SUBMISSIONS

ON

CONCLUSIONS

on behalf of

NATIONAL SERVICES SCOTLAND

THE SCOTTISH NATIONAL BLOOD

TRANSFUSION SERVICE

in the matter of

THE UK INFECTED BLOOD

INQUIRY

Part 1: Apology and acknowledgement of impact on infected and affected people

1. At the outset National Services Scotland Scottish National Blood Transfusion Service (SNBTS) would like to express our sympathy, sadness and sorrow for the devastating impact transfusion transmitted infections have had on the lives of patients, and on those of their families and friends. There are times where on reflection we feel that the organisation could and should have done better in the past. We are sorry for that and have addressed these specifically in our submissions below.

Part 2: Statement of approach

2. SNBTS has approached these submissions with the following considerations in mind:

3. We have focussed on those issues which have been highlighted by the Inquiry or by representatives of the infected and affected core participants as being of specific importance and which are germane to SNBTS's remit, responsibilities and actions. We do not think it appropriate to comment on the responsibilities and actions of other organisations except where they have or had an impact on SNBTS's responsibilities or actions.

4. As directed by the Chair of the Inquiry we have not attempted to rehearse all the relevant evidence in these submissions, but to articulate the position of the current senior management of SNBTS reflecting on the chronology of events and evidence that has been brought before the Inquiry. We have cross-referenced documents where we feel this would assist the reader who may wish to review specific evidence for themselves. SNBTS does not have the resources to review the extensive amount of evidence laid before the Inquiry itself and this process is therefore necessarily selective. We apologise in advance if we have omitted relevant evidence either in support or against a position we have advanced and would welcome this being drawn to our attention.

5. We respectfully remind the reader that no members of the current senior management of SNBTS were part of the organisation during the earlier periods under consideration by the Inquiry and therefore with respect to factual accuracy of historical events we are as reliant as other Core Participants on the evidence brought before the Inquiry, the personal statements and testimony of former colleagues and the detailed chronology of events in Scotland presented by the Penrose Inquiry (INQY0000102).

6. The positions we articulate in these submissions reflect the perspective of the current senior management of SNBTS after review of the evidence available to us and our understanding of contemporaneous and current practice. We have offered specific apologies on behalf of the organisation where, in our view and with the benefit of reflection, we feel the organisation could or should have done better. These are not intended to supplant the opinions of past colleagues who may, or may not, agree with our opinion.

7. There have been substantial changes in science, technology and medicine over the more than 50 years under consideration by the Inquiry. Where we make suggestions as to recommendations they relate to current practice and our core responsibilities to ensure and enhance the sufficiency, quality and safety of blood components and other substances of human origin used in the treatment of patients in Scotland at the present time.

8. We recognise that some positions may be contested by other core participants and/or that the Inquiry may take a different view and will give any such responses very close consideration

Part 3: Contextual Remarks

9. We are mindful that the primary focus of the Inquiry has been on events which occurred in the past and would ask the Chair of the Inquiry to take cognisance of current information when considering those of his recommendations which may pertain to current practice. Whilst the fundamental challenges in managing a Blood Service in respect of ensuring the sufficiency, quality and safety of blood components and other substances of human origin (tissues, cells and organs) persist over the long term, science and technology, clinical and operational practice, quality management and the regulatory environment have evolved significantly over the past 50 years and continue to do so.

10. SNBTS is responsible for the procurement, testing, manufacturing and supply of a range of substances of human origin (including blood components, tissues, cells and starting materials for advanced therapies manufacture) for patients in Scotland. The historical and current structure, management and governance of the organisation is described in Section 1 of our first Witness Statement (WITN3530007). We currently provide around 179,000 products to approximately 32,000 patients each year. Some of these are lifesaving, some life enhancing and some enabling of other clinical interventions.

11. With regard to blood components, SNBTS has a clinical and ethical duty of care to meet demand for blood components at all times across Scotland – a demand over which SNBTS does not have control (because the decision to transfuse blood is taken by clinicians within territorial health boards) and which can be unpredictable and volatile due to changes in clinical practice (as seen over the past few years during the SARS-CoV-2 pandemic) and in response to major incidents with mass casualties. One of the key SNBTS responsibilities is therefore to maintain sufficiency of blood, tissue and cell stocks to ensure support of ongoing patient care and to provide contingency in the eventuality of untoward events.

12. Similarly, SNBTS is not wholly in control of the supply of blood and other substances of human origin as they are provided through the altruism of voluntary non-remunerated donors, at a degree of inconvenience and a small risk to themselves. We discuss the importance of self-sufficiency below (Part 4), but here would like to record our gratitude and duty of care to the 100,000 or so donors who supply the starting material for these products and without whom our Service would not be possible (Part 5).

13. We believe that it is important to understand the separation of functions and responsibilities between SNBTS and other UK Blood Services, independent Advisory Committees, Regulatory Authorities, UK and Scottish Governments and the broader healthcare system including public health authorities, primary and secondary healthcare and individual clinicians. Some of these structural issues are reviewed in Sections 3 and 5 of our first Witness Statement (WITN3530007).

14. SNBTS works closely with the other UK Blood Services through the UK Forum which comprises of the Chief Executives / Directors and Medical Directors with other professionals invited as required. The Forum itself meets four times a year to discuss matters of collective importance and share experience.

15. A number of professional groups are funded by and accountable to UK Forum including:

    - UK Blood Services Joint Professional Advisory Committee (JPAC) and its Specialist Advisory Committees: the expert professional advisory committees which are responsible for publishing detailed guidelines for the UK Blood Services (the Red Book).
    - Serious Hazards of Transfusion (SHOT): the UK haemovigilance scheme that allows oversight of reported adverse events linked to blood transfusion.

- Systematic Reviews Initiative (SRI): a clinical research group set up to develop the evidence base for the practice of transfusion medicine through systematic reviews and other evidence-based medicine research projects.

16. Together these formal channels of collaboration alongside many informal collaborations allow the UK Blood Services to ensure consistency of approach and shared learning with respect to the quality and safety of blood, tissues and cells.

17. UK Forum will work together on recommendations made by the Inquiry.

18. All medical treatments involve a balance of benefit and risk whether they be surgical intervention, medicinal products or vaccines. In respect of blood components and other substances of human origin some risks are intrinsic to the human condition and therefore can be mitigated but not avoided altogether. These include the potential for transmission of microbial agents associated with the human body, neoplastic (cancerous) cells, drugs or toxins and genetic or immunological incompatibility.

19. These risks can be mitigated to a significant extent, though not completely eliminated, through donor selection (see Part 5.5) and screening (Part 6).

20. The current residual risk of missing an infection with current donor selection and screening procedures in the UK is low as evidenced by the UK Serious Hazards of Transfusion (SHOT) haemovigilance system (https://www.shotuk.org) and discussed by Professor Mark Bellamy in his Witness Statement (WITN7312001). However, the risk of transmission of infection by substances of human origin cannot be completely eliminated because of limitations to the sensitivity of assays, the emergence of new infections and the continuing genetic evolution of established infectious agents - as we have seen with the emergence of SARS-CoV-2 and its variants over the past 2 years. Moreover, the risk of transfusion or transplantation transmission of infection is contingent on the prevalence and distribution of infection in the general population (such as, for example, the transmission of Hepatitis C through intravenous drug use (IVDU) and the food-borne transmission of Bovine Spongiform Encephalopathy and Hepatitis E).

21. Further, there is a material difference between managing a known risk and managing a potential risk from a new or emergent infection which may or may not pose a risk to the blood supply. In the face of uncertainty, the choice lies between waiting until the evidence base develops to inform the correct action and risk avoidable infections and acting on a precautionary basis and risk having acted unnecessarily or taken inappropriate action.

22. A proactive approach to horizon scanning, research and development is a critical part of reducing uncertainty around whether a new or emergent risk will impact upon the safety of blood and in developing solutions to mitigate that risk in a timely manner. In scientific research the outcome or solution, by definition, is unknown and a variety of approaches often need to be explored, usually in collaboration with other groups, before a preferred approach emerges (Section 10 of our first Witness Statement (WITN3530007).

23. A key issue is the question of what is the level of risk that is acceptable in the context of blood safety and how the precautionary principle should be deployed when the nature or level of that risk is uncertain. Blood Services, as part of the wider healthcare system, are financially and operationally constrained, never more so than in the current and forthcoming public sector funding environment. Commitments of resources to research and development or implementation of precautionary measures are vital but do elicit opportunity costs in respect of other benefits forgone either within the Blood Services themselves, or the wider healthcare system. On a societal level there is therefore a balance to be struck between the imperative to protect the sufficiency, quality and safety of the blood supply and the broader ethical problem of equity of access to resources and care.

24. Internationally, risk-based decision making in the field of transfusion medicine was formally inaugurated in 2011 at an international consensus conference on "Risk-Based Decision Making for Blood Safety" (RLIT0001876). The effective framework for risk-based decision making in transfusion medicine aims to include scientific, medical, ethical, legal, regulatory, economic, patient and public policy perspectives, as well as societal values and historic context and has been adopted by the Alliance of Blood Operators (Alliance of Blood Operators).

25. ***SNBTS recommendation:*** in our June submission (SUBS0000009) to the Inquiry, we invited the Chair to consider the nature and appropriate level of tolerability of risk in regard to transfusion / transplantation transmitted infection, the extent to which conventional cost effectiveness calculations should be applied in the field of transfusion / transplantation safety and the broader societal responsibility to mitigate the prevalence of serious infections in the general population which then impact on transfusion safety.

26. ***SNBTS position:*** we believe that a risk-based decision making framework is an appropriate methodology for balancing the multiple factors inherent in complex decisions around blood safety and should continue to be embedded in the decisions of UK Blood Services, Advisory Committees, Regulators and Governments.

Part 4: Self-Sufficiency in blood components

27. SNBTS regards voluntary non-remunerated donation as a fundamental ethical principle on which our Service is based. We also consider that there is a clinical and ethical imperative to maintain sufficient blood component stocks to meet elective and emergency demand for all blood components and compatible blood groups throughout the whole of Scotland at all times. A person involved in a road traffic accident in Shetland requires the same availability of life saving blood components as they would in central Edinburgh.

28. The complexity and challenges in maintaining the sufficiency of the historic and modern blood supply is discussed in Section 8 of our first Witness Statement (WITN3530007).

29. Around 90% of blood is donated by regular donors who provide the core of planned sessions and, as discussed below, provide a structured way of adjusting supply to balance variation in demand for different blood group and component stocks. Regular donors have, by definition, been selected and screened before and therefore have lower rates of deferral and test reactivity.

30. Scotland has been and is self-sufficient in the provision of blood components. There are caveats to this statement. We do from time to time receive red cell concentrates from donors with rare blood groups or rare HLA/HNA matched platelets for specific patients from other UK Blood Services if we don't have a suitably matched donor ourselves. Similarly, all four UK Blood Services provide mutual aid to each other in times of shortage based on the principle of equity of access of patients in the UK to blood and tissues.

31. Since our first Witness Statement was written, sufficiency of the blood supply has become very challenging as a result of the SARS-CoV-2 pandemic and its aftermath. This is partly due to changes in blood donation (Part 5) including reduction in donor numbers, the requirement for infection control measures at donor sessions and the incidence of SARS-CoV-2 infection amongst donors and staff, and partly due to an increase and volatility in demand for blood components after many years of sequential reduction (Part 9) – probably due to patients having to wait longer for treatment and more serious illnesses being prioritised. The risk of blood component shortages is currently a major concern to UK and international Blood Services and will require further changes to our blood donor engagement and donation, integrated supply chain and demand management models.

32. It is important to appreciate that for other substances of human origin such as tissues, cells and organs, the concept of self-sufficiency is partially realised on a UK-wide basis and specific products are frequently supplied across the home nation boundaries.

33. The issues relating to self-sufficiency in plasma products are discussed in Part 8.

Part 5: Donation

34. The supply of blood components, tissues, cells and organs in Scotland and the wider UK is wholly dependent on the altruism of voluntary non-remunerated donors as articulated by Richard Titmuss in 'The Gift Relationship' (HSOC0019917) and the World Health Organisation in its unanimous declaration of commitment and support for voluntary blood donation in May 2005 (Towards 100% voluntary blood donation: a global framework for action (who.int)). SNBTS regards this as a fundamental ethical principle underpinning its Service and has never paid donors. We recognise our duty of care to the 100,000 or so people in Scotland who regularly donate with a degree of inconvenience, some discomfort and a small risk to themselves, in order to support the lives of others.

5.1 Donor Engagement.

35. Thompson's Solicitors have highlighted in their submission to the Inquiry the importance of measures which seek to improve donor engagement and investment in the system in which they play such an important part (SUBS0000011; paragraph 15) - a suggestion with which SNBTS agrees.

36. The ways in which SNBTS engages with its regular donors (who provide 90% of the blood in Scotland) and with the wider public has evolved very significantly over the past 50 years due to the emergence of the internet, social media and mobile telephony platforms.

37. SNBTS uses its Scotblood website as a primary platform for general communication with donors and the general public (Scotblood | Homepage).

38. General information contained on the website includes campaign information for donor recruitment and retention and information on how to become a platelet or plasma donor. Information on Tissues & Cells donation (musculoskeletal, cardiovascular and ophthalmic tissues, pancreatic islet cells and haematopoietic stem cells) is also signposted. SNBTS supports other partners, such as the other UK Blood Services, the

Anthony Nolan Trust and DKMS on the "Our Partners" section of the site, and directs interested people to their web pages.

39. The Scotblood website also allows potential donors to complete a preliminary quiz to self-determine whether they are eligible to give blood, to register as a donor, to search for their nearest fixed site or community donation session and to make an appointment to donate. Information on Scotland's blood stock levels is updated and published daily (Monday – Friday) and empowers donors to manage their own attendance, donating blood when stocks of their blood group are low or taking a break when stocks are at higher levels.

40. We also make extensive use of social media platforms as below:

Channel	Link to Site	Followers
Facebook	Facebook.com/Scottish National Blood Transfusion Service	79,993
Twitter	Twitter.com @givebloodscot	11,700
Instagram	Instagram.com/givebloodscotland	519 (launched in June 2022)
YouTube	Scottish National Blood Transfusion Service - YouTube	160 subscribers
TikTok		launched in Autumn 2022

Table 1: SNBTS social media platforms

41. Donors like to be able to see the difference their blood donations make to patients and in view of this we share patient stories through our social media platforms and the general media as often as possible and receive support from patients in this area. We have specific campaigns that demonstrate the end-to-end process from donor to patient (The Gift - YouTube) and when required conduct specific campaigns to encourage new donors to come forward. These are particularly important given the challenges Blood Services are facing in maintaining blood stocks following the SARS-CoV-2 pandemic, in recognising the increasing diversity of the blood donor base in Scotland and the need to communicate more effectively using new technologies with the younger generations of people required to support the blood donation system in the future.

42. Our current marketing strategy, "People Like You", was launched in June 2022. This strategy was developed following both quantitative and qualitative research with the

target audience – over 1,000 members of the Scottish public. Emerging themes were altruism and communitarianism and with this understanding SNBTS is trying to broaden the perceptions of who can donate blood. This is particularly important as we aim to increase diversity and reduce discrimination in the donor base, with increased youth, LGBTQ+ and ethnic minority representation (see paragraph 51).

43. Our flagship TV advertisement can be seen here: People like you: Street (Full length) - YouTube. This and the subsequent follow up advertisement are currently being aired on terrestrial television, video on demand, paid advertisements on YouTube and other social media.

44. In 2015, Scotland developed the "Right Donor Right Time" strategy with the objective of optimising the supply chain for each of the different blood groups and components and helping donors understand that specific donors may be needed to help specific patients. This means that donations from some blood donors are needed more often than others (for example if they are O negative red cell donors or platelet apheresis donors). We publish extensive information on the "Blood Types" section of the Scotblood website and this is the most visited page on the site after the home page. SNBTS also ensures that the donor blood group is highly visible on every invitation (home donor health check) sent to donors. We actively inform donors if stocks of their group are high, meaning that they are not needed to donate at that time and we contact donors and cancel their appointment if this is the case. Donors react well to this, and understand we are aiming to make the best use of every gift. This blood group awareness among the donor population, combined with intelligent inventory control and close monitoring of demand maximises the availability of components and minimises expiry rates (Part 9).

45. Specific calls to action and updates about blood group levels are also advertised on social media, and in times of need extended to other channels such as television and radio.

46. SNBTS continues to work on its engagement with its donors and the general population in Scotland to encourage people to donate blood, tissues and cells and to enhance understanding of sufficiency, quality and safety issues. This is particularly critical given the challenges to self-sufficiency currently being experienced by Blood Services worldwide in the aftermath of the SARS-CoV-2 pandemic and the subsequent cost of living crisis (Part 4). The nature of engagement will continue to evolve in response to broader changes in technology and society.

47. Specific initiatives planned over the next few years include:

- Refreshing the Scotblood website.
- Texting to donors to inform them which hospital their donation has been issued to. We are currently undertaking Omnibus research in partnership with YouGov and asking people if they would appreciate this.
- Continuing to encourage user generated content from both donors and patients about the importance of donating and receiving blood. SNBTS have recently launched an Instagram channel and TikTok channel to support this activity.
- Expanding the current "People Like You" advertising campaign to a patient focus "People Like you Saved People Like Me." We have plans in place to deliver this for Christmas 2022. This campaign will further enhance the critical relationship between donor and patient, and we are grateful to all patients who are supporting this activity.

48. ***SNBTS position:*** We will give further consideration to how we can utilise the Scotblood website and our social media platforms to provide general information and raise awareness amongst donors, patients and the public on the benefits and risks of both donation and receipt of blood components and other substances of human origin.

5.2 Donor Information and Consent.

49. All blood donors are provided with the SNBTS donor information leaflet and are required to provide written consent by signing the 'donor declaration' prior to donating. The historical development of Donor Information and Consent policy in SNBTS is described in Section 2 of our first witness statement (WITN3530007). A new donor information leaflet was published in April 2022 renamed 'Giving Blood: process, risk and information'. This leaflet is provided at donation sessions and is also available on the Scotblood website (Scotblood | Donor information leaflet) .

50. The leaflet includes information about the process of donating blood, the possible risks of blood donation (including what donors can do to reduce these risks), instruction that those with a blood borne virus or those who have taken part in a high risk activity must not donate, information about the testing that will be performed on the blood donor, what the donation may be used for, information on storage of donor information and signposting to the data protection notice, information on Duty of Candour legislation and consent and what the donor should do if they become unwell post donation. In addition, the donor receives a small post donation information card entitled 'After giving blood'

which provides the donor with a thank you message, information on post donation self-care and what to do if unwell.

5.3 Donor Adverse Events

51. Donors are given written information as they leave their donation session to contact SNBTS if they experience any adverse effects of donation or if any subsequent post-donation information which could impact upon the safety of their blood becomes available after the event. This service is available 24/7 through the Clinical Support Team and the on call SNBTS Medical team.

52. Donors who do experience adverse events are managed by the nursing staff at the donation session and are provided with additional verbal and/or written information. Donors with more significant adverse events are followed up after the donation session by the Clinical Support Team (nursing and medical staff) and Duty of Candour is applied where relevant. The clinical support team provides support and signposting of donors to the correct clinical service. There is ongoing follow up by SNBTS until the donors' symptoms resolve or up to 1 year.

53. SNBTS is required by the Blood Safety and Quality Regulations 2005 (as amended) to record all adverse events in blood donors. SNBTS records adverse events in blood donors using the International Haemovigilance Network/AABB (Association of Advancement of Blood and Biotherapies) definitions published December 11th, 2014 (Home - International Haemovigilance Network (ihn-org.com)). Numbers, categories, and trends in adverse events are monitored through SNBTS and NSS clinical governance systems.

54. SNBTS submits serious adverse events of donations data annually to the Serious Hazards of Transfusion haemovigilance system (SHOT) and this is included in the annual SHOT report. In the UK in 2021 the rate of serious adverse events of blood donation was 0.26 per 10,000 donations. Over the next few years, the UK Blood Services plan to implement the Haemovigilance Network/AABB severity grading tool for donor adverse events which considers the impact of any adverse event on activities of daily living.

5.4 Donor Records

55. Following discussion with the IBI legal team, we have interpreted record keeping arrangements to refer to how information on blood donors and their donations is stored and used in the management of the blood supply in Scotland. The historic and current

arrangements in this regard are detailed in Section 2 of our first Witness Statement (WITN3530007).

5.5 Donor Selection

56. Modern donor selection employs a complex set of criteria recommended on a UK-wide basis by the JPAC Specialist Advisory Committee on the Care and Selection of Donors through the Donor Selection Guidelines (Welcome to JPAC (transfusionguidelines.org)). These are designed both to protect the health of the donor and that of recipients and continuously evolve in response to changes in scientific and medical knowledge and recognition of new and emergent infectious diseases. As discussed below the latter have become more challenging as a result of global travel, trade and climate change (Part 6). It should be appreciated that higher and lower risk is a continuum associated with background and behaviours and categorical approaches to donor selection are therefore a relatively blunt donor risk reduction tool. With the introduction of the FAIR recommendations in June 2021 (fair_sabto_20201211.pdf (windows.net)), the UK Blood Services have started to move towards a more individualised risk-based approach to blood and tissue donor risk assessment whilst taking cognisance of evolving societal perspectives on acceptability and discrimination.

57. The history of Donor Selection in SNBTS from 1970 onwards is documented in Chapter 18 of the Penrose Inquiry Final Report. Four issues are of particular historical importance:

5.5.1 Intravenous drug use (IVDU)

58. It appears that during the 1970s and early 1980s, whilst a recent or current history or physical evidence of injecting drugs were grounds for exclusion, there was relatively little systematic face-to-face questioning of donors, though an association of IVDU with Hepatitis B (HBV) infection was recognised from at least the early 1970s.

59. In response to the emergence of the Acquired Immunodeficiency Syndrome (AIDS) in 1982 a leaflet 'AIDS and Blood Transfusion' was issued by the Edinburgh and SE Scotland Blood Transfusion Service in 1983 including IVDU amongst those people at risk of contracting AIDS and asking them to avoid donating blood.

60. Appendix Figure 4.1 of the Expert Report to IBI on Statistics (EXPG0000049) shows evidence of low levels of IVDU in Scotland in the 1970s but a very rapid rise through the 1980s.

61. ***SNBTS position**:* our view is that it would have been better to have excluded IVDUs earlier than we did through more systematic donor selection across all SNBTS regions given the evidence of increased prevalence of HBV in this population and we apologise for not doing so.

5.5.2 Donations in Institutions

62. The collection of blood in prisons was a common practice by both non-profit and commercial blood donation services for many years. In 1971 the World Health Organisation (WHO) 'guidelines on forming a suitable donor panel' suggested that prisons were one of the optimum places to collect blood (PRSE0002035.pdf). In the early 1970s UK Home Office policy supported collection within prisons as it was felt that encouraging prisoners to become donors would help with their rehabilitation, and that it would be socially and psychologically undesirable to exclude prisoners from the donor population (PRSE0004729.pdf). In 1975 the UK Department for Health and Social Security (DHSS) warned Regional Medical Officers that blood donations from prisoners might have a higher risk of containing hepatitis B, but stated that as long as donations were screened for HBV there was no reason to cease collecting from prisons (PRSE0000009.pdf).

63. During the late 1970s and early 1980s work was carried out at the Glasgow and West of Scotland Regional Transfusion Service on the development and use of various screening tests for hepatitis. In the course of these studies the levels of the various markers including liver enzymes were studied in the general population and in institutionalised donors. In 1972 significantly increased levels of HBV were found in prisoners compared to the general population (PRSE0004840.pdf). It appears that this high prevalence was ascribed to 'social habits and hygiene' at the time, though in retrospect it appears more likely that, particularly in the early 1980s, this was due to IVDU. Similarly increased levels of HBV as measured by Hepatitis B surface antigen (HBsAg) and the liver enzyme Alanine Transaminase (ALT) were found in prisoners in 1981 (PRSE0001035.pdf). Together with other data, these suggest that male prison donors were at higher risk of transmitting HBV compared to the general population.

64. SNBTS collected blood in prisons from 1957 until between December 1981 and March 1984 dependent on the Regional Blood Transfusion Service. Prison donor sessions were often arranged when the general supply of blood was low, for example during the Trades Holidays when most large employers used to close for two weeks with a consequent negative impact on workplace donor sessions. During the 1970s it is

estimated that prison donations represented around 2.4% of the total blood collected in Scotland falling to 0.11% in 1984 (PRSE0002164.pdf).

65. In 2004 the European Blood Alliance conducted a survey of member states with regard to their policies past and present on collecting donations from prisoners both during incarceration and after release. Of the 17 countries responding to the survey, 3 countries had never collected blood from prisoners, 3 countries introduced deferral of prisoners in the 1970s, while the majority stopped collecting from prisoners in the 1980s and 4 not until the 1990s (PRSE0002164.pdf). In the United States the Food and Drug Administration did not ban the collection of blood from prisoners until 1995. Similarly Chapter 26 of the Penrose Inquiry Final Report documents significant variation in international practice.

66. Between 1994 and 1996 a study was carried out of the prevalence of Hepatitis C (HCV) amongst prisoners in 5 Scottish prisons. The study found an overall prevalence of HCV of 20% amongst prisoners, of 49% amongst those reporting IVDU and 3% amongst those reporting no IVDU (PRSE0001200).

67. We are aware that concerns have also been raised around donation of blood in military institutions. The amount of blood collected from military institutions in Scotland was less than that in prisons (approximately 0.2% of donations) and we are not aware of evidence that military personnel based in Scotland were at higher risk of HBV, HIV or HCV infection than the general Scottish or UK donor population.

68. ***SNBTS position:*** we understand that there were various arguments for holding donation sessions in prisons in the past including genuine concerns around the sufficiency of the blood supply and a desire to encourage altruistic behaviour amongst prisoners. We consider that there was probably an over-reliance on HBsAg testing to provide safety in this context due to an under appreciation of the concept of the window period and of the risk of transmission and severity of non-A non B (NANB) hepatitis. Whilst there was a range of international practice and the practice in SNBTS was not dissimilar in this regard to that in other Blood Services, the view of the current SNBTS senior management is that it would have been better to have demitted from prison donations much earlier, arguably in the first half of the 1970s when evidence of high HBV prevalence amongst prison donors emerged and we apologise that this was not the case.

69. SNBTS regards the principle of voluntary non-remunerated donation as a key ethical principle and an important contribution to blood safety and does not now, or in the future intend, to collect blood from people in penal institutions.

5.5.3 *Donor selection in response to the emergence of Acquired Immunodeficiency Syndrome (AIDS)*

70. The emergence of AIDS in 1982 and the evidence that it could be transmitted through blood products to patients with haemophilia in 1983 precipitated efforts to defer or exclude donors belonging to broadly defined groups considered to be at higher risk of infection. In May 1983 the Edinburgh and SE Scotland Blood Transfusion Service started working with clinicians specialising in sexually transmitted diseases and representatives of the gay community in Scotland to develop a leaflet asking specific groups of people at higher risk of AIDS to refrain from donation. A number of versions of the leaflet were developed to try to achieve maximum clarity with minimum offence, discrimination and stigmatisation. The leaflet was circulated on 15th June 1983 and a UK wide leaflet followed in September 1983. Further drafts followed through 1984 and 1985 as the situation evolved including a requirement for donors to sign a statement to say that they had read the leaflet. When HIV testing of blood donors was introduced in October 1985 (*vide infra*) the leaflet required further revision.

71. ***SNBTS position:*** we consider that the Edinburgh Service was at the forefront of development of leaflets to defer groups of people at higher risk of AIDS from donating blood and appreciate the difficulties encountered in trying to minimise discrimination, the sensitivity of asking donors about their sexual behaviour (which was unprecedented at the time) and the negative impact on blood donation. It is unfortunate that these early leaflets were not more widely adopted prior to the release of a UK-wide leaflet in September 1983.

5.5.4 *Donor selection in response to Creutzfeldt-Jakob Disease (CJD)*

72. Transmission of sporadic CJD has occurred in the past through substances of human origin such as corneal and dura mater grafts and cadaveric pituitary derived human growth hormone and gonadotrophins. A series of epidemiological case control, look back and surveillance studies over the last 35 years have not revealed any confirmed cases of transmission of sporadic CJD by blood components, plasma products, or peripheral tissues (such as bone, skin and heart valves) (DHSC0032289_056). However, as a precautionary measure, UK Blood Services apply agreed UK and European exclusion criteria (in line with WHO recommendations) to exclude anyone who could have an increased risk of iatrogenic or familial CJD from donating blood, tissues or cells.

73. UK Blood Transfusion Services' criteria for excluding blood and tissue donors who have, or who could have, an increased risk of human prion diseases include:

- Diagnosed with any form of CJD, or other human prion disease.
- Identified at increased risk of developing CJD or another form of human prion disease. This includes:
  - Individuals at familial risk of CJD or another form of human prion disease (have had two or more blood relatives develop CJD or another form of human prion disease or have been informed following genetic counselling that they are at risk)
  - Individuals who have been told that they have been put at increased risk from surgery, transfusion or transplant of tissues or organs.
  - Individuals who have been told that they may be at increased risk because a recipient of blood or tissues that they have donated has developed a human prion disease.
  - Recipients of dura mater grafts.
  - Recipients of corneal, scleral or other ocular tissue grafts.
  - Recipients of human pituitary derived extracts.

74. A different form of Creutzfeldt-Jakob disease – variant CJD - was first reported in March 1996 (HSOC0010099). Unlike sporadic CJD, this disease affected younger people (a median age at death of 28, range 14-75 years old). The clinical presentation was also different. Variant CJD patients show signs of behavioural disorder, depression and anxiety followed by problems with sensation and co-ordination leading to progressive dementia and death over a period of on average 14 months (range 6-114 months). The clinical, epidemiological, neuropathological and experimental data point to variant CJD having been caused by the same strain of prion as Bovine Spongiform Encephalopathy (BSE) (MHRA0021347 and DHSC0004125_011).

75. In the early stages of the variant CJD outbreak, between 1996 and 2004, there was concern that variant CJD was at higher risk of being transmitted by blood transfusion due to the fact that it is a different strain of prion from those seen in sporadic, iatrogenic and familial forms of CJD, that accumulation of prions had been detected in the peripheral lymphoid tissue of patients with clinical variant CJD (DHSC0004747_040 and DHSC0038548_050) and that, at the time, given the widespread exposure to BSE amongst the UK population, it was unclear how many people may have had subclinical infection and would eventually develop clinical disease (RLIT0001877).

76. Withdrawal and recall of any blood components, plasma derivatives, cells or tissues obtained from any individual who later develops variant CJD was announced in December 1997.

77. Universal leucodepletion was introduced in the UK in 1999 as a precautionary measure (BART0002084_002, DHSC0041249_091and DHSC0004790_066), partly as a result of experimental data that suggested that peripheral white blood cells might be involved in the early pathogenesis of the infection (RLIT0001878). Studies in mouse (NHBT0085451 and DHSC0006455_067), hamster (NHBT0098007 and RLIT0001879), sheep (NHBT0052146_002, DHSC0004575_014 and WITN5592014) and primate (RLIT0001880) animal models showed that where infectivity is found in the peripheral blood, a large proportion is associated with the white blood cells and that leucodepletion removes a proportion of that infectivity, but is unlikely, by itself, to remove all infectivity (SCGV0001016_021, HCDO0000254_710 and RLIT0001881).

78. To date there have been 178 definite and probable cases of variant CJD in the UK, 28 cases in France, and 26 cases elsewhere in the world. Some of these latter cases are thought to have acquired the disease in the UK. The other patients are thought to have been infected in their country of origin, but possibly through eating beef of UK origin. The eventual number of individuals within the UK population likely to develop variant CJD remains uncertain, though the number of new cases is diminishing with none reported in the past 5 years. All cases of clinical variant CJD, except three from the UK discussed below, are believed to be primary cases resulting from eating BSE contaminated meat.

79. In December 2003, the first presumed transmission of variant CJD by blood transfusion was described by the Transfusion Medicine Epidemiology Review (TMER) (Part 7.3). The transfusion occurred in 1996; the blood donor was well at the time but went on to develop symptoms of variant CJD in 1999. The recipient was diagnosed with variant CJD in 2003 (NHBT0008743_013). A probable transmission of variant CJD prions, not leading to clinical disease, was reported in July 2004. On this occasion the patient received blood in 1999 from a donor who went on to develop symptoms of variant CJD 18 months later. The recipient died of unrelated causes 5 years after the transfusion with no evidence of neurological disease but at post-mortem was found to have evidence of abnormal prion accumulation in the spleen and a lymph node (DHSC0004215_039). The second presumed blood-associated transmission leading to clinical disease was reported in February 2006. The patient developed symptoms about 8 years after receiving a blood transfusion from a donor who developed symptoms of variant CJD

about 20 months after donating blood (RLIT0000157). A third presumed blood-associated transmission leading to clinical disease was reported in January 2007 in a patient who developed symptoms just over 8 years after receiving a blood transfusion from a donor whose symptoms of variant CJD appeared about 17 months after donating this blood. This donor was also associated with one of the earlier transmissions (PHEN0002470).

80. Consequent on materialisation of the risk of transmission of variant CJD by blood, plasma and tissue products a number of further risk mitigation measures were taken by UK Blood Services:

- Importation of clinical Fresh Frozen Plasma (FFP) for patients born on or after 1st January 1996, initially proposed by SNBTS and announced on 16 August 2003 and implemented by the end of June 2004. This was extended to all patients under the age of 16 by July 2005. As those born on or after 1st January 1996 began to turn 16 from 1 January 2012, this rule reverted to its original wording to ensure that these individuals continued to receive imported plasma past their 16th birthday. This measure was rescinded by SaBTO in September 2019.
- Exclusion of whole blood donors who state that they have received a blood component transfusion in the UK since 1st January 1980 was implemented in April 2004 (NHBT0035101). This led to the loss of around 5% of regular donors. This was extended to whole blood and apheresis donors who may have received a blood component transfusion in the UK since 1st January 1980 in August 2004 and to any donors who have been treated with UK plasma derived intravenous immunoglobulin or have undergone plasma exchange. This was further extended in November 2005 to transfusions anywhere in the world.
- Exclusion of live bone donors who have been transfused since 1st January 1980 was implemented in July 2005.
- Exclusion of blood donors whose blood has been transfused to recipients who later developed variant CJD, where blood transfusion cannot be excluded as a source of the variant CJD infection and where no infected donor has been identified was implemented in July 2005.

81. No instances of transfusion-transmission of variant CJD are known to have occurred since universal leucodepletion was introduced in the UK in 1999 though the development of clinical disease in those patients did not manifest until between 2003 and 2007 (NCRU0000109_090).

82. ***SNBTS position***: the implementation of universal leucodepletion in 1999 appears to have prevented further transmission of variant CJD manifesting as clinical disease.

Part 6: Donation Screening

83. SNBTS holds the primary responsibility for the quality, safety and sufficiency of the blood supply in Scotland. This responsibility has not changed substantively with regard to blood components since the organisation was created, though up until around 1991 SNBTS consisted of Regional Blood Transfusion Services and the responsibility would have been more distributed than it is currently as discussed in Sections 1 and 4 of our first Witness Statement (WITN35300007). SNBTS held the responsibility for the quality and safety of its plasma products until it ceased manufacture of these in 2006 as discussed below.

84. The organisational structures and functions employed to maintain the quality and safety of blood, tissue and cell products including its current donor selection and screening policies, the role of external advisory bodies, its clinical governance and quality management systems, the legal and regulatory environment and the steps taken to ensure that the organisation keeps abreast of medical and scientific research and developments are described in our first Witness Statement (WITN3530007).

85. In their Submissions on Recommendations to the Inquiry Thompson's Solicitors advocate in favour of the early adoption of new donor (microbiological) tests (SUBS0000011). SNBTS agrees with this principle in general terms and would like to clarify the contemporary position in this regard.

86. All medical interventions involve a balance of potential benefit and risk to the patient. The current residual risk of missing an infection with current donor selection and screening procedures in the UK is generally low as evidenced by the UK Serious Hazards of Transfusion (SHOT) haemovigilance system (https://www.shotuk.org), however the risk of transmission of known transfusion transmissible infectious agents by substances of human origin cannot be completely eliminated because of limitations to the sensitivity of assays. There are a large number of potential transfusion transmitted infections, some of which are new and emergent due to genetic change, zoonotic transmission or geographic spread due to the effects of climate change, globalisation and international travel. Moreover, established infectious agents are subject to continuous genetic evolution as one can see from the continuing emergence of SARS-CoV-2 variants during the current pandemic. Furthermore, the risk of transfusion or transplantation transmission of infection is contingent on the prevalence and

transmission of infection in the general population (such as, for example, the food-borne transmission of Bovine Spongiform Encephalopathy and Hepatitis E).

87. The decision as to whether or not to implement a new donor screening assay in Scotland rests with Scottish Ministers and Government usually acting on the advice of the UK Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO). The separation of functions between SNBTS, Advisory Committees and Government, both historically and current, is described in Section 5 of our first witness statement (WITN3530007) and we regard this as a key principle. SNBTS would not normally be in a position to act unilaterally in introducing a substantive blood safety measure (such as a new blood test) because of the financial and operational costs involved and the requirement for systemic lookback for previous recipients of products from repeat donors who are found to be confirmed positive on the new test (Part 7). The recent introduction of a further test for occult HBV (anti-HBc antibody) exemplifies this process as highlighted in the Scottish Government's Submission on Recommendations from June 2022 (SUBS0000017).

88. Further issues which need to be considered during the implementation of new tests include the sensitivity and specificity of assays (i.e. the frequency of missed infections and the frequency of falsely reactive tests respectively), the requirement for confirmatory tests (to ensure that donors are not falsely diagnosed with infections they do not have), validation of modern automated testing platforms and IT systems and regulatory compliance. All tests must be licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) under the UK Medical Devices Regulations 2002. The MHRA has recently published results of its consultation on the new Medical Device Regulations to come into effect in July 2024.

89. There are a number of issues of historical importance which SNBTS feels it is appropriate to comment further on. More detail is described in our first and second Witness Statements (Section 10 WITN3530007 and WITN3530085).

6.1 Testing for Hepatitis B.

90. The chronology relating to the introduction of HBV testing by SNBTS is detailed in Chapter 25 of the Penrose Inquiry Final Report. Systematic study of virus transmission by blood products was ongoing in SNBTS in the late 1960s and work on screening tests in Edinburgh in 1970. There appear to have been concerns around assay sensitivity and competing views at the Department of Health and Social Security as to whether screening for the Australia antigen (later renamed Hepatitis B surface antigen - HBsAg)

should await development of uniform methods of testing or reagents or be introduced as soon as possible despite the limitations. In September 1971 the Advisory Group on Testing for the Presence of Australia (hepatitis-associated) antigen and its antibody (the Maycock Group) recommended that testing be implemented as soon as possible – it was estimated that this would reduce the incidence of serum hepatitis by around 25-30%. Screening was implemented across Scotland by the end of 1971 or early 1972 but was recognised to provide only a partial solution given the relative insensitivity of the tests at the time. During the 1970s work continued on improving the sensitivity of assays and the Glasgow Regional Blood Service was at the forefront of research and development into HBV testing at this time. In 1976 the Glasgow and West of Scotland Blood Transfusion Service had evaluated a test developed by Abbott Ltd (a Radio Immuno-Assay (RIA) which was shown to be more sensitive than the existing Reversed Passive Haemagglutination Assay (RPHA), however the Maycock Group decided to recommend RPHA as it could be introduced more quickly (PRSE0000964). As a consequence, the Scottish Home and Health Department (SHHD) declined to meet SNBTS's request for funding to allow it to continue implementation of the RIA test.

91. By the mid-1970s it was becoming clear that a proportion of long-incubation post-transfusion hepatitis was unrelated to HBV. Despite this evidence the second report of the Maycock Group in October 1975 and a World Health Organisation (WHO) report of the same year recommended that donors with a history of jaundice should no longer be permanently excluded from donating provided that the donor had not suffered from hepatitis or jaundice in the previous 12 months. We are of the view that this inconsistency may have been a reflection of the prevailing (and in retrospect erroneous) view at the time that hepatitis, if not due to HBV, was not a serious condition. Following the availability of a test for Hepatitis A in 1978 the first cases of post-transfusion Non-A Non-B (NANB) hepatitis in Scotland were identified in 1979. Work on identifying the extent of NANB hepatitis commenced in the Glasgow Service thereafter and through the first part of the 1980s on grant funding, but a full prospective study would have needed to be wide ranging and could not be undertaken without external financial support.

92. The issue of surrogate testing for NANB hepatitis is picked up in Section 6.4.

6.2 Surrogate testing for HIV.

93. The question of whether the introduction of Hepatitis B core antibody (anti-HBc) testing could have been used as a surrogate marker for Human Immunodeficiency Virus (HIV) infection in the early 1980s (before the introduction of HIV testing in 1985) resolves into two questions – whether or to what extent a person infected with HBV was or is more

likely to be infected with HIV, and whether anti-HBc would have added much to the HBsAg testing already in place.

94. SNBTS has carried out a search of the international literature on the prevalence of HIV in blood donors who are found to be HBV positive. It appears that whilst HBV coinfection is not uncommon in people who are HIV positive, there are no relevant data we can find on the prevalence of HIV in people known to be HBV positive, particularly in the context of a donor population already screened for HBsAg.

95. ***SNBTS position:*** our view is therefore that the question as to whether anti-HBc testing could have been used as a surrogate for HIV infection in the early 1980s is probably unresolvable.

6.3 Introduction of HIV testing.

96. The HIV virus was first identified by Montagnier *et al* in May 1983 and confirmed by Gallo *et al* in April 1984. However as narrated in Chapter 29 of the Final Penrose Report it took some time to translate academic-based assays into the scaled up and commercialised tests which can be used for the routine testing of thousands of blood donors each day.

97. The first commercial assays underwent field testing in the USA towards the end of 1984. Significant limitations in sensitivity and specificity were described (PRSE0003419) thereby giving rise to concerns about the impact of false positive results on donors. First generation tests were introduced in the USA in March / April 1985 though there were ongoing problems with specificity and initial supplies were not sufficient to meet demand in the US market and there was a lack of availability of kits for large scale export.

98. As we understand it, at the time there was no legal framework to regulate the import and sale of testing kits in the UK (unlike today where we benefit from the Medical Device Regulations which came into law from 2002 onwards). The Department of Health and Social Security (DHSS) decided that further evaluation of the HIV test kits would be required to inform implementation and a national evaluation programme was established in 1984 though SNBTS was not involved.

99. The Abbott HIV test kit became available for evaluation at the Glasgow and West of Scotland Blood Transfusion Service in January 1985 but this was apparently opposed by the SHHD who indicated that "the commencement of routine HIV donation testing in Scotland would be determined by Ministers, on the advice of DHSS and that this date would apply across the UK" (PRSE0003395). Thereafter SNBTS clinicians and scientists participated in the UK Expert Advisory Group on AIDS (EAGA), a non-

departmental body established to provide the UK Health Departments with Expert Advice on AIDS.

100. It appears that the initial phase test evaluation commenced in the Public Health Laboratory Service in Colindale in April 1985 and completed by the end of July 1985. A second phase evaluation was commenced by the National Blood Transfusion Service (NBTS) in England however this appears to have been truncated and a decision was made by the EAGA on 25th September 1985 to implement in October 1985.

101. HIV testing was officially introduced on 14th October 1985 although SNBTS started testing donations before the official date so that all SNBTS stock and that held by NHS Scotland hospital blood banks was tested by the official start date.

102. ***SNBTS position:*** SNBTS started testing donations before the official date and all stock in Scotland was tested by 14th October 1985. At this distance in time SNBTS is not able to form an opinion on whether it would have been in a position to implement HIV testing earlier had it been allowed to proceed with an independent evaluation. We respectfully submit that the question is speculative because the SHHD elected to follow the policy of DHSS in relation to HIV test evaluation and implementation which specified a uniform UK start date.

6.4 Surrogate testing for Non-A Non-B hepatitis.

103. In the late 1970s / early 1980s evidence emerged of a correlation between elevated Alanine Transaminase (ALT) levels and the presence of Hepatitis B core antibodies (anti-HBc) in blood donors and an increased risk of NANB hepatitis in recipients (PRSE0001650; NHBT0111483_001; PRSE0004356; PRSE0001533). The question was raised as to whether these could be used as surrogate markers of NANB in the absence of a specific test for what later became known as Hepatitis C (HCV) (Part 6.5). The main concerns with introducing such testing related to the level of sensitivity (i.e. the number of cases of NANB amongst donors that would be missed and therefore the positive predictive value of the test) and specificity (i.e. the number of people who have elevated ALT or the presence of anti-HBc in the absence of NANB and therefore the negative predictive value of the test). For example, the US National Institutes of Health (NIH) studies suggested that 30-40% of cases of NANB hepatitis might be prevented by ALT testing, whilst 70% of donors with elevated ALT were not associated with transmission of NANB hepatitis. There was concern that the introduction of testing would lead to the loss of an estimated 3% of donors, that information on the significance of elevated ALT for donors was unknown and that at that time the natural history of NANB

hepatitis was uncertain – it was therefore difficult to assess the cost-benefit. There were mixed views at the time as to whether properly designed prospective randomised controlled studies should be conducted to help resolve the uncertainties. Unfortunately no such clinical studies were carried out.

104. In February 1979 an *ad hoc* meeting of the Medical Research Council concluded that a survey of post-transfusion hepatitis was not warranted. Despite this, work was progressed at the Edinburgh and South East Scotland Regional Blood Transfusion Service and in June 1981 a protocol for a prospective study of post-transfusion hepatitis in the UK (to be carried out in Edinburgh and Manchester) based on the original US TTV study was tabled at a meeting of the Medical Research Council Working Party on Post Transfusion Hepatitis (PRSE0004584). The proposed study was not supported, apparently on the grounds that a previous study had been carried out in 1974. A further proposal for a prospective study of NANB hepatitis was made to the Working Party in 1982 / 83 but again this was not supported and such a study was not conducted in the UK (PRSE0004669).

105. ***SNBTS position:*** we regard the failure to progress prospective clinical studies as a missed opportunity which, had they been progressed, might have informed a decision as to whether or not to introduce surrogate testing for NANB in the UK in the mid-1980s.

106. In early 1986 the accumulating data suggesting that chronic NANB hepatitis led to cirrhosis in 10-20% of cases and the unlikelihood of a specific test becoming available in the near future led to a precautionary decision by the Blood Products Advisory Committee of the US Food and Drug Administration to recommend both ALT and anti-HBc testing which was introduced widely in the USA and by some European countries in 1986/87.

107. Opinion in Europe was divided, partly because it was considered that most European countries had a lower incidence of NANB hepatitis than the USA and it appears that some countries introduced ALT testing either fully or partially (and a few anti-HBc testing) whilst others did not (Penrose Inquiry Final Report Table 27.1; INQY0000390).

108. SNBTS submitted a funding bid for the implementation of surrogate testing to the Public Expenditure Survey (PRSE0001473) in 1986. This was declined, apparently due to lack of evidence around incidence of transfusion-transmitted NANB hepatitis, underestimation of the longer-term seriousness of the infection and lack of prospective data on the utility of ALT and anti-HBc testing in a UK context.

109. In March 1987 SNBTS Directors recommended that surrogate testing should be introduced in light of the decision by the FDA to recommend surrogate testing and the impending introduction of the Consumer Protection Act 1987 (PRSE0004163) and submitted a further Public Expenditure Survey making provision for introduction of surrogate testing in financial years 1988/89 and 1989/90. This was again declined by SHHD on the grounds that further research was required.

110. In 1987 there was a chain of correspondence in the Lancet arguing against the introduction of surrogate testing without a national UK study to assess the prevalence of raised ALT levels and anti-HBc in donors in different parts of the country, the incidence of post-transfusion NANB hepatitis and how many of those developed evidence of chronicity and long-term clinical sequelae (NHBT0000025_010; PRSE0000239; PRSE0002104). A letter in response from SNBTS Directors agreed that whilst the size of benefit to be gained by surrogate testing could not be accurately established without such a study (as proposed in 1981), the time for such a study had already passed and that testing was inescapable (PRSE0001444). In August 1987 a further grant application was made to the Chief Scientist's Office for funding to enable the Edinburgh Service to participate in a proposed UK multi-centre study into surrogate markers in donors (PRSE0001722) but this was declined in October 1987. In April 1988 the English part of the multi-centre study was funded and it was accepted by SNBTS Directors that they could not introduce surrogate testing until a decision was made at UK level dependent on the outcome of the multi-centre study. There was discomfort that SNBTS was excluded from this research and with regard to the further delay involved (PRSE0004647). The final report of the study showed a prevalence of 3.4% of donors with a raised ALT and 0.63% anti-HBc positive, though it was difficult to conclude how many of these might have transmitted NANB hepatitis because the study did not involve prospective follow up of recipients (PRSE0001695). In the event the announcement by the Chiron Corporation of the identification of HCV superseded this work and no further consideration was given to surrogate testing after November 1989.

111. When SNBTS introduced HCV testing in September 1991 the prevalence of infection amongst donors was found to be 0.088%, which was higher than that in other parts of the UK - probably due to the higher prevalence of HCV-infected ever-IVDU in Scotland as indicated by Professor Bird in her testimony of 9th November 2022. Of those identified in the first 6 months and who attended for counselling, 59% had ALT levels above the upper limit of normal, though the majority of these were below the level of cut off that would have been used for donor screening. Once more sensitive HCV tests became available a retrospective study of stored samples from prison donors between 1980 and

1984 showed that 65.6% of samples with an ALT> 2.5 times the upper limit of normal were positive for HCV. However, this is clearly a selected population with a higher incidence of HCV than the general population.

112. ***SNBTS position:*** we consider that it was very difficult to resolve the uncertainties relating to the sensitivity and specificity of ALT and anti-HBc testing in preventing transmission of NANB hepatitis in the absence of adequately powered prospective clinical studies and that these should have been supported in order to allow informed decisions to be made in a timely manner. SNBTS advocated such studies from 1981 onwards but was not able to progress these unilaterally without external funding and support.

113. We feel that on balance, in the absence of such data and with the emergence of more evidence of the long-term effects of HCV infection in some patients, surrogate testing should have been introduced in Scotland as a precautionary measure. Again, it was not possible for SNBTS to introduce such testing without external funding and UK Government support. In reaching this conclusion we acknowledge that the data is complex and caveated and it's difficult to conclude with any certainty what the magnitude of benefit would have been had such testing been introduced.

6.5 Introduction of HCV testing

114. The Hepatitis C virus (HCV) was identified by the Chiron Corporation in May 1988 and details published in April 1989 (NHBT0000025_021 and PRSE0003989). On 5th July 1988 SNBTS wrote to Chiron asking for access to some of their kits for evaluation and to Ortho seeking confirmation they would be marketing the kit in UK and asking when it would be available (PRSE0000670 and PRSE0002363). Ortho had its first generation tests available for sale for *in vitro* diagnostic use at the end of November 1989.

115. It was considered that the EAGA did not have the remit to advise on the introduction of tests for other viruses and a new advisory group, the Advisory Committee on the Virological Safety of Blood (ACVSB) was proposed in July 1988 and established in April 1989 under the aegis of the Department of Health (DoH) and reporting to the Chief Medical Officers. Proceedings of this committee were confidential.

116. In June 1989 SNBTS commenced a research evaluation of the Ortho first generation test kits in parallel with an evaluation that was being carried out in NBS Edgware Centre. In August 1989 SHHD indicated that a decision to commence routine donation testing would be made simultaneously throughout the UK as was done in the case of the HIV test (PRSE0001692 and PRSE0000402). There were clearly concerns around the

sensitivity and specificity of the first generation tests and the need for a confirmatory assay when screening low prevalence groups (NHBT0000025_025 and NHBT0083819). In Autumn 1989 Ortho offered to sell first generation kits in the UK and the routine screening of blood donations for HCV was advocated in principle subject to a number of conditions by UK Blood Services on 9th October 1989 (ACTTD) (PRSE0002888) but this position was not supported by ACVSB (PRSE0001071). In November 1989 Ortho intimated that an export licence had been approved by the FDA for their ELISA test for *in vitro* diagnostic use. The SNBTS study reported in October 1989 and the NBTS study in April 1990 concluded that the first generation Ortho test had an acceptable level of sensitivity and specificity.

117. It appears that following an Ortho symposium in London (PRSE0004275), the view in SNBTS in February 1990 was that screening of donations should be introduced (PRSE0001562 and PRSE0004402). Despite the reservations some countries did implement this first generation assay for blood donor screening around this time (including Finland, France, Belgium and Luxembourg), however ACVSB continued to express reservations in respect of sensitivity, specificity and lack of a confirmatory assay and appear to have delayed a decision. It was made clear that the decision as to whether to introduce HCV testing of blood donations was a matter of policy to be decided by the UK Government on the basis of advice from ACVSB rather than being a matter for the Blood Services (PRSE0002519).

118. In May 1990 the FDA approved the first generation HCV assay and Ortho confirmed the availability of a Radio Immunoblotting Assay (RIBA) as a supplementary / confirmatory test. The USA moved to implement HCV testing at this time. On 2nd July 1990 ACVSB decided to recommend the implementation of HCV testing and also a comparative study of the Abbott and Ortho tests (PRSE0000976). The final report from this study did not become available until February 1991. In its meeting of 21 November 1990 ACVSB further recommended implementation of HCV testing with a potential start date of 1st April 1991 discussed (PRSE0000976). It appears that there was further slippage in 1991 due to a lack of decision on a start date and funding concerns in England. In addition an evaluation of the second generation Ortho test by Glasgow and West of Scotland Blood Transfusion Service proved promising. In February 1991 DoH proposed delaying implementation until 1st July 1991 and funding remained a problem with no new allocation for introduction of screening (PRSE0002280). In addition ACVSB apparently agreed to a further evaluation of the Ortho and Abbott first and second generation tests prior to implementation. Between March 1991 and August 1991 there were successive delays with tensions arising between those who felt that SNBTS should implement as

soon as possible and those who felt that SNBTS should stick to the UK Government date of 1st September 1991. In the event SNBTS remained formally aligned with the UK Government instruction. SNBTS introduced HCV screening of blood donations using second generation ELISA and RIBA tests and removed reactive units prior to the official start date so that all SNBTS and hospital blood bank stock had been tested negative by 1st September 1991 .

119. ***SNBTS position:*** It is difficult to understand why it took more than two years to implement HCV testing. In his judgement in the case of A v National Blood Authority (2001) 3 All E R 289, Lord Justice Burton provides a table illustrating the position in 25 countries across Europe, the USA, Canada, Australia and Japan. Of those countries the last two to implement HCV screening were the UK and Ireland.

120. Much greater urgency should have been given to the implementation of HCV testing. It is not clear to us why it would not have been possible in principle to introduce a first generation test as early as April 1990 and by April 1991 at latest. The delays appear to be mainly related to delays in decision making by ACVSB and the UK Government instruction to comply with a single UK-wide implementation date.

121. In retrospect there are concerns around the independence, transparency and breadth of representation on ACVSB, an apparent bias in favour of scientific rigour rather than a precautionary action leading to delays in decision making and, following the decision to implement, the lack of clear plan and commitment to funding. Secrecy and confidentiality in regard to ACVSB was clearly a problem for SNBTS and it is difficult to understand now why this was considered necessary.

122. Lord Penrose criticised SNBTS for not more robustly arguing the case for implementation in Scotland on 1st April 1991 at latest and for not making a formal request to the SHHD to be allowed to do so. SNBTS accepts this criticism though whether such a request would have been accepted by the Secretary of State for Scotland, given the stated position of the UK Government at the time remains uncertain.

6.6 Variant CJD Tests.

123. The types of tests that are used to screen blood and tissue donations for viruses cannot be applied to variant CJD because, unlike a bacterial or viral microorganism, the pathogenesis of this disease involves an abnormal conformational change in prion protein widely expressed by human tissues which does not elicit an immune response or contain foreign genetic material (RLIT0001882). Many research groups, including those in SNBTS and NHSBT, were unsuccessful in developing an assay with sufficient

sensitivity to differentiate the normal from the abnormal form of prion protein (RLIT0001883, RLIT0001884, WITN7065034 and RLIT0001884). Researchers from the MRC Prion Unit developed a blood test which has been demonstrated to be sensitive enough to detect abnormal prion in the blood of some patients with clinical variant CJD (NHBT0033626 and WITN3093010). Similarly, two international groups have developed assays which can detect prions in the blood of experimentally infected animals (RLIT0001886, RLIT0001887, WITN3093002 and WITN5592004). Unfortunately, neither of these assays has moved into commercial translation as a test which could be deployed at large scale for the rapid testing of blood and tissue donors (RLIT0001888).

Part 7: Lookback

124. The Inquiry has investigated the performance of lookback in the context of introduction of HIV and HCV and a historic account of SNBTS's involvement in these processes is provided in our second Witness Statement (WITN3530085).

125. Lookback is not unusual in the context of repeat donors who develop evidence of a new infection or disclose a previously unknown risk factor (targeted lookback), or in the context of a person who is diagnosed with an infection which may have been transmitted by a previous blood component transfusion or tissue, cell or organ transplant (reverse lookback or traceback). Both require maintenance of full traceability between the donor and the recipient(s) across the organisational boundaries of the Blood Service and the Hospital and this is a legal requirement since the introduction of the Blood Safety and Quality Regulations 2005.

126. In the context of a repeat donor newly diagnosed with a transfusion transmissible infection, previous donations from that person are identified and the blood components manufactured therefrom are traced to the hospital blood bank to which they were sent. The hospital blood bank holds the information on which patients received the implicated blood components. The medical notes held by the hospital will indicate whether the patient is alive or deceased and if alive whether they are still under the clinical care of the hospital or have been discharged back to primary care. The attending clinician will normally contact the patient to arrange for blood tests and provide any follow up clinical care required.

127. In the context of a person who is identified as having an infection which may have been transmitted by a previous transfusion or transplant, provided the medical notes or hospital blood bank can be found and contain a record of the donation numbers of the

components received, then the Blood Service should be capable of identifying the original donation and donor. In some cases the donor may have been tested for the infection in question at the time or at subsequent donations, otherwise efforts are made to contact them to invite them for testing. If a donor is identified as being positive for an infection as a result of this investigation, then they are excluded from further donation and a lookback for other recipients of previous donations is carried out as described in the paragraph above.

128. Some Blood Services, including SNBTS, retain a frozen archive of residual plasma (normally around 1-2 ml) from the original donor testing sample. This is not a legal requirement but can help identify when a donor first became infected (such that recipients of blood components prior to that date don't have to be traced) or clarify whether a specific donation was the source of infection in the case of a reverse lookback. Once a sample is used for an investigation in this way there is usually no, or very little, residual plasma left. For this reason the blood donor sample archive is not used for research purposes or for general epidemiological studies.

129. The further one goes back in time the more challenging lookback becomes. SNBTS retains donor records more or less in perpetuity, but prior to the introduction of the national Progesa IT system in 1998 donor records were managed on a regionalised IT system (DOBBIN) as noted in Section 2 of our first Witness Statement (WITN3530007). Data on all donors registered in DOBBIN were transferred to Progesa alongside the results from the most recent donation recorded. Information on earlier donations is only available on the original DOBBIN system which can be searched but has suffered some degree of data corruption so is not as complete as it once was. Prior to 1988 / 89 donor records are only held on microfiche or regional paper records. These records are held off site, are more patchy and can only be searched by hand which is an arduous and time consuming undertaking. In addition during the period of time before the Service was national, regional donor, donation and sample numbers could be repeated both in time and across regions giving rise the risk of the wrong donor being investigated or the wrong donation being implicated or excluded.

130. Moreover, it is unusual for hospital blood bank records to be retained for a substantial length of time. The Blood Safety and Quality Regulations imposed a retention period of 30 years when they came into force in 2005, but of course this could not be applied retrospectively if records had already been destroyed. In practice, therefore, it is very difficult to carry out an accurate lookback prior to around 1991 and really these only start to become reliable from about 1998.

131. A large scale systematic lookback such as may be required following introduction of a new assay is more unusual and is a major undertaking. A systematic lookback needs to be considered from the perspective of the healthcare system as a whole. SNBTS does not have the expertise, capacity or authority to carry out a systematic lookback unilaterally, the authority of the Scottish Government is required, alongside the expertise of Public Health Scotland and the participation of hospital blood banks, primary and secondary care in tracing, informing, testing and, where required, clinically managing recipients.

132. The Inquiry has asked the question as to whether, on the introduction of a new test, lapsed donors could be identified and tested or traced. Within SNBTS it would be possible in principle to undertake such an exercise utilising a search of its core donor database eProgesa which holds data back to 1998 but we would identify in the order of 750,000 donors of whom 85,000 we would consider currently active (i.e. having donated in the past 12 months), leaving 665,000 people from whom archive samples would need to be retrieved and tested or who would need to be individually contacted. The tracing alone would be an enormous task and the testing would represent a 4 fold (400%) increase over the current sample capacity of the SNBTS donor testing facility. There would need to be significant Governmental investment and establishment of a separate laboratory to achieve this without compromise to the current blood supply. Moreover, this is likely only something that could be done once given the limited sample volumes available. An alternative strategy would be to trace and contact past donors and ask them to be re-tested. Again this would be a very significant public health exercise involving the testing of perhaps 12% of the population of Scotland.

133. The need or otherwise for lookback is not captured in the European Blood or Tissue Directives or related UK legislation. The decision as to how far a lookback should extend both in terms of scope and time is a difficult balance of the ethical, legal and medical imperative to inform a person who may have been put at risk of infection, against the diminishing practicality and cost benefit as one expands the scope to those people who are no longer active donors and the further one goes back in time. In our opinion these are not decisions which can or should be made by Blood Services alone because whilst the scientific, operational and clinical issues are surmountable, the broader issues of financial and opportunity cost pertain to the healthcare system more broadly and societal priorities.

134. There are three national lookbacks of historical importance which SNBTS feels it is appropriate to comment upon:

7.1 HIV Lookback

135. In the latter half of 1984 commercial test kit companies and academic centres for virology in the USA, UK and France developed testing methods for the identification of antibodies to HIV. The first commercially available kits for routine testing of specimens in large numbers were released to transfusion services in the USA in April 1985, though difficulties with supplies initially led to a patchy introduction. Nevertheless, the US transfusion services jointly agreed that they would attempt to identify previous recipients of blood from donors found to be positive for the virus. A time limit of 5 years was put on this retrospective search for affected patients, reflecting the length of time HIV was thought to have been present in humans.

136. In the UK test kits were not available for routine testing until later in 1985, though some preliminary testing was carried out in the Blood Services. While this was in progress a working party of the UK Regional Transfusion Directors was set up with a remit to develop procedures and protocols for screening of donors, confirmatory testing and communication with and further management of donors found to be positive. The report produced by the working party was accepted by the Regional Directors at their meeting on 11 July 1985. This included a statement that efforts should be made to trace recipients of donations found to be positive and to inform the consultant in charge of the patient (DHSC0000406). This report formed the basis of standardised procedures implemented after a training exercise for donor centre staff held at SNBTS Headquarters in the run-up to the implementation of routine screening on 15 October 1985. Full testing commenced in October 1985, by which time the UK Blood Services had agreed to carry out lookback on the same basis as in the USA. Procedures were agreed and standardised and staff trained before testing commenced (PRSE0004042).

7.2 HCV lookback

137. The chronology of events in relation to HCV lookback are documented in Chapter 35 of the Final Penrose Report and in the SNBTS paper on lookback submitted to the Penrose Inquiry (PRSE0004042).

138. From the introduction of HCV screening in September 1991 donors confirmed positive for HCV were offered face-to-face counselling by a member of SNBTS medical staff, including repeat testing and onward referral for appropriate further investigation and treatment. In some cases, at the request of the donor, this was carried out by the GP, who was supplied with appropriate documentation by SNBTS.

139. The procedures to follow in counselling such donors and ensuring appropriate medical follow-up were codified in a report (PRSE0004114) prepared by a SNBTS working party. It was approved by the Scottish Regional Centre Directors in September 1990 and formed the basis of guidelines employed throughout the Scottish donor service from the start of routine testing for HCV in September 1991. This report recommended that lookback should be introduced at the same time as testing and this was endorsed by SNBTS Directors. In November 1990 SNBTS wrote to the Department of Health requesting that the ACVSB should discuss lookback (PRSE0001573). The minutes of the meeting of ACVSB of February 1991 recorded the decision that lookback "should not be undertaken as a service" (PRSE0002280). This became accepted UK policy. However lookback was introduced in Edinburgh and South East Scotland Blood Transfusion Service at the onset of routine testing of donations in September 1991 and designated a pilot study.

140. Subsequently a UK wide HCV lookback was launched in 1995. The CMO letter of April 1995 (WITN3530095) provides a detailed account of the processes and procedures followed with appendices providing guidelines on counselling and specimen letters etc. The outcomes of the HCV lookback were provided in a letter from SNBTS to the Scottish Office, dated 28th April 1998 (PRSE0003277), containing a report prepared by Dr J Gillon, dated 9 April 1998, which detailed the results of the lookback in Scotland up to that date (SCGV0000167_192). These results were also provided by the Health Minister to the Health Committee of the Scottish Parliament on 31 January 2006.

141. ***SNBTS position:*** The principle of tracing recipients of potentially infectious blood had been established by the precedent of introducing lookback at the time of commencing screening for HIV in 1985. The question which the pilot study set out to address was whether the same approach to HCV was logistically feasible, which was answered in the affirmative. It is our view that lookback could have been undertaken throughout Scotland from September 1991, as testing with second generation assays was backed up with confirmatory tests including PCR for virus RNA. However it would have been very difficult for SNBTS to progress this unilaterally in light of the ACVSB and UK Government's decision to reject HCV lookback as a policy and given that the systematic engagement of hospital blood banks, clinicians and GPs was required to trace, test and counsel recipients. Certainly the institution of a contemporary lookback in regard to the recent introduction of anti-HBc testing for occult hepatitis B has required the support of Scottish Ministers and Chief Medical Officers in order to secure engagement of the wider healthcare system to ensure that transfusion recipients identified as being exposed to

blood components from a potentially infectious donation are managed so as to give the best possible outcomes.

7.3 Transfusion Medicine Epidemiology Review (TMER).

142. The TMER was established in 1997 as a collaboration between the National CJD Surveillance Unit in Edinburgh and the UK Blood Services in order to establish whether those people who developed CJD had donated blood (and if so the fate of those donations and whether the recipients had developed variant CJD) and whether they had themselves received blood (and if so whether the donors had developed variant CJD). In other words the TMER was a forward and reverse lookback process.

143. Eighteen people who later developed variant CJD were traced as blood donors and gave blood donations that were transfused to recipients. Sixty-seven recipients of blood components from these donors were identified of whom 14 were still alive, all of whom survived for at least 10 years after the blood transfusion. Their doctors were informed of their exposure to these products (http://www.cjd.ed.ac.uk/TMER/TMER.htm) (NCRU0000109_092 and WITN7034034).

144. Three recipients of blood from donors who subsequently went on to develop variant CJD themselves developed variant CJD and a further patient was found to have evidence of subclinical infection as described in Section 5.4.4.

145. Eleven blood donors who later developed variant CJD contributed to 25 plasma pools from which 191 plasma product batches were manufactured.

146. A presumed transmission of prions by plasma products was described in February 2009 as a result of the TMER (Section 7.3) and post-mortem surveillance studies in patients with haemophilia and primary immunodeficiencies (HCDO0000799). The patient suffered from haemophilia and had received batches of Factor VIII to which a donor who subsequently developed vCJD had contributed plasma. He died of other causes but was found at post-mortem to have evidence of prion accumulation in his spleen (Part 8.8).

147. ***SNBTS position:*** The TMER facilitated early identification of cases of donor to patient transmission of variant CJD. It is not clear whether these transmissions would have been detected in the absence of this initiative and we consider that this was an exemplar of the benefit of a proactive surveillance strategy to allow early detection of transfusion transmission of new and emergent infections.

148. ***SNBTS recommendation*:** We would invite the Chair to consider the circumstances under which a systematic lookback should be carried out, the scope of such lookbacks and the extent to which cost effectiveness should be considered alongside the views of blood recipients and broader ethical, legal, operational and societal considerations. We also invite the Chair to consider whether or to what extent the duty to perform systematic lookback could or should be included in relevant legislation.

Part 8: Plasma products

149. The chronology of the early treatment of Haemophilia in Scotland is documented in Chapter 20 of the Final Report of the Penrose Inquiry. Cryoprecipitate was introduced for the treatment of Haemophilia A (Factor VIII deficiency) in 1964. The administration of 10-15 pooled donations was sufficient to raise the Factor VIII level high enough to stop haemorrhage. However, cryoprecipitate does not contain sufficient concentrations of other coagulation factors to treat patients with Haemophilia B who required Fresh Frozen Plasma until the development of a 4 factor concentrate (PPSB) in 1968.

150. SNBTS manufactured plasma products from Scottish plasma in the 1950s and 1960s on a relatively small scale within the Blood Products Unit (BPU) at the Edinburgh and SE Scotland Blood Transfusion Service including anti-measles immunoglobulin, fibrinogen, albumin and an early version of Factor VIII. In 1975 an improved and larger scale manufacturing facility, the Protein Fractionation Centre (PFC) was opened at Liberton in Edinburgh as discussed below (Section 8.2). More detail is provided in Chapter 19 of the Penrose Inquiry Final Report and Section 6 of our first Witness Statement (WITN3530007) and the documents referenced therein.

151. During its period of activity the PFC manufactured a wide variety of plasma products including coagulation factors, immunoglobulins and albumin.

8.1 Sufficiency of supply of Scottish plasma to meet demand for coagulation factors.

152. In December 1974 the UK Government decided that the UK should aim to become self-sufficient in the provision of plasma products within 2 to 3 years (PRSE0004264). The role of SNBTS was to achieve this for Scotland using only blood or plasma donated voluntarily from non-remunerated donors in Scotland. This objective required plasma to be obtained by replacing whole blood transfusions with transfusion of red cell concentrates augmented by donor plasmapheresis where required. The scale and yield

of coagulation factor manufacturing capacity at PFC also had to be increased substantially (Part 8.2).

153. Unfortunately, as discussed below (Part 8.2) the planning assumptions at that time significantly underestimated the substantial growth in demand for coagulation factor concentrates due to previously unmet clinical demand and increasing demand due to the move towards home therapy to allow earlier treatment as illustrated in Figure 21.4 Chapter 21 of the Penrose Inquiry Final Report.

154. Figure 18.1 Chapter 18 of the Penrose Inquiry Final Report shows that the resultant demand for plasma was principally met by an increase in blood donation from around 210,000 donations in 1975 to just over 300,000 donations in 1990.

155. The Table in paragraph 21.62 of the Final Penrose Report shows that at all times between 1975/76 and 1989/90 SNBTS had sufficient Factor VIII available to meet average demand if cryoprecipitate was considered to be suitable to supplement Factor VIII concentrate. Beyond that time cryoprecipitate data is not available (PRSE0001083). If cryoprecipitate is excluded from the analysis of sufficiency, then the availability of SNBTS Factor VIII concentrates was sufficient to meet average demand in the years up to 1998/99 apart from 1978/79 and 1979/80 (though a transition to recombinant Factor VIII becomes evident from 1997/98).

156. This is not the same as saying that all FVIII used in Scotland over this period was provided by SNBTS because clinicians had the freedom to purchase and use commercial Factor VIII concentrates if they felt they were clinically indicated.

157. ***SNBTS position:*** Between 1975/76 and 1987/88 sufficient plasma was available from whole blood donation in Scotland to meet average demand if Factor VIII and cryoprecipitate are taken into account. During this period there was therefore no requirement to introduce plasmapheresis. Whilst SNBTS always aimed to be the provider of choice, clinical preference meant that some commercial concentrates continued to be prescribed in Scotland over this period (Penrose Report Figure 21.5).

8.2 Processing capacity at the Protein Fractionation Centre (PFC)

158. During the planning of PFC it was anticipated that it would be commissioned with an initial capacity of 1,500 litres of plasma per week and capable of being increased to 3,000 litres per week and that this would include plasma from Northern Ireland and a third of England's plasma. Subsequently the DoH contributed 30% of the capital cost of building the PFC.

159. Over the period between 1969 and 1973 there was considerable uncertainty around the levels and pattern of future demand for coagulation factors because of increasing clinical preference for plasma concentrates over cryoprecipitate, the introduction of new surgical techniques, changing expectations relating to the benefit of more active patient lifestyles and a developing interest in home therapy to allow earlier treatment. As a result, the PFC and BioProducts Laboratory (BPL) in Elstree were planned and commissioned against a background of insufficient projected production capacity to fully meet UK requirements.

160. In 1973 the first UK licences for US commercially manufactured Factor VIII concentrates were granted and it was recommended by an Expert Group on the Treatment of Haemophilia (PRSE0004706) that the UK should aim to become self-sufficient as soon as possible and that close cooperation across the UK nations would be required to achieve this.

161. Continuous flow plasma fractionation for the manufacture of immunoglobulin and albumin by ethanol fractionation was developed and patented by SNBTS in 1969. Although this design was modified in 1973, the basic infrastructure to accommodate this process was built into the PFC during its construction. At that stage coagulation Factors VIII and IX were both prepared by batch processing. Research on applying the concept of continuous processing to thawing plasma for the recovery of cryoprecipitate was initiated in 1976. The principles on which this was based were published in 1978 (PRSE0001426). Pilot-scale equipment was introduced for the production of Factor VIII concentrate during 1979 and the final design introduced in January 1981. Factor IX concentrate was prepared from the cryo-depleted plasma.

162. Additional freeze drying capacity was installed at PFC in the late-1970s for the preparation of FVIII concentrate and again in the early 1980s. Freeze drying capacity was extended further in the mid-1980s to accommodate Intravenous Immunoglobulin as well was Factor VIII concentrate.

163. By the time the PFC started commissioning in 1975 the estimated use of coagulation factors was over 4 times that reported in 1969. PFC was fully operational by 1976 against a backdrop of concern that there was significant use of cryoprecipitate and commercial concentrates particularly in the west of Scotland. A meeting in October 1976 estimated a UK requirement of 40 million units of FVIII rising to 50 million units over the next 3 years (4–5 million units for Scotland) (PRSE0002069). This projection exceeded by a considerable margin the production targets on which PFC and BPL were planned

and constructed. In Scotland the facilities were sufficient in scale or flexible enough to adapt to growing demand until the end of the 1970s.

164. A key problem appears to have been the absence of a centralised planning system and in particular the absence of a central purchasing system or database that allowed visibility over true demand (i.e. for both NHS and commercial concentrates).

165. ***SNBTS position:*** Between 1975/76 and 1987/88 sufficient plasma products were available from PFC to meet average demand in Scotland if Factor VIII and cryoprecipitate are taken into account (see paragraph 149). However, clinical preference meant that some commercial concentrates continued to be prescribed in Scotland over this period (Penrose Report Figure 21.5).

8.3 Could PFC production capacity have been expanded to support England.

166. The primary limit on FVIII production capacity at PFC (other than plasma and yield) was freeze drying capacity. This could have been increased as required, but would have needed significant funding and planning as it typically took 18-24 months to purchase install and commission a new freeze drier.

167. The IBI explored the possibility that with shift working, PFC could have taken time-expired plasma from BPL and enabled BPL to process more fresh plasma for FVIII production, pending the installation of additional freeze drying capacity at PFC (IBI transcript 24 March 2022, page 145).

168. ***SNBTS position:*** it should have been possible with appropriate investment to increase the processing capacity at PFC to support England.

8.4 Development and implementation of virus inactivation up to the end of 1984 to inactivate the HIV virus.

169. Considerable research was undertaken from 1944-1969 to eliminate the risk of hepatitis transmission by blood and blood products, including heat treatment, UV-irradiation and treatment with a variety of chemicals (PRSE0002291). None of these were successful other than the pasteurisation of albumin. This led to the view that freedom from hepatitis transmission could only be achieved by the physical removal of viruses (WITN6914095).

170. Heat treatment of plasma by the method of J Garrott Allen (WITN6914097) was studied at PFC (formerly the Blood Products Unit - BPU), with a report published in the Lancet in 1958 (RLIT0001903). Pasteurised albumin was introduced by BPU in 1964.

171. During the 1970s, research was undertaken at BPU/PFC on the physical removal of hepatitis virus by precipitation and by chromatography, with consideration also given to the use of high-speed centrifugation for this purpose.

172. The main focus of PFC research in the 1970s was increasing factor VIII yield for two reasons. First, to minimise the need for imported concentrates, which were considered to have a much greater risk of hepatitis infection. Second, to provide a sufficient yield to enable additional processing to be adopted, knowing that any extra step(s) e.g. for virus elimination, would carry a yield penalty. Such studies at PFC have been previously described as 'Platform Technologies' (PRSE0002291).

173. The discoveries made at PFC concerning yield went on to support virus inactivation technologies for the inactivation of NANBH, not only by PFC, but also by BPL (8Y), Behringwerke (higher yielding pasteurisation) and by solvent-detergent treatment (WITN6914071).

174. The introduction of a test for HBV in 1972 engendered the hope that this would eliminate post-transfusion hepatitis in people with haemophilia. However, by 1975 clinical studies were indicating that there were one or more other infectious agents responsible for a significant proportion of post-transfusion hepatitis.

175. Studies in the 1970s found that a combination of fractionation and pasteurisation (heating at 60C for 10 hours) was effective in inactivating HBV in human albumin solution.

176. However, the scientific and technical issues in extending this work to other viruses and more labile plasma proteins such as coagulation factors were substantial, both in respect of developing methods that would inactivate HIV (and later HCV) and in ensuring that the product was not denatured by the heat treatment leading to reduced yield, loss of efficacy or increased immunogenicity or thrombogenicity (in the case of Factor IX). These are discussed in some detail in Chapter 23 of the Penrose Inquiry Final Report.

177. Research on heat treatment of Factor VIII had begun at PFC in 1981 following reports at an international meeting that Behring had made a breakthrough in the pasteurisation of Factor VIII if suitably protected by chemical stabilisers in a high purity product. The yield however was low (8%) (Penrose Final Report page 944 section 23.41). By late 1982 SNBTS had eliminated irradiation and physical virus removal as options for increasing Factor VIIII safety and the objective of research was to achieve heat treatment of 30% of the PFC's output of Factor VIII during 1984/85 at the earliest

(PRSE0001111). At that stage the objective was designed to give priority to the prevention of NANB transmission in patients who were not already infected.

178. With the emergence of reports of AIDS in patients with haemophilia in the UK the focus of the research programme shifted to this new virus. In a memorandum of 3rd May 1983 (PRSE0001111), it was proposed that the objective of applying heat treatment to PFC's Factor VIII be accelerated and applied to all Factor VIII on the assumption that the disorder of AIDS might be caused by a blood borne infectious agent that might be destroyed by heat treatment. A technical approach to achieve this was outlined. This proposal was accepted by SNBTS and an initial request for funding for the required PFC building works was submitted to SHHD though not authorised until over a year later (August 1984). The research progressed despite the absence of external funding and the approach was used to prepare two batches of pasteurised Factor VIII concentrate (NY 761) for clinical evaluation towards the end of 1983. The results were satisfactory in two patients but one patient experienced a significant adverse reaction, the cause of which was uncertain. This approach did not therefore progress to routine manufacture (Penrose Inquiry Preliminary Report page 471 section 11.158 and Final Report page 972 section 23.147).

179. PFC experimented on dry heat treatment in December 1983, finding that its Factor VIII concentrate (NY) could not tolerate the degree of heat treatment (60ºC for 72 hrs) being applied by Baxter to Hemofil-T. It became known by SNBTS, at about this time, that NANB hepatitis continued to be transmitted to patients by Hemofil-T (PRSE0001736). The main focus of PFC in 1984 remained on examining different pasteurisation conditions to bring the degree of virus inactivation closer to that obtained during the pasteurisation of albumin (based on marker virus inactivation studies at PFC). A number of further batches (ZHT) were prepared for clinical evaluation. PFC also began practical work on increasing Factor VIII purity to address the 'adverse reaction' should that turn out to be generic.

180. In late September 1984 Bayer published a report in the Lancet of dry heat treatment at 68ºC of a murine retrovirus added to FVIII (CBLA0001898). The results suggested that this retrovirus might be more sensitive to dry heat than infective agent(s) responsible for NANB Hepatitis. Whilst SNBTS had determined that PFC's Factor VIII (NY) could not withstand dry heating at 60ºC for 72 hrs (the conditions used by Baxter), SNBTS had not determined the degree of dry heating that NY could withstand. In light of the report by Bayer and the fact that the AIDS virus (HIV) was a retrovirus the possibility had emerged that HIV might be inactivated by dry heat treatment and a preliminary

experiment was carried out to obtain this information. The first PFC dry heat study at 68ºC was initiated on 26th October 1984.

181. On 29th October 1984 PFC first learned that three Edinburgh haemophilia patients had tested positive for HIV. Some vials of Factor VIII (NY) with a variety of different additives had already been prepared with the aim of increasing yield over the final stages of processing. It was decided to use these to see if any of these additives might extend the degree of dry heat treatment at 68ºC. This was the second PFC dry heat study at 68ºC.

182. The results of the first dry heat study at 68ºC were available on 30th October 1984 and showed that the batch of NY that had been used could withstand dry heating at 68ºC for 3 hours. Beyond that, the samples failed to meet the specification for reconstitution time.

183. At the Groningen symposium on 2nd November 1984 CDC reported that 5 logs of HIV added to FVIII had been fully inactivated by pasteurisation at 60ºC for 10 hours. For dry heating at 68ºC, 4 logs had been inactivated at 1 hours and 5 logs at 24 hours. Colleagues present at the meeting agreed to recommend the immediate application of 68ºC dry heat to NY.

184. On 5th November 1984 samples of NY from a number of batches were examined to confirm that they would all withstand dry heat at 68ºC for 3 hours. It was found that many batches did not, but that all batches could tolerate dry heating at 68ºC for 2 hours – double the time required to inactivate 4 logs of HIV according to CDC.

185. On 14th November 1984 the PFC spray cabinets that were used to pasteurise Albumin at 60ºC were validated for the dry heat treatment of FVIII (NY) at 68ºC for 2 hours and on 18th November 1984 dry heat treatment of NY at 68ºC for 2 hours was begun. Heat treated Factor VIII was available for clinical evaluation from 3rd December 1984 and issued to Regional Transfusion Centres in Aberdeen, Belfast, Dundee, Edinburgh Glasgow and Inverness for general use and all unheated FVIII recalled.

186. From the results of the second PFC dry heat study at 68ºC that had been initiated on 29th October 1984, it was subsequently discovered that the addition of 2% sucrose to NY could allow dry heating at 68ºC to be extended to 24 hours.

187. On 20th January 1985 processing of plasma was restarted after a 3-month shut-down for Medicines Inspectorate building modifications to PFC. NY was formulated with the addition of 2% sucrose to enable dry heat treatment at 68ºC to be extended to 24 hours.

188. After donor screening for HIV had been introduced it was demonstrated that two of the first batches of the dry-heat treated Factor VIII had been prepared using donations from a donor infected with HIV and that no transmissions had occurred (STHB0000159).

189. Commercial dry-heat treated coagulation factor concentrates were not licensed by the UK Medicines Control Agency for release in the UK until February 1985.

190. ***SNBTS position:*** The progressive development of virus inactivation for HIV reflects the profound initial uncertainty and rapid evolution of events in the context of a global pandemic of an emergent infectious disease – a context with which we are all now unfortunately very familiar from our recent experience with SARS-CoV-2. Since it is not possible to know *a priori* which (if any) avenues of research may prove to be successful in detecting or inactivating a new virus a variety of different approaches are normally explored by different groups. As evidence of both successes and failures emerges it is usual for the community to focus on a smaller number of options. Close contact with other researchers in the field and adequate contingency capacity is essential to achieve rapid progress and flexibility of response.

191. There had been concern since the early 1980s (PRSE0002343) that heat induced damage to the factor VIII molecule might produce antibodies to factor VIII (inhibitors) in patients. As late as January 1985, immunology experts opposed the introduction of heat treatment for this reason (PRSE0003980). The data of late October and early November described above were from an *in vitro* virus inactivation study, in which HIV was added to samples of Factor VIII, freeze dried, heat treated and tested for residual infectivity. PFC introduced dry heating as soon as there was preliminary data from the first in vitro HIV inactivation study and the key objective of heat treating all of PFC's output of Factor VIII to prevent AIDS transmission, was therefore achieved in December 1984.

192. ***SNBTS position:*** SNBTS does not think that PFC could have reasonably introduced HIV inactivated Factor VIII any more rapidly than it did in December 1984. It could be argued that to have done so earlier would have put patients at risk of inhibitor formation without any evidence to justify it.

8.5 Development and implementation of virus inactivation from 1985 and 1991 to inactivate the NANB agent.

193. There was no expectation that PFC's dry heat treatment at 68ºC for either 2 hours or 24 hours would inactivate the agents(s) responsible for NANB hepatitis, as it was known that FVIII from Cutter/Bayer dry heated at 68ºC for 72 hours had continued to transmit NANB hepatitis.

194. During 1985, PFC continued to focus primarily on the development of a pasteurised Factor VIII as this was the only virus inactivation technique for which evidence was available to demonstrate freedom from NANB hepatitis transmission. PFC's development of a very high purity Factor VIII was advancing well. This was aimed at removing concerns associated with the adverse reaction to PFC's pasteurised low purity Factor VIII and was regarded as also consistent with either the solvent-detergent technique, under development at the New York Blood Centre, or 80ºC dry heating of 8Y, whichever proved most effective against NANB and remained high yielding.

195. The first batches of Factor IX dry heat treated at 80°C for 72 hours were released to a few Scottish centres in August 1985 and across the country by October 1985. Existing stocks were recalled and destroyed.

196. The situation changed in December 1985, when PFC received a pre-publication copy of a Lancet paper which found that the inactivation of HIV by dry heat at 60ºC for 30 hours was much less than expected. At a meeting at PFC in late December 1985 it was agreed that in light of this we should introduce a greater degree of heat treatment as soon as possible to allay concerns over HIV transmission that could result when the Lancet paper was published. It had been discovered at PFC that the reason why 8Y could withstand dry heat at 80ºC for 72 hour was not due to its higher purity but to the way in which it was freeze dried. It was agreed that the quickest way of achieving a greater degree of heat treatment would be to adapt the earlier PFC pasteurisation process (ZHT) to dry heat FVIII at 80ºC (Z8).

197. Pilot manufacturing runs of Z8 took place in June 1986, with full-scale preparation in August 1986. Surprisingly, many vials of Factor VIII from first full scale production batch failed to meet the specified reconstitution time. The problem was traced to variations on the ice crystal structures that had formed when the FVIII solution was frozen within the freeze drier. The problem was solved by the end of September and a production batch of Z8 which had entered processing in early October 1986 was successful and placed at issue in early December 1986.

198. There were also problems in regard to clinical trials which did not start until February / March 1987. Z8 was made available for general use in April 1987.

199. The challenge facing all manufacturers was to achieve a method of virus inactivation that was not only effective against NANBH, but which had a high enough yield to be able to be applied to all of their FVIII production. The additional challenge facing state manufacturers, such as BPL and PFC, was to provide sufficient FVIII to meet the needs of their patient population (i.e. self-sufficiency).

200. Comparative information assembled by the Penrose Inquiry (Chapter 24 Tables 24.1) shows that PFL/BPL were the first fractionators able to apply a virus inactivation method to all of its Factor VIII production (8Y) from September 1985 which was later shown (October 1986) to have reduced NANB transmission (and finally confirmed as HCV safe in 1993). As noted above, PFC was able to make a Factor VIII product (Z8) available for clinical trial from December 1986 and sufficient amounts to meet the needs of all Haemophilia A patients in Scotland from April 1987. Table 24.1 of the Penrose Final Report shows that most commercial manufacturers released similar products between 1986 and 1990. As noted elsewhere the agent responsible for NANB (HCV) was identified in 1989.

201. With regard to Factor IX, both PFL/BPL (9A) and PFC (DEFIX) were able to make a product shown (in due course) to be safe from NANB transmission for all patients with Haemophilia B from October 1985. Table 24.2 of the Penrose Final Report shows that most commercial manufacturers released similar products between 1991 and 1992.

202. ***SNBTS position:*** PFL/BPL were the first fractionators in the world to manufacture a Factor VIII product (8Y) shown to be safe from NANB transmission. The development of a NANB inactivated Factor VIII product by PFC (Z8) took a further 18 months because the two manufacturing processes were not the same and therefore the BPL process could not be directly imported and a number of development problems had to be addressed.

203. The release of Factor IX products from both PFL/BPL (9A) and PFC (DEFIX) was aligned in October 1985, well ahead of commercial manufacturers.

204. It is surprising and a credit to the scientists involved that UK fractionators achieved virus inactivated products ahead of or contemporaneous with commercial fractionators given the substantially greater financial and research resources available to the latter.

8.6 Differential risk of cryoprecipitate vs coagulation factor concentrates

205. The question has been asked as to whether it would have been feasible and/or desirable to move back to cryoprecipitate once the risks from HIV and NANB hepatitis became clear.

206. The choice of product for the treatment of the patient is the responsibility of the attending clinician. However, it is clear that whilst cryoprecipitate could be (and indeed was) used for many years in a hospital treatment environment, various features of the product including lack of accurate potency, the need for it to be stored at -30^{O}C and the difficulty of reconstituting it for use, made it inappropriate or at least difficult for home therapy.

Factor concentrates on the other hand are of known potency, don't require freezing and are easier to reconstitute and are therefore more suitable for home therapy. For this reason factor concentrates were seen to afford more rapid treatment and a better quality of life.

207. The key questions from an SNBTS perspective are whether or to what extent it would have been possible to revert to cryoprecipitate for the treatment of Factor VIII deficiency and FFP for Factor IX deficiency and to what extent that may have reduced the incidence of infection amongst people receiving factor concentrates.

208. Edinburgh's first case of HIV was diagnosed in 1983 and as the decade went on the city's infection rate rose to nearly 7 times the national average. SNBTS introduced HIV inactivation of Factor VIII concentrates in December 1984 and HIV testing in October 1985. So, in retrospect, whilst cryoprecipitate was probably of less risk than factor concentrates from an HIV perspective in 1983/84 due to the lower degree of pooling, it would have been slightly more risk between January and October 1985.

209. With regard to NANB, in retrospect, the risk from cryoprecipitate was lower than that from factor concentrates through to the introduction of virus inactivation in April 1987, but then higher until the introduction of HCV testing in September 1991.

210. An analysis carried out for the Penrose Inquiry estimated the probability of infection with HCV via treatment with cryoprecipitate prior to the implementation of testing (WITN6666007). In 1974, patients with haemophilia A in the South East of Scotland were treated on average with 500 IU factor VIII/kg body weight /year. On this basis a typical adult patient with haemophilia would have received 313 units of cryoprecipitate per annum. Assuming an incidence of HCV in the donor population of 0.3%, it can be calculated that the probability of exposure to infection would have been 60% after one year and 85% after two years of treatment. If the prevalence was 0.1% in donations, then 27% of patients would be exposed to HCV at 1 year and 46 % at 2 years, reaching 95% after 10 years. This level of treatment did not encompass home therapy, nor did it include major reconstructive surgery, nor other elective or general surgical procedures, nor treatment of inhibitors with large amounts of factor VIII.

211. With modern treatment, a person with haemophilia A receives on average 2000 IU of Factor VIII thirty times per annum. This higher level of treatment would have required treatment with about 600 units of cryoprecipitate per annum, giving a probability of exposure to HCV (assuming a HCV prevalence of 0.3% in the donor population) of 83% after one year of treatment. After many years of treatment, for example from 1977 until effective heat treatment against HCV in the mid-1980s, this figure would approach 100%

exposure. For a lower prevalence of Hepatitis C of 0.1%, these figures would be a probability of exposure of 45% at 1 year, 70% at 2 years, and 95% at 5 years.

212. 70-80% of cases of NANB were associated with the first dose of concentrate the patient received. On the other hand once the lifetime exposure reached approx.100 donors (about 5 infusions) the risk of NANB infection approached 100% (WITN6666007).

213. The Inquiry has taken evidence on the manufacture of freeze-dried cryoprecipitate at Law Hospital up until March 1982 when it was closed following an adverse Medicines Inspectorate report (SBTS0000407_006). It would not have been possible to manufacture this product within PFC and new GMP manufacturing facilities would have had to have been established. Given that freeze-dried cryoprecipitate could not be heat treated, the same considerations in respect of risk of transmission of infection apply as to standard cryoprecipitate.

214. ***SNBTS position:*** Cryoprecipitate was probably of less risk of transmitting HIV than concentrates in 1983/84 due to the lower degree of pooling. PFC concentrates would have been safer than cryoprecipitate following the introduction of virus inactivation for HIV in December 1984 until the introduction of HIV testing in October 1985.

215. On the balance of probability, the majority of patients requiring large amounts of Factor VIII over prolonged periods of time would have been exposed to the risk of HCV infection irrespective of whether they received cryoprecipitate or Factor VIII concentrate. Cryoprecipitate would have posed less risk of exposure to HCV for those requiring small amounts or short duration of Factor VIII treatment up until the introduction of virus inactivation in April 1987.

8.7 Product labelling, information and warnings

8.7.1 Hepatitis Risk

216. In section 2.6 of page 2 of the PFC FVIII Product Licence Application of 30th March 1978 (WITN6914078), PFC wrote "*Product may carry the risk of transmitting serum hepatitis*"

217. The term 'serum hepatitis' had been replaced by 'hepatitis B' in 1947 (RLIT0001904). That PFC should have chosen to use an expression that was 30 years out of date indicates that it understood that the risk of transfusion transmitted hepatitis extended beyond HBV.

218. The product information leaflet used the expression "*..the general complications of hepatitis..'* without referring specifically to any particular form or strain of infectious agent.

219. The product information leaflet did note that the blood donations had "*been screened for the presence of the HB surface antigen using a radioimmunoassay"* which was a factual account of the screening test used but did not suggest that HBV was the only virus of concern. No other tests were listed as none were carried out.

8.7.2 AIDS Warning

220. All product warnings had to be agreed by the Committee on Safety of Medicines (CSM) before a product licence was granted and the CSM had a duty to advise licence holders of the need to provide warnings (Professor Michael Rawlins IBI transcript, 7 June 2022, page 77, lines 16-18).

221. PFC submitted an application for the renewal of its Product Licence for FVIII (NY) on 23rd September 1983. This was granted by CSM on 26th September 1983 without an AIDS warning, despite the risk of AIDS having been discussed at a CSM meeting on 13th July 1983 (PRSE0002300).

222. It appears that there was a meeting between SNBTS Directors and Haemophilia Directors in November 1983 in which the addition of an AIDS warning was discussed but not supported due to concerns around causing patients 'unnecessary anxiety' (PRSE0001244).

223. On 7th March 1984, the CSM approved an AIDS warning to be issued with a commercial FVIII concentrate (WITN6914080), but do not appear to have advised PFC to add an AIDS warning.

224. ***SNBTS Position:*** The view of the current SNBTS management is that whilst the labelling of plasma products in the 1980s was consistent with the practice of other plasma product manufacturers and compliant with the regulatory standards of the time, it would not be considered sufficient by modern standards and in retrospect the warnings given could have been much more explicit.

8.8 The move away from UK plasma in 1998

225. In 1998 the use of UK plasma for fractionation was banned by the then CSM on a precautionary basis due to concerns that variant CJD may prove to be transmissible by plasma products (MHRA0009455, MHRA0009404, DHSC0004790_065 and MHRA0034749_015). Historically, there was a significant amount of epidemiological data which showed no evidence of transmission of sporadic CJD by either blood components or plasma products (MHRA0009455, MHRA0009404, DHSC0004790_065 and MHRA0034749_015). However, there was recognition that variant CJD was a

different strain of prion disease, that there was evidence of prion accumulation in peripheral lymphoid tissues and that the incidence and prevalence of infection could be much higher due to the widespread exposure of the UK population of BSE infected beef. UK plasma was withdrawn from fractionation therefore as a precautionary measure to reduce both the risk of further transmission of infection and the risk of plasma product shortages due to withdrawal of plasma product batches if a donor developed vCJD.

226. The TMER (Section 7.3) identified 11 blood donors who later developed variant CJD who had contributed to 25 plasma pools from which 191 plasma product batches were manufactured.

227. The CJD Incidents Panel (since disbanded) requested a model to help assess the level of risk of exposure to variant CJD for recipients of plasma products. This model was developed by the Health Protection Agency and is now maintained by its successor body, the UK Health Security Agency (UKHSA). The model allowed the public health services to calculate a dose of each product (in implicated or non-implicated batches) beyond which it was likely that an infection-control threshold would be surpassed. It was kept under regular review and informed patient notification (and de-notification) exercises (DHSC0004206_072 and PHEN0000502). Patients recognised to have been at increased risk of exposure were, where possible, informed of their exposure to these products and precautionary steps taken to minimise the risk of any onward transmission through blood, tissue or organ donation, or by medical or surgical instrumentation. Further information can be obtained from the UKHSA website: https://www.gov.uk/government/collections/creutzfeldt-jakob-disease-cjd-guidance-data-and-analysis.

228. A presumed transmission of prions by plasma products was described in February 2009 as a result of the TMER and post-mortem surveillance studies in patients with haemophilia and primary immunodeficiencies (HCDO0000109_013, HCDO0000799 and WITN7034001 paragraph 4(d) (ii) page 13). The patient suffered from haemophilia and had received batches of Factor VIII to which a donor who subsequently developed variant CJD had contributed plasma. The patient died of other causes but was found at post-mortem to have evidence of prion accumulation in his spleen.

229. Considerable research was carried out by SNBTS PFC on the potential for the plasma fractionation process to remove abnormal prion aggregates and therefore reduce the risk of transmission of variant CJD by plasma products (RLIT0001888, RLIT0001889, IPSN0000214, RLIT0001890 and SBTS0003646_030.

230. Clinical studies carried out subsequent to 2009 provided evidence that it was unlikely that any UK clinical variant CJD cases were infected through exposure to fractionated plasma products (DHSC5574448 and WITN7034048).

231. In February 2021 the Commission on Human Medicines rescinded the ban on the use of UK plasma for manufacture of immunoglobulin products.

8.9 The closure of PFC in 2008

232. PFC products were supplied free of charge by SNBTS. However, the move from the use of recovered Scottish plasma to the purchase of international plasma (which accounted for 50% of PFC's operating cost) in association with the clinical introduction of recombinant coagulation factors and increased regulatory requirements led to the decision in June 2006 that the PFC was no longer economically viable and the closure of the facility in 2008.

233. Since 2006 SNBTS has acted as the wholesale distributor for commercial plasma products for NHS Scotland. These plasma products are procured through NHS National Services Scotland's (NSS) National Procurement (NP) function but are physically stored and distributed to hospitals by SNBTS under our Wholesale Dealers Authorisation.

Part 9: Clinical Transfusion Practice

234. The Inquiry will be aware of the complexities of the clinical use of blood and the importance of safe and appropriate, or effective, transfusion practice so that patients who need blood get the right blood, at the right time, for the right reason and in the right dose.

235. Whilst the Inquiry is rightly focused on the risk of contracting an infection from a blood component transfusion, it is now recognised that there are greater risks to patients from getting the wrong blood, getting too much blood too quickly or not getting blood when it is needed for acute bleeding or critical anaemia (https://www.shotuk.org).

236. Over the years covered by the Inquiry, and up to the current day, the improvements in clinical transfusion practice have come from the recognition that clinical staff need access to education about the benefits and risks of transfusion so that they can make evidence-based decisions to offer a transfusion to a patient.

237. Good practice emphasises the importance of accurate and accessible information for patients to support shared decision-making and, after being given the opportunity to ask questions, to allow them to give informed consent to be transfused, or to refuse transfusion, as is their right.

238. SNBTS has both led and participated in clinical initiatives to ensure that blood is transfused safely and appropriately. The Inquiry has heard evidence that the Edinburgh and SE Scotland Regional Transfusion Service developed an Effective Use of Blood project in the early 1990s, produced the first Handbook of Transfusion Medicine in 1989, and, with other doctors and nurses from Scotland, participated in the first Better Blood Transfusion (BBT) UK workshop in the late 1990s.

239. The BBT framework, the detail published in Scotland in a Medical Executive letter in 1999 (NHS MEL 1999 no 9 (scot.nhs.uk) (WITN7102002), has provided the clinical governance structure for blood transfusion which is in place throughout NHS Scotland today. From 2003 onwards, safe and effective clinical transfusion practice is supported by an SNBTS team of Transfusion Practitioners who work as transfusion subject matter experts in every Territorial Health Board.

240. The Inquiry will be aware that every hospital that transfuses blood must have a Hospital Transfusion Committee (HTC) to provide oversight and assurance that up-to-date policies are in place, that role-based transfusion training is available to all clinical staff that are involved with transfusion, that audit and monitoring of blood usage and wastage is undertaken and that any adverse incidents related to blood are fully investigated. The Hospital Transfusion Team is the multidisciplinary team that provides subject matter expertise to the HTC but also ensures that the day-to-day operation of a clinical transfusion service is delivered to the right standard and patients get the transfusion support that they need (WITN3530051).

241. The LearnBloodTransfusion (LBT) e-learning programme was started in 2004 and, until recently, was used throughout the UK. In Scotland it is mandated that all those in clinical transfusion practice complete the Safe Transfusion Practice module within the first few weeks of starting work in a Scottish hospital and compliance with this requirement is monitored by the HTC. Other modules available in the LBT e-learning portfolio include Blood Components and Use, Transfusion Reactions, Consent for Transfusion and resources to support Safe Sampling and Blood Collection. The SNBTS Transfusion Team signpost the modules to be completed by each staff group and ensures the modules are kept up to date. LBT modules are included in undergraduate programmes for Nursing and Midwifery students and Medical students so that new nurses and doctors are prepared for clinical transfusion practice.

242. The Account for Blood (AfB) development started in 2008 working with one Health Board and one Laboratory Information Management System (LIMS) provider. The feasibility of working with the LIMS system suppliers to provide an automated feed of data was

proven and during 2008-2009 was rolled out with other LIMS providers. The database was developed by the NSS Business Intelligence team during 2009 and by 2010 both the database and automated data feeds were complete. Each LIMS installation provides two data extracts overnight (a stock extract and a patient transfusion extract) and these are transferred, validated and loaded in the AfB database every morning.

243. The database now covers 95-98% of blood transfusions in Scotland and allows reports/dashboards/analysis to be produced on the use of blood components within and across health boards or hospitals. There are various measures of interest and performance including stock levels, wastage rates and transfusion rates. In addition, there are features of the blood component that are of interest (component age from donation, blood group) and features of the patients that are of interest (blood group, age, sex). Trends across time and variation across hospitals are important outputs. The data is used throughout NHS Scotland in hospitals in support of audits and quality improvement initiatives and by SNBTS for supply chain management, customer engagement, Service Level Agreements, quality improvement and demand planning. This database is important to SNBTS for resilience and longer term demand planning.

244. The Scottish Transfusion Epidemiology Database (STED) uses the patient data from Account for Blood system and links with hospital inpatient records via an automated monthly record linkage. Blood component use by clinical speciality, per condition/procedure and the proportion of patients transfused are important measures and, when combined with clinical and patient features, support clinical audit and research and allow insights on historical trends and practice variations to be explored. This clinical transfusion database provides clinical staff with information to demonstrate their compliance with best practice guidance and to track changes in blood usage related to implementation of quality improvement initiatives. It also provides a denominator for understanding adverse events of transfusion. The AfB data has been used to provide statistical information on clinical transfusion practice data for the Inquiry (EXPG0000049).

245. ***SNBTS position***: The current model of clinical transfusion governance and practice has enhanced the safety of transfusion throughout Scotland but there are still areas where improvements can be made. By working together with our colleagues in the Territorial Health Boards through the Scottish National Blood Transfusion Committee (SNBTC) and the Haematology and Transfusion Scotland (HaTS) Managed Diagnostic Network

we have identified that consent for transfusion and shared decision making, as recommended by the updated SaBTO consent guidance in 2020, needs to be improved and have developed a UK-wide patient information leaflet and a Scottish National Transfusion Record which guides clinicians through the consent process by virtue of a checklist.

246. SNBTS, along with other UK Blood Services has noticed an increase demand for blood over the past 12 months, reversing the trend of gradual reduction in blood usage over the last 15-20 years. In order to maintain sufficiency of supply, SNBTS aims to work with clinicians to ensure that evidence-based Patient Blood Management principles are being applied to patient care through a combination of providing blood use data, as previously described, as well as convening a Scottish Appropriate Use of Blood group as a sub-group of the SNBTC.

247. SNBTS works closely with the SHOT UK haemovigilance scheme to ensure that learning from adverse events is shared, recommendations are implemented and systems are thereby improved (WITN7312001).

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Part 10: References

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PRSE0004042	SNBTS Report titled 'Lookback Procedures to identify, trace and offer counselling and testing to patients who received blood components from donors subsequently found to be positive in tests for HIV and HCV'
PRSE0004114	Letter from Dr J Gillon to J D Cash Donor Counselling - HCV
PRSE0004163	Minutes of a Directors' Meeting Held in HQ Unit on 3 March 1987. Issues raised include AIDS and heat treatment, donor literature, donor attendance, HTLV-I and HTLV-II, surrogate testing for NANB, product liability, clinical trials and minimum ages for donation. (CT) (DT) (HT)
PRSE0004264	Letter from (Not stated) to regional Administrators, titled 'Blood products production' content describes the need to provide more concentrate', dated 24 December 1974.
PRSE0004275	Report on Ortho HCV Symposium
PRSE0004356	Annals of Internal Medicine, "Hepatitis B Virus Antibody in Blood Donors and the Occurrence of Non-A. Non-B Hepatitis in Transfusion Recipients" by Cladd E. Stevens et al. 1984
PRSE0004402	Report of HCV Symposium Organised by Ortho regarding HCV and the blood transfusion service
PRSE0004584	Proposal for a prospective study of post transfusion hepatitis in the UK.
PRSE0004647	Minutes of SNBTS Directors' meeting held on 27 September 1988
PRSE0004669	Minutes of UK Working Party on Transfusion associated Hepatitis. Discussion on hepatitis in haemophiliacs and surveillance of Oxford haemophiliacs in addition to comments on AIDS in the UK and how to prevent high risk groups donating without causing a scare.
PRSE0004706	Meeting minutes of the Expert Group on the Treatment of Haemophilia. Provides several recommendations to the DHSS, including discussion of: reinstating a national central register for haemophiliacs; Dr Biggs' paper on haemophilia treatments; the increasing demand for AHG concentrate to supply prophylactic treatments; need for UK to become self-sufficient in AHG concentrate; cooperation between England, Wales, Northern Ireland and Scotland.
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