blood to the ISBT	WITN3456003
2007	"Guidelines for policies on alternatives to allogeneic blood transfusion. 1. Predeposit autologous blood donation and transfusion" (British Journal of Haematology 2007)	WITN3456004
2005	Redacted complaint	WITN3456005
2003	F Boulton (2003). The Impact of variant CJD on transfusion practices in the UK: Transfusion and Apheresis Science, 28,	WITN3456006

	107-116	