Presentation Note on the Belfast Haemophilia Centre

Introduction

1. This Note is intended to provide an overview of the Belfast Haemophilia Centre ("the Centre") and its activities, based on the documents received by the Inquiry. The oral presentation on 30-31 March 2021 will draw on these documents (as well as referring to evidence of people who were treated at the Centre and to the written evidence of Dr Mayne). The oral evidence of Dr Benson on 1 April 2021 will address the practices of the Centre from 2008 onwards in more detail. The Inquiry is seeking statements from other clinicians involved in providing treatment in Northern Ireland and any statements received will of course be disclosed.

Overview of Centre

The Centre

2. The Belfast Haemophilia Centre was established by Professor Nelson in 1958 and was located within the Clinical Pathology Department. It appears that in 1958 there were 44 patients with Haemophilia A registered at the Centre and one patient with Haemophilia B [RHSC0000067_002 p.2]. This remained the number during the 1960s [WITN0736009 at §8.1]. In 1968, it is noted that there was no physical location of the Centre, nor any dedicated staff or in-patient facility. At that time there were forty-four families registered [WITN0736008 at §2.2[1]].

3. Professor Bridges has estimated that there were approximately 10 patients with bleeding disorders attending the Children's Hospital prior to 1979 [WITN4569001 at §6].

4. During the 1970s and early 1980s, the number of patients at the adult Centre increased and the staff team also grew, to include a part-time physiotherapist from 1983, a full-time nurse, a secretary and a part-time social worker.

[1] There are two paragraphs §2.2 in the statement. This refers to the second of these paragraphs.

5. Until 1981, the Centre was included in the Oxford supra-region [HCDO0000405 at p.6]. However, in February 1980 it was agreed that Belfast should become a Reference Centre[2] and in the UKHCDO minutes of 14 September 1981, it was noted that Dr Thornton, DHSS Northern Ireland Office, had written to Professor Bloom confirming the Royal Victoria Hospital had been designated as a Haemophilia Reference Centre [LOTH0000012_122 at p.1].

6. The Centre served patients drawn from all over Northern Ireland with a reciprocal arrangement with the Centre in Dublin, enabling a small number of patients from the Republic of Ireland to attend Belfast for travel convenience, and Belfast patients to receive free treatment at southern Centres when in the Republic [HSOC0022947 at p.9].[3] Treatment on short visits was not cross-charged but more substantial treatment requirements were [BHCT0000622].

7. During the mid-1980s, there was added to the team a full-time Medical Registrar, a second nurse, a part time aromatherapist and reflexologist, another secretary, receptionist and finally a full-time scientist [HSOC0022947 at p.8]. By 1989, there appears to have been a further nurse caring for haemophilia inpatients [HSOC0022947 at p.8].

8. In relation to patient numbers in 1985 there were 189 persons on the register, with 124 patients with haemophilia A, 16 with haemophilia B, 45 with von Willebrand's, 2 with Factor X deficiency, 1 with Factor XIII deficiency and 1 with Factor XI deficiency [BHCT0000503].

9. In 1988 there were approximately 80 patients per year treated at the Belfast Centre [SBTS0000297_008 at p.2]. The documents provide slightly different figures for the numbers of patients registered: one document states that there were 125 patients with Haemophilia A, 13 with Haemophilia B, 55 with von Willebrand's disease and 20 with other inherited disorders [RHSC0000067_002 at p.2]; another gives the same figures

[2] Although a document authored by Dr Mayne in 1985 appears to suggest that it became a Reference Centre in 1976 [BHCT0000503].
[3] It appears that some payment was made by the Republic of Ireland for treatment received in Belfast, at least in 1984, albeit this was by the provision of concentrates rather than money: BHCT0000623.

for Haemophilia A and B but states that there were 69 with von Willebrand's and 11 with other inherited disorders [HSOC0022947 at p.8].

10. The physical facilities had also developed such that by 1989, there was a designated Day Centre and an inpatient unit with 16 designated beds, with at least 25% of them being occupied by haemophiliac patients most of the time [HSOC0022947 at p.8].

11. By March 1988, a joint haemophiliac/orthopaedic clinic was being held every three months [RHSC0000067_002 at p.7] and in 1989 it was noted that there was also a regular dental clinic for the management of patients with bleeding disorders [HSOC0022947 at p.8].

12. An audit of the Centre in 1991 by Dr Ludlam on behalf of the Haemophilia Centre Directors of Scotland and Northern Ireland noted that there needed to be improvements in the privacy of bedside and telephone conversations, with a need for dedicated rooms. It also highlighted a need for more social work and physiotherapy input [LOTH0000051_089]. In a report of the Regional Centre in 1991, Dr Mayne recorded that there had been attendances, either outpatient or inpatient, of 147 patients with Haemophilia A, 14 with Haemophilia B, 61 with von Willebrand syndrome and 7 symptomatic carriers of Haemophilia A [WITN0736010]. By 1999 there were 300 people on the haemophilia and bleeding disorder register [WITN0736009 §8.1].

13. In 2001/2002 haematology services at the Royal Victoria Hospital were amalgamated with the City hospital and the Centre is now based at the Belfast City Hospital. It is co-located with the haematology and oncology outpatient clinics. Patients attend the Centre for routine outpatient appointments and acute unscheduled care during the hours of 9-5, Monday to Friday. Out-of-hours care is now provided via a telephone helpline and attendance at the Royal Victoria Hospital emergency department if required [WITN3082015 at §14-15]. The Centre comprises three consulting rooms, a phlebotomy room, nursing room, resource room, secretary/receptionist office and a waiting area [WITN3082015 at §16].

14. Patient numbers in 2008 were 41 with severe haemophilia A and B; 1 with Type 3 von Willebrand's and 2 with Bernard Soulier [WITN3082015 at §37]. There was a total of

292 patients with a bleeding disorder registered. Staffing in 2008 consisted of a single-handed consultant, two nurses, a specialty doctor and a clinical scientist together with a secretary, receptionist, a specialty registrar on rotation and two band 7 biomedical scientists in the specialist coagulation laboratory [WITN3082015 at §18]. By 2008, the only specialist clinic that operated was an HIV service [WITN3082015 at §20].

15. As of 2020, patient numbers have increased to 64 patients with severe haemophilia A and B, 3 with type 3 von Willebrands, 6 with Bernard Soulier, 1 with Glanzmann thrombasthenia, and a total of 596 patients with a bleeding disorder [WITN3082015 at §38]. The staff has also increased to two consultant haematologists (of which one post is vacant), a specialty doctor, four nurses (constituting 3 wte), a dedicated haemophilia social worker, physiotherapist, occupational therapist and two clinical scientists [WITN3082015 at §18].

16. The HIV joint clinic continues to run on a 3-4 monthly basis. Since 2008, new clinics were established including a combined obstetric haematology clinic [WITN3082015 at §24]. A satellite review service was established at Altnagelvin Hospital.

17. From the evidence of Dr Mayne, it appears that children transferred to adult care, from the Royal Belfast Hospital for Sick Children to the Royal Victoria Hospital, at approximately 13 years old [WITN0736006 at §22]. However, Professor Bridges notes that he would have referred a child requiring factor concentrates, rather than cryoprecipitate, to Dr Mayne at the adult hospital because of her clinical experience [WITN4569001 at §5].

18. By 2008, the transition took, and takes, place from the age of 14 but usually at around 16 [WITN3082015 at §25].

Dr Elizabeth Mayne

19. Dr Mayne trained in Belfast, working as a Senior Registrar in Haematology at the Royal Victoria Hospital from 1968 to 1972. She completed her MRCPath in 1970 and became a Consultant Haematologist in 1972. Dr Mayne remained at the Royal Victoria,

Belfast throughout her career, until her retirement in 1999. She was the Director of the Northern Ireland Haemophilia Reference Centre from 1978 to 1999 [WITN0736001 at §1.2], [HSOC0022994 at p.7].

20. Dr Mayne was a member of a wide range of committees/organisations; she was the Vice President of the World Federation of Haemophilia, and the Chair of the UKHCDO from 1990-1993. She was also a trustee of the Macfarlane Trust and the Eileen Trust in the early 1990s.

21. Several witnesses have criticised her tone and manner towards them, or said that she made inappropriate comments [for example, WITN1371001 at §20-§21]. Dr Mayne has responded to a number of the witnesses and addressed the circumstances raised in their statements. She denies that she made inappropriate comments and defends her tone and manner [WITN0736005], [WITN0736007].

Other clinicians

22. Professor John Bridges was appointed as Consultant Clinical Pathologist at the Royal Group of Hospitals in Belfast, based at the Royal Belfast Hospital for Sick Children. From 1979 he only spent 50% of his time in clinical practice, following his appointment to the Chair of Haematology at Queen's University Belfast. He primarily worked at the adult hospital thereafter, in leukaemia and general blood disorders, only providing cover for Dr Mayne in relation to patients at the Centre. Dr Dempsey took on his work at the Children's Hospital. Professor Bridges retired in 1994 [WITN4569001 at §2].

23. Dr Moulod El-Agnaf worked as a Registrar in Haematology at the Royal Victoria Hospital from August 1982 until July 1983 before moving to the Belfast City Hospital, where he worked until 1985. In 1985 he joined the Northern Ireland Blood Transfusion Service for around four months before returning to work as a Registrar at the Royal Victoria from August 1985 until December 1987. In January 1988 he became the Acting Consultant Haematologist at the Belfast City Hospital. In August 1988 he became the head of the Haematology department at Altnagelvin Area Hospital. In

March 1993 he became the head of department at the South Eastern Trust / Ulster Hospital.

24. Dr Orla McNulty worked in the Centre from 1992, becoming a Staff Grade doctor in 2000 and Associate Specialist in 2008 [WITN0921001 at §2.2 and §2.9].

25. From 1999 to 2001, Dr Frank Jones was acting Director and in 2001 Dr Julia Anderson was appointed as a full-time haemophilia consultant [WITN0921001 at §2.7]. She remained in post until 2005 and there was then a further period in which Dr Jones acted in a supervisory capacity until Dr Benson was employed (with a brief interlude of six months in which Dr Dennis O'Keeffe was appointed consultant in 2006).

26. Dr Gary Benson was appointed in February 2008 and continues in post as Consultant Haematologist and Clinical Director for Blood Services within the Trust [WITN3082015]. He was joined by Dr Christopher McCauley from August 2016 to March 2020

Use of blood products

27. The Inquiry has received evidence describing treatment at the Royal Victoria Hospital with fresh frozen plasma and whole blood during the late 1950s and 1960s [for example, WITN3356001]. Prior to the advent of factor VIII and factor IX it appears the main product of choice was cryoprecipitate.

28. Professor Bridges states that during his time at the Children's Hospital, that is, until 1979, the main treatment for children with haemophilia was cryoprecipitate [WITN4569001 at §5]. He did not use factor concentrates because he was unfamiliar with them. Dr Mayne states that the decision to keep children on cryoprecipitate rather than switch to home treatment with concentrates was her decision and was one which Professor Bridges was happy with. The decision was made in the early 1970s because *"I was anxious and apprehensive about repeatedly injecting patients with any material, particularly over periods of weeks and months via the intravenous route."* [WITN0736009 at §14.3].

29. In 1989, Dr Mayne, setting out the history of haemophilia care, described patients as being "*ecstatic*" with the advent of cryoprecipitate [RHSC0000067_002 at p.2]. However, in her HIV Litigation Report of May 1991, she described difficulties in the use of cryoprecipitate: *"A major disadvantage was the unpredictability of infused dosage... A further disadvantage was the necessity of storage of the product within a deep freeze unit. Advantages were efficacy, low donor exposure and simplicity of manufacture"* [CBLA0000072_024 at p.7]. She stated that the development of factor concentrates *"had an estimated dose content. They enabled accurate calculated doses of Factor VIII to be given in small volume, associated with a decreased chance of clinical side effects. They represented manifest advantages over cryoprecipitate"* [CBLA0000072_024 at p.7].

30. There were concerns about the units of factor VIII per pack of cryoprecipitate. Nevertheless, Dr Mayne noted on various occasions that clinically the cryoprecipitate was still effective [BHCT0000492], [BHCT0000496], [BHCT0000494], [BHCT0000495], [BHCT0000651] and [BHCT0000491].

31. Correspondence suggests that the treatment of patients with inhibitors was, however, considered challenging, the inhibitors rendering cryoprecipitate "*virtually useless*" [BHCT0000651]. Moreover, any treatment that was required raised concerns about future difficulties in achieving haemostasis [BHCT0000647].

Early use of concentrates

32. The Inquiry is aware of a patient receiving factor VIII concentrate for the first time in February 1970. It seems that Dr Mayne was cautious about its use, saying: *"In view of the importance of this knee joint to [X's] everyday life and well being, and in consideration of the fact that he had received no cryoprecipitate for at least one year, we decided to treat him with Factor VIII concentrate on this occasion"* [BHCT0000784]. It appears that the caution arose because of this particular patient's previous reactions to cryoprecipitate and the concern that he may be developing an inhibitor, rather than any concern specific to factor concentrates *per se* [BHCT0000795]. It is notable that Dr Mayne had decided not to inform the patient or his parents about the possibility of inhibitor development. However in her witness

statement, Dr Mayne refers to the first use of factor concentrate being in November 1971 in relation to a patient with severe intestinal bleeding who had developed inhibitors [WITN0736009 at §10.2].

33. In Dr Mayne's statement, she has indicated that Hemofil was the only concentrate that was used for the first three years [WITN0736009 at §10.3]. In June 1972, she sought the advice of Dr Rizza when deciding which factor concentrate to prescribe for a patient to carry on holiday [BHCT0000743_001] considering switching a patient to factor concentrates.

34. By January 1974, Dr Mayne reported that in Northern Ireland they were using material prepared from approximately 10,000 donors and a stock was kept of commercial concentrate [CBLA0000187 at p.6].

Choice of factor concentrates

35. In one of her witness statements, Dr Mayne states that in the mid-1970s when she *"initiated a Home Treatment (HT) programme for severely affected patients commercial Factor Concentrate had to be used. The following policy for the NI Haemophilia Centre was drawn up by myself and is as follows:*

    i) All HT patients would be treated with only one product: KRYOBULIN Immuno Ltd Vienna
    ii) All non HT patients would be treated with HEMOFIL Travenol Laboratories USA.
    iii) *All children would continue to be treated with cryoprecipitate. There were two exceptions; namely 2 severely affected children who were entered into the HT group."* [WITN0736006 at §5].

36. According to another document authored by Dr Mayne, this policy was adopted in 1977 [WITN2658002 at p.14].[4]

[4] Another document indicates that home treatment commenced in 1974 but suggests that the same policy applied [RHSC0000067_002 at p.3].

37. Dr Mayne explains that she chose Kryobulin because *"I found the company business-like, straightforward and their packaging was ideal. Incidentally, the source of their donors was within Europe."* Hemofil was chosen because she had been familiar with it since 1971 [WITN0736006 at §7]. Subsequently, in late 1982, Factorate was also introduced.

38. However, in a meeting with a director of Speywood on 10 October 1978, further evidence is provided as to the possible reasons for the loyalty to Hemofil. In a memo of the meeting, David Williams notes: *"Dr Mayne is not prepared to change her present policy concerning human factor VIII. She uses Hemofil for operations and Immuno for home treatment (22 patients). She realises this is an expensive policy, but feels that treatment changes are something best avoided with Haemophiliacs. She is very concerned about liver enzyme changes, but at least she knows what to expect with products which have been used for some years. There is also loyalty to Hemofil, because Baxter obviously gave her considerable financial help in the early days"* [IPSN0000332_021].[5] It is presently not known what the "*considerable financial help*" related to. In January 1979, Dr Mayne indicated that Koate was more expensive than the two products she was using at that time [IPSN0000332_017]. However, due to a price reduction in February 1979, Dr Mayne went on to order 30,000 units of Koate [IPSN0000332_015 and IPSN0000332_016]. It is unclear how this evidence fits with her avowed intention of not switching between products.

39. With regards to factor IX concentrates, Dr Mayne has described research she undertook to develop a concentrate for Haemophilia B. When she presented this to Dr Bidwell of the Plasma Fractionation Unit at Oxford, she was initially dismissed. The next day however Dr Bidwell telephoned Dr Mayne to inform her that her research was excellent but was too late: a French product was being released 6 weeks later. Dr Bidwell thereafter provided Dr Mayne with Oxford Factor IX, 9D, until (according to Dr Mayne) commercial products were introduced in the mid-1980s because UK supplies could not cope with demand [WITN0736005 at §§3.3.2-3.3.4].

40. The available annual returns demonstrate the following:

[5] Related correspondence can be found at [IPSN0000332_019] and [IPSN0000332_020].

a. In 1976, 37 patients with haemophilia A were treated, of whom 6 had factor VIII antibodies, and 6 patients with haemophilia B. Cryoprecipitate, Hemofil and Kryobulin were used together with NHS Factor IX and a small quantity of Prothromplex [HCDO0000054_006].

b. In 1978, 51 patients with haemophilia A were treated, of whom 9 had factor VIII antibodies, and 4 patients with haemophilia B. There were 7 patients with von Willebrand's disease. Cryoprecipitate, NHS factor VIII and IX, Hyland and Immuno were used together with FEIBA and Proplex. The von Willebrand's patients received cryoprecipitate and Immuno fibrinogen. In her letter to Miss Spooner, Dr Mayne noted that '*a few patients are treated in the peripheral hospitals'* and as a result it was '*impossible to obtain accurate records of the therapeutic materials such as cryoprecipitate used in these hospitals.*' [HCDO0001231].

c. In 1979, 63 patients with haemophilia A were treated, of whom 10 had factor VIII antibodies, and 2 patients with haemophilia B. There were 8 patients with von Willebrand's disease. The largest factor VIII used was Hyland, followed by Immuno. A smaller amount of Cutters factor VIII was used, as well as cryoprecipitate and NHS factor VIII. A very small amount of bovine/porcine factor VIII was used. One carrier of haemophilia was treated with Kyrobulin. The return states that all haemophilia B patients received NHS factor IX. The von Willebrand's patients received plasma, cryoprecipitate and DDAVP [HCDO0001300].

d. In 1980, 65 patients with haemophilia A were treated, of whom 8 patients had von Willebrand's disease. 4 patients with haemophilia B were treated. Haemophilia A patients received cryoprecipitate, NHS factor VIII, Armour, Immuno and Hyland factor VIII. A small amount of Speywood porcine factor VIII and Immuno FEIBA was also used. Haemophilia B patients were treated with NHS factor IX [HCDO0001394].

e. In 1983, 72 patients with haemophilia A, 2 carriers of haemophilia A, 16 patients with Von Willebrand's disease and 5 haemophilia B patients were treated. In

relation to patients with haemophilia A, the product used to the greatest extent was Factorate – some 289,630 units in hospital and 505,844 units in home treatment. 27,419 units of Kryobulin were used in the hospital and 422,497 units in home treatment. 159,090 units of NHS concentrate were used and only in hospital. Only NHS Factor IX concentrate was used for patients with haemophilia B. There were 9 haemophilia A patients with antibodies, and the annual return notes that five patients responded well to Hyate C. This was the majority treatment used for patients with inhibitors, alongside Factorate, Autoplex, Hemofil, Kryobulin and FEIBA [HCDO0000153_003], [HCDO0000153_004] and [HCDO0000153_005].

f. In 1984, 82 patients with haemophilia A were treated, of whom 1 was a carrier. 8 patients had von Willebrand's disease and 4 patients had haemophilia B. 8 patients had factor VIII antibodies. In addition to cryoprecipitate and NHS factor VIII, Armour, Immuno and Travenol factor VIII were used. There was a significant increase in use of porcine factor VIII but the majority of this appears to relate to one patient. NHS factor IX concentrate was used for the haemophilia B patients [HSOC0016545].

g. In 1986, 81 patients with haemophilia A, 2 carriers of haemophilia A, 11 patients with Von Willebrand's disease and 4 haemophilia B patients were treated. In relation to patients with haemophilia A, it appears that the product used to the greatest extent was NHS Factor VIII concentrate with 1,421,490 units in hospital and 775,980 in home treatment. 475,666 and 125,452 units of Profilate were used in hospital and for home treatment respectively. Small quantities of Factorate and Hemofil were also used. Only NHS Factor IX concentrate was used for patients with haemophilia B [HCDO0000362_008].

41. A document written by Dr Mayne on 1 August 1985 records the following: *"Up until December 1984 the [home] treatment was virtually all commercial imported material and up until the end of 1982 this all originated from Immuno in Vienna, namely European Factor VIII. Thereafter the scare and implications for AIDS made great inroads into the European supplies, therefore we were grateful to receive American material from Armour... They were already regular suppliers of material for inpatient*

surgery." [BHCT0000503]. She states that NHS Factor VIII only became available in December 1982. Figures are then given:

a. 1982: Immuno 648,707; Armour 478,137; NHS 12,960.

b. 1983: Immuno 451,497; Armour 505,844; NHS 159,090.

c. 1984: Immuno 441,408; Armour 506,184; NHS 525,710.

42. Dr Mayne records that *"It is clear from these figures that the increased use of NHS material should have produced an economy in the purchase of commercial material but, due to extensive orthopaedic surgery being necessary following a series of road traffic accidents and bone fractures, the increase in NHS material was inadequate for needs"* [BHCT0000503].

43. A completed survey form in April 1985 indicates that by then the Centre was primarily using heat-treated factor VIII and un-heat-treated factor IX from Scotland. There appears to have been occasional use of heat-treated commercial factor VIII and occasional use of cryoprecipitate for children [BHCT0000907]. The use of heat-treated product is addressed further below.

Prophylaxis and home treatment

44. Dr Mayne records that the first patients in the home treatment programme commenced home treatment in around 1976 [WITN0736001 at §2.1].[6] One of her statements suggests that of 110 annually treated patients, 43 (or perhaps 47) were on home treatment [WITN0736006 at §8]. By 1989 50 patients were on home treatment [HSOC0022947 at p.9].

45. It appears that initially the Eastern Area Health and Social Services Board had some reservations about home therapy and the training of non-medical personnel to give the

[6] Another document dates its commencement at 1974: RHSC0000067_002 at p.3.

therapy. However, there is no evidence that this concern went further than raising questions about it [BHCT0000573].

46. In 1979, Dr Mayne, in an article for the Haemophilia Society, set out the difficulties faced by haemophiliacs when attending hospital and having to deal with doctors who were not sufficiently competent in the treatment of haemophilia. In addition, she advocated the use of prophylaxis to avoid *"stressful situations developing. Certainly I have found that, coming up to exams etc, a small dose of factor VIII is all that is necessary to keep the haemophiliac on an even keel. I think it is because he realises that people are concerned and in some way this sorts out the bleeding problems!"* [HSOC0022869 at p.3]. Similarly, in 1989 "*non-therapeutic injections*" were noted as being used "*before times of known or possible stress*" [HSOC0022947 at p.9].

Mechanics of supply

47. It is clear from the documents that throughout the 1970s and 1980s, Dr Mayne was personally addressing product supply. Consequently, she was in communication with PFL arranging for factor concentrate for a particular patient for surgery [BHCT0001061_002], BPL for the provision of factor IX [CBLA0004486], corresponded with Speywood about possible supply of Koate and sampling Hyate:C [IPSN0000332_017] as well as arranging for particular products to be ordered through the Royal Victoria Hospital pharmacy [IPSN0000332_015].

48. In September 1980, Dr Mayne raised the question of whether there was any way for plasma collected from Northern Ireland to be fractionated, in order to help with the shortage of supply. She was assured by Dr Walford that this was being looked into [PRSE0003946 at p.7]. It was not until 1982 that any progress appears to have been made in relation to this.

49. From 1 April 1981, BPL planned to supply products on a pro rata basis according to the plasma supplied by the region. At the time the Northern Ireland Blood Transfusion Service ("NIBTS") was said to be receiving over 1000 vials of factor VIII from BPL annually. NIBTS at that time was unable to supply fresh frozen plasma to either BPL or PFC and so would not under the pro rata system proposed be entitled to factor VIII.

Initially it was planned that NIBTS would still receive blood products while they worked to scale up supply of cryoprecipitate and established a mechanism for transporting fresh frozen plasma to BPL or PFC [CBLA0001294 at p.2]. Subsequently, the service was transferred to PFC and the Blood Transfusion Service was required to pay for all products supplied [RHSC0000066_024 at p.2]. It was agreed that Northern Irish fresh frozen plasma would be sent to PFC and they would then receive a pro-rata supply of factor VIII [CBLA0001287 at p.3]. A formal request for the transfer of the supply of blood products from BPL to PFC was made by letter dated 7 May 1981, with the expectation that plasma would be sent to Liberton by October 1981 and finished products would be received from March 1982 [SCGV0000104_134]. It was subsequently noted that these arrangements in 1982 were put in place *"in response to a number of issues one of which was the major financial outlay on commercial products"* [NIBS0001721]. Until the changeover occurred in March 1982, BPL provided factor VIII to Northern Ireland [CBLA0001388 at p.2]. Thereafter, plasma was donated and transported by the Blood Transfusion Service and a charge was made for fractionation and appropriate heat treatment before the material was returned to Northern Ireland [RHSC0000067_002 at p.6].[7]

50. On 25 May 1984, the Eastern Health and Social Services Board noted that in monitoring the arrangements with the Scottish Health Services they had received advice that *"there is now a sufficiency of the NHS product to cover all current demand for Factor VIII"*. The letter states that there was now self-sufficiency of product and requested that Dr Mayne explain which patients would require commercial concentrate and the clinical reasons for that [NIBS0001721]. In a memo dated 25 October 1984, the Eastern Health and Social Services Board recorded an agreement that, with effect from 1 December 1984, all blood products identified on the schedule (which the Inquiry does not presently hold) must be purchased from the NI Blood Transfusion Service, and not be purchased or obtained by a UMG directly. The rule would also apply to new blood products coming on to the market [BHCT0000501]

[7] This process is also reflected in Dr Mayne's request at the Scottish Factor VIII Working Party meeting of 8 September 1988 that the figures for supply of plasma from Northern Ireland to PFC should be presented separately to the other data on supplies of plasma into PFC [SBTS0000297_032 at p.2].

Shortages and budget constraints

51. By letter dated 10 September 1976, Dr Mayne raised concerns with the Group Accountant of the Royal Victoria Hospital that the laboratory was paying for the treatment of all patients with bleeding disorders in Northern Ireland. She asked whether some of the costs could be recouped from other districts of the Eastern Area Board [BHCT0000502]. The difficulties do not appear to have been resolved because on 22 November 1983, Dr Mayne wrote to Professor Bloom asking for information about how funding was addressed in Wales because *"there has been considerable unrest in the Finance Department of this Hospital due to the large drug expenditure for the treatment of haemophiliac patients. ... The vast majority of patients under treatment in this Centre are resident in the three boards outside our own region"* [BHCT0000504].

52. On 25 March 1988, Dr Mayne wrote a document headed "A Profile of the Management of Haemophilia in Northern Ireland" [RHSC0000067_002]. She stated that *"The funding of therapeutic materials for the Haemophilia Centre has not been clearly thought out and appropriate guidelines established"* (at p.5). She notes that until the early 1980s, the cost of purchasing commercial concentrates was borne by the Royal Victoria Hospital pharmacy budget. Thereafter in 1985, it was transferred to the Northern Ireland Blood Transfusion Service. This coincided with a reduction in the volume of commercial concentrate that was purchased and the commencement of the use of NHS Factor VIII from the Scottish Home and Health Department.

53. Funding was a difficult issue for the Centre in 1988 such that on 1 April 1988, Dr Mayne wrote to all home treatment users asking them to be more economical in the use of their home treatment material because the Eastern Health and Social Services Board ("EHSSB") were threatening to cut the Blood Transfusion Service budget by one million pounds [BHCT0000572_001].

54. The Treasurer's Department of the EHSSB produced a paper in February 1989 which provides insight into the financial issues at that time. It notes that the Northern Ireland Blood Transfusion Service bore the cost of all clotting agents issued from the Haemophilia Centre for all patients in Northern Ireland. No cross charging was used. The paper notes the significant overspend by the Blood Transfusion Service and states

that *"The major cause of increased costs has been the availability of improved treatment for the rare group of inhibited haemophiliacs (11 people in Northern Ireland at present) who do not receive relief from the 'normal' Factor VIII produced by PFCE"*. The cost of treatment for these patients was £1.3m in 1987/8 and just over £0.8m in 1988/9 [RHSC0000066_024 at p.4].

55. Financial issues were not the only concern. In her litigation report in relation to one patient, Dr Mayne notes that it was difficult to maintain large stocks of material, particularly Kryobulin, because it was distributed to home treatment patients. Moreover, in late 1982 and throughout 1983, there were supply issues with Kryobulin, resulting in the introduction of Factorate, produced by Armour [WITN2658002 at pp.15-16]. Subsequently, Dr Mayne, in a witness statement produced for the Inquiry, has stated that the reason for the introduction of the Armour product was because demand exceeded supply [WITN0736006 at §7].

56. Budgetary concerns appear to have continued throughout the 1980s and 1990s culminating in a lengthy paper drafted by Drs Mayne and Dempsey for the Regional Medical Services Consortium in 1996 setting out the ongoing overspend of the transfusion service budget due to the purchase of commercial products [RHSC0000285].

Self sufficiency

57. In her HIV Litigation report in 1991, Dr Mayne refers to the concerns of the UKHCDO regarding the delays in achieving self-sufficiency. Of note, she records her "*personal recollections of discussion at that time*" in relation to the suggestion towards the end of 1975 that Scotland could supply more Factor VIII. She states that *"during prolonged subsequent negotiations it transpired that a shift system of staffing would be necessary to render the suggestion operational. Such arrangements were unacceptable to trade union policies, then in operation, thus causing further delays in a possible field of improvement. Other highlighted difficulties were in the collection, transport and delivery of plasma to the plasma fractionation centre in Edinburgh"* [CBLA0000072_024 at p.24].

58. She goes on to state her view that had the Department of Health provided further financial support at an earlier time, it would "*probably*" have "*accrued significant patient benefit*". Having quoted the lower HIV infection rates in the Netherlands, she notes that *"the treaters of the Haemophiliac patients would feel it to be likely but it is by no means certain"* that a similar result might have been achieved in the UK (at p.25).

Heat treated factor products

59. In her HIV Litigation Report, Dr Mayne notes that in 1984 commercial heat-treated products were available but *"preliminary reports suggested that the viral infectivity problem was far from resolved"* [CBLA0000072_024 at p.28]. She notes confirmation in 1984 that heat treatment destroyed the HTLV-III virus but states that fears of inhibitors were only dispelled in 1985. While she refers to the use of commercial concentrates on a named patient basis, Dr Mayne gives no indication in the Litigation Report as to her own personal practice.

60. Infusions of dry heated Factor VIII were used in Edinburgh in late November / early December 1984. Belfast was to receive the first vials of the dry heated material on 10 or 11 December 1984. These vials were anticipated to be a one month's supply. These supplies were not dedicated batches from the specific regions. Thereafter the plan was for PFC to provide Belfast, and the Scottish centres, with twice their minimum /maximum stock level so that stocks could be replaced. Centres were asked to make arrangements for non-heat treated material to be recalled ready for PFC to collect it in the New Year [PRSE0002675].

61. On 13 November 1986, Dr Cash noted that PFC intended to begin routine production of a new heat-treated product, Z8. It would be dry heat treated at 75°C for 72 hours. Dr Boulton was asked to liaise with Dr Mayne, Dr Ludlam and Dr Forbes *"with a view to obtaining t/2 and % recovery data on this product."* It was hoped that data should be obtained from a total of six patients [PRSE0002335]. Other documents suggest that Dr Mayne started using Z8 in July 1987 and she wrote that by February 1988, 28 patients had been treated "*on many occasions*" with seven batches [PRSE0000129 at p.39]. There had been one adverse event in keeping with non-A non-B hepatitis but it

transpired that this was likely to have been caused by an "*old generation*" Z8 product that had not been heat treated to the same degree [SBTS0000495_242] [PRSE0000129 at p.35].

62. At the meeting of the Factor VIII Working Party for Scotland and Northern Ireland on 9 November 1988, Dr Mayne stated that *"she was not convinced that any single treatment could be considered a gold standard and she believed that current evidence suggested that final vial dry heat treatment was as good as any other."* [SBTS0000297_053 at p.4]. She raised concerns about the long-term effects of solvent-detergent exposure and in relation to Monoclate, the continual exposure to mouse proteins.

63. In March 1989 Dr Mayne stated that *"...it has been agreed that heat treatment sometimes renders the haemostatic effect of the material less effective*" thus it was "*necessary*" to maintain a store of some commercial concentrate [RHSC0000067_002 at p.6]. However, the documents also show that at this time, Dr Mayne had agreed with the SNBTS that Northern Ireland would receive a smaller allocation of NHS product in favour of commercial concentrate.

64. In 1988 it appears that an agreement was reached that contradicted earlier arrangements for pro rata provision of factor products according to plasma supply: the Belfast Centre was to receive less Scottish NHS Factor VIII and to receive the equivalent number of Factor VIII units of Profilate instead. At the UKHCDO meeting on 5 September 1988 the minutes record:

> *"Dr Ludlam raised the question of the position in Scotland where there was going to be a shortfall of 2million units in the current year.... Dr Mayne suggested that because some Scottish material was presently sent to Northern Ireland whether or not a more realistic arrangement could be made between the two countries. It was agreed that Dr Ludlam and Dr Mayne should meet to determine the best way to cope with the Scottish BTS shortfall"* [HCDO0000431 at p.3].

65. In a letter dated 26 September 1988, Dr Mayne stated that she was *"happy for us to try this arrangement as long as the treatment of the children here and the small number of*

other patients is safeguarded ... It would be interesting to see the reactions of the patients to the change over and to see if the number of units consumed is reduced" [NIBS0001762]. It is unclear what if anything patients were told about this arrangement.

66. The position is more fully explained in a letter from Dr Mayne to Professor Cash dated 23 November 1988, in which she noted Dr Ludlam's concern that there would be a shortfall of NHS material in Scotland requiring the topping up of needs with commercial concentrates:

> *"In view of the widespread discussions regarding alterations in immunological tolerance in multi-transfused patients, I made a suggestion to Chris. There exists in Scotland children and other patients who have only been exposed to the NHS donor population. They have never received commercial concentrate at any time. In Northern Ireland up until 1985, all patients except children were exposed to commercial factor VIII: therefore I suggested to Chris that it might be worthwhile to consider an exchange basis to enable all patients who had never received other than NHS factor VIII to continue to do. I would be happy to let them have my allocation of NHS factor VIII, barring the needs for the children here and one or two patients who were in the same category as those in Scotland, namely never exposed to commercial material.... It was felt appropriate to try it out until the end of the financial year"* [NIBS0001767].[8]

67. The letter goes on to decline their request for the Eastern Health and Social Services Board to make a formal request for these arrangements because *"it would appear that I was requesting commercial factor VIII in preference to NHS factor VIII. That is not the case. The arrangements were made purely and solely to try and produce the best therapeutic benefit for the most patients"*.

68. Dr Ludlam makes no mention of this arrangement in his article in the Haemophilia Society Bulletin No 4 of 1989 and, having noted Dr Mayne's involvement in the

[8] Further documents concerning these arrangements are: SBTS0000384_066, SBTS0000435_006, NIBS0001770, HCDO0000003_061, PRSE0004188 and LOTH0000006_031.

Scottish Factor VIII Working Party, records the policy of Dr Davies to use only locally produced blood products [PRSE0001853 at p.13].

69. The arrangement appears to have continued into the 1989 financial year with the allocations by the Scottish Factor VIII working party to Northern Ireland being predominantly of commercial concentrate and much reduced NHS concentrate, and the complex cross-charging arrangements are also recorded [PRSE0003487 at p.4]. The Northern Ireland participants are recorded as "*keen to continue the arrangements for the transfer of products*" in April 1989 [PRSE0000921 at p.2]. Even after 1989, until at least 1996, the documents suggest that there was a substantial requirement for Northern Ireland to purchase commercial products, despite the plan in 1989 being that Scottish Factor VIII would be the main source of supply [RHSC0000285 at p.1].

70. In November 1989, Dr Mayne wrote to Dr Cash and mooted the suggestion that Northern Ireland might move their plasma supply to Elstree. She reiterated her *"disappointment at the delays in producing the new S8"* because of her *"periodic dissatisfaction"* with Z8 and delays in producing S8, together with concerns about the increased purchase of commercial factor VIII for Scotland [LOTH0000006_031][LOTH0000006_032].

71. On 23 April 1990, Dr Mayne highlighted her concerns about Z8 at a meeting of the Factor VIII Working Party for Scotland and Northern Ireland. She stated that her staff were reluctant to use Z8 due to poor solubility. She had produced a paper evidencing her concerns. Dr Perry, of PFC, explained the difficulties in the manufacturing process and Dr Mayne agreed that she expected Northern Irish demand to increase as long as the improvement was sustained [NIBS0001666 at p.2].

72. In October 1990 Dr Mayne had been invited by Dr Ludlam to express her "*views on the future product to be available from SNBTS*" [SBTS0000041_119].[9] Notably, she remained unhappy with Z8[10] stating that *"I can no longer regard Z8 as acceptable for all patients and at the present time I would consider 8Y to be satisfactory but not*

[9] The substance of her views in 1990 are set out below in relation to high purity products.
[10] Despite an apparent resolution of the issues in May 1990: NIBS0001794, such that by September 1990, Dr Mayne had increased supplies of Z8: NIBS0001668.

ideal". She suggested that Northern Ireland might consider sending their plasma to Elstree to be converted to 8Y as a short-term measure.

73. It seems that matters had been resolved to an extent by 25 January 1991, when Dr Mayne wrote to Dr Ludlam expressing disquiet that the SNBTS would be using Lille technology, producing a non-licensed product. It appears that because Elstree had also pursued a non-licensed pathway, Dr Mayne decided to continue the Scottish arrangement. She indicated that she would need to use up all of her commercial supplies before using the new high purity product [NIBS0001474].

74. However, the picture remains somewhat unclear because in 1991 she reported that 3,221,831 units of Factor VIII and 100,975 units of Factor IX had been used that year. The allocation from Edinburgh was 2.8million units per year *"and therefore it required a top-up utilising the NHS 8Y material from BPL in England"* [WITN0736010].

75. The "*semi-tartan*" high purity product was phased in from March 1992 and it was anticipated that all the stocks of Z8 would be used up by August/September 1992 [NIBS0001514] [GGCL0000114].

76. As to DEFIX, in the 1996/97 Annual Report of the Coagulation Factor Working Party for Scotland and Northern Ireland it was noted that the licence for DEFIX HT had been extended to include patients with acquired deficiencies of factors II, IX and X [SBTS0000389_005 at p.2]. The high purity double virally deactivated factor IX concentrate, HIPFIX, was being trialled in Scotland and Northern Ireland. There had previously been difficulties with precipitate formation but a new process was being used and the reformulated concentrate was expected to be used in clinical trials shortly thereafter. The Annual Report noted the difficulties in supply of FIX when the HIPFIX trial was suspended in September 1996 because of the precipitate problems. The supply difficulties appear to have arisen from the arrangements for the supply of commercial FIX. Consequently *"The Working Party was concerned that patients may have had to change treatment to one or more different concentrates for reasons not related to supply by manufacturers and that such changes were against previously agreed practise and also UK guidelines. The difficulties for patients were further compounded by the lack of*

the usual consultations before deciding upon the most appropriate concentrates" [SBTS0000389_005 at p.3].

77. It is clear that on an ongoing basis, the Centre was meant to be allocated factor concentrates from PFC according to the plasma input from Northern Ireland. However, it appears that this could not always be provided. Consequently, in May 1991, it was noted that the "*considerable carry over*" from the previous year and the increased plasma input that year meant their entitlement had risen but usage of Z8 would be a "*considerable way short of this [entitlement] figure*" [NIBS0001492]. It is unclear how this interrelates with the agreement to reduce the Northern Ireland allocation in exchange for commercial factor.

78. On 27 November 1992, a similar letter was sent to Dr Mayne regarding the 1992/93 entitlement – Northern Ireland was to receive increased supplies of HP8 from PFC because of a reduced supply earlier in the year. There are then estimates provided of likely supply in light of plasma input and yields [NIBS0001529].

79. Equally, usage at the Belfast Centre could run substantially ahead of the allocation, for example in 1994 and 1995, requiring consideration to be given to patients' usage of Factor VIII and to the purchase of commercial concentrates [NIBS0001571] and [WITN1383006].

High purity products

80. In a newspaper article in September 1990, Dr Mayne is quoted as saying that there were some "*tenuous*" indications that HIV positive haemophiliacs benefited from high purity factor VIII but that *"there are constraints in the financial field"* [NHBT0005445].

81. As noted above, in 1990 Dr Mayne was asked for her views as to the future products to be produced by PFC. She stated that:

> *"Our future treatment aims, as I see them, are:*
> *a) High purity factor VIII*
> *b) Safety and efficacy*

c) *Usage of licensed products*

d) *UK self-sufficiency for high purity factor VIII"* [SBTS0000041_119].[11]

82. She considered that UK plasma-derived monoclonal factor VIII should be the ultimate goal.

83. The PFC continued with their planning in relation to the Lille technology and in a document dated 19 April 1991 the plan for PFC production is outlined. There would be three stages before reaching production of high purity "*Tartan*" factor VIII. Firstly, product would be made in Lille from French donor plasma. Secondly, product would be made in Lille from SNBTS and NIBTS plasma. Finally, product would be made in PFC using the Lille technology, from SNBTS and NIBTS plasma. At each stage product would be available on a clinical trial basis [PRSE0002157].

84. Dr Mayne expressed *"some continuing disquiet"* about the plan, recognising that *"it will be necessary to expose our patients to a different, large donor population, although I realise this is only for a short time"* [NIBS0001474].

85. In September 1991 the Haemophilia Society discussed the issue of high purity products with Dr Mayne. They were informed by her that ion exchange products were as pure as monoclonal products. Consequently, they agreed to change their policy [HSOC0017199 at p.3]. Shortly afterwards, in an article for the Haemophilia Society Bulletin in November 1991, Dr Mayne wrote expressing concern about articles that had been published in the previous Bulletin edition about high purity products. She stated that *"More than 80% of the factor VIII concentrate used in the United Kingdom is intermediate purity material. This material has been in use since the summer of 1985 and has been shown to be clinically effective and most importantly, safe from infection. ... it should be made clear that there are alternative forms of high purity factor VIII which are considered by some to be as good and even possibly superior to the monoclonally prepared materials"* [HSOC0022977 at p.7]. She noted that Scotland and Northern Ireland had opted to use high purity material prepared by ion exchange and

[11] See also [PRSE0001539].

that monoclonally prepared products were under investigation in relation to the development of inhibitors.

86. The first deliveries of the "*semi Tartan*" high purity factor VIII were due to arrive in Northern Ireland in January 1992 and Dr Mayne noted that informed patient consent would be sought in relation to its use in clinical trials [NIBS0001507]. However, it seems it did not arrive until March or April 1992. The first supplies of "*Tartan VIII*" arrived in Northern Ireland sometime before 20 May 1992 and Dr Mayne anticipated needing to use them from 1 June 1992 [NIBS0001518]. Tartan VIII was due to become available generally to all haemophiliacs in Scotland and Northern Ireland by August/September 1992 [NIBS0001514] and [PRSE0004830 at p.1]. The Z8 product licence would be terminated in December 1992 [PRSE0000300 at p.1].

87. The clinical trials of the high purity products were subsequently published by the Haemophilia Directors for Scotland and Northern Ireland [PRSE0000082].

Other products used

88. In her HIV litigation report, Dr Mayne records the development of porcine Factor VIII in 1981. She notes that it was efficacious in patients with inhibitors but that treatment could not be continued indefinitely *"due to the development of refractoriness or the occurrence of reactions... Its advantages are the lack of known viral transmission and its disadvantages are its limited suitability and the occurrence of side effects"* [CBLA0000072_024 at p.11]. The determination of suitability is not explained.

89. It is clear that porcine factor was used at an early stage in Belfast, as part of clinical trials [IPSN0000332_013] [BPLL0002571_086]. Thereafter, the documents indicate, as noted above, that Hyate:C was used in Belfast to good effect. A note from Speywood records that Belfast was their largest customer in 1983 *"so clearly [they] have no reservations about using Hyate:C"*. They were the second largest customer in 1984 [IPSN0000036_012 at p.8]. Dr Mayne also described in her litigation report the use of DDAVP for patients with mild to moderate Haemophilia or von Willebrand disease [CBLA0000072_024 at p.12]. She noted that was *"to be used with care and careful*

selection of suitable patients", according to Factor VIII levels but should not be used in older patients or those with Type IIB von Willebrand.

90. In addition, Dr Mayne described the use of tranexamic acid in the treatment of menorrhagia for those with von Willebrand disease and in mild and moderately affected haemophiliacs with superficial gum bleeding or bleeding following dental extraction [CBLA0000072_024 at p.12].

Recombinant

91. In 1994, patients in Belfast were involved in Phase III trials of Recombinant VIII:SQ [LOTH0000051_027 at p.4]. Dr Mayne's approach to recombinant was noted to be "*conservative*" sharing concerns with Professor Briet, in the Netherlands, seemingly about possible inhibitor development.

92. In 1995, it appears that there were discussions between Scottish clinicians and Dr Mayne about formulating proposals for the use of recombinant that were to be presented to the Management Executive at SOHHD. Dr Mayne proposed the following groups to be the first to be considered for recombinant:

> *"1. PUP's*
> *2. Infrequently transfused patients with mild/moderate haemophilia A*
> *3. Children up to mid teens (This group could be sub-divided into those who have only received virally inactivated concentrates (or who are HCV negative), i.e. less than approximately 10 years of age, and those who received other products and are HCV positive)."* [HIGH0000013].

93. She noted in May 1995 that the main limiting factor would probably be the cost of introduction [SBTS0000839 at p.5].

94. Haemophilia Directors for Scotland and Northern Ireland produced formal guidelines for the use of recombinant Factor VIII on 13 September 1996 [PRSE0002401]. The guidelines listed patients in descending order of priority over eight different types of patients: starting with PUPs as the most important group to receive recombinant and

ending with patients already infected with HCV at the lower end of the spectrum. The guidelines were revised in September 1997 where the total number of different priority groups was 11 [PRSE0002401].

95. By February 1997, Dr Mayne reported that all previously untreated patients and children were on recombinant products [HCDO0000460 at p.4].

96. The 1997/98 Annual Report of the Coagulation Factor Working Party for Scotland and Northern Ireland recorded that the transition to recombinant had continued and the Recombinant Factor VIII Consortium had been established. The agreed plan was for an orderly transition to recombinant for all patients by 2000. It was noted that recombinant Factor IX would be available from July and would be funded using the same criteria as for Factor VIII [SBTS0000389_009].

97. Since at least 2008, all patients with haemophilia A have been on recombinant factor VIII. All but one patient with haemophilia B have been on recombinant factor IX. All patients with von Willebrand's disease have received DDAVP or intermediate purity plasma derived clotting factor [WITN3082015 at §39].

Knowledge of, and response to risk

98. It appears that there was a "Blood club" operating in Northern Ireland and Ireland in the 1980s, seemingly as an opportunity for haematology clinicians to meet and discuss matters [BHCT0000623]. The frequency and content of those meetings is presently unclear.

Hepatitis

99. In relation to patients at the Children's Hospital, Professor Bridges has stated that *"The risk of hepatitis was not widely known during the time I was treating children with cryoprecipitate [up to 1979] and therefore there was no discussion with the parents about risk"* [WITN4569001 at §32]. However, Professor Bridges is noted to have attended the UKHCDO meeting at Middlesex Hospital on 29 March 1977, where Dr

Craske outlined his study of hepatitis in haemophiliac patients treated with NHS and commercial factor VIII [PRSE0002268].

100. By 1988 patients at the Children's Hospital were being tested routinely for Hepatitis B, and a vaccination programme for Hepatitis B was getting underway [PRSE0000129 at p. 66].

101. As to the treatment of adult patients, Dr Mayne attended a UKHCDO meeting on 5 April 1971 in place of Dr Nelson. At that meeting, there was discussion about the incidence of jaundice in patients with haemophilia A and B arising from the survey of patients treated during 1969 and 1970. There was considerable discussion about the precautions required to prevent the spread of Australia antigen [HCDO0001014 at p.3]. Dr Mayne treated and addressed issues arising from the infectivity of, patients with Australia antigen in the early 1970s, so would have been familiar with risks of hepatitis [BHCT0000768], [BHCT0000757] and [BHCT0000765].

102. Although her recollection was that hepatitis B was *"almost non-existent"* in Northern Ireland, she acknowledges [see WITN0736009 at §26.3] that this is contradicted by an article in the Ulster Medical Journal (April 1989) which stated that 11 haemophiliacs had suffered acute Hepatitis B infections between 1970 and 1987 [WITN3082021].

103. Dr Mayne has described that throughout the 1970s liver function tests were performed on patients *"because of my apprehension about the adverse effect of prolonged IV treatment"* [WITN0736007 at §2].[12] She states that it was suggested that she stop testing her patients because she was finding it upsetting but she declined to do so [WITN0736009 at §26.4]. In her most recent statement, Dr Mayne states that by *"the late-1970s and the mid-1980s, there was increasing evidence that NANB hepatitis was not as benign as had been thought but could progress from chronic persistent hepatitis to cirrhosis."* She was also aware that the size of donor population was *"an important factor in transmission"*. She seeks to emphasise that it was an *"evolving picture"* [WITN0736009 at §22.3]. Despite this, it appears that in 1976, no information about the risks of factor concentrates was given to patients: Dr Mayne states that at that time

[12] This is echoed in her recent witness statement: *"Always I had concerns regarding the repeated injections of IV material in relation to the risk of as yet unknown viruses being transmitted"* [WITN0736009 at §10.8].

she believed the treatment was *"both effective and safe"* [WITN0736001 at §2.2]. She states that *"There were few facts available regarding viral infections at this time, apart from the historical and rare transmission of Hepatitis B.... Risks of viral infection were discussed at the hospital clinic and at Annual patient meetings held in Craigavon Area Hospital each November"* [WITN0736001 at §5.2].

104. An affected daughter describes her father's early treatment at the RVH in the 1970s. Within his UKHCDO records is a document titled 'M.R.C Cryoprecipitate Working Party Group' [WITN3209004] which states that it is a 'Survey of Instance of transfusion jaundice in haemophiliac and Christmas disease patients.'[WITN3209004] The witness considers that these documents demonstrate that "*doctors were aware that there were problems with the treatment' for haemophiliacs in the 1970s"* [WITN3209001 at §13].

105. The majority of the available witness evidence from infected individuals and their affected family members suggests that patients at the Centre were not routinely informed of the risks posed by blood products prior to their use. In contrast, one patient recalls a discussion with Dr Nelson in April 1980 about the potential risk posed by blood products. She underwent a tonsillectomy in April 1980 and was given Kryobulin Factor VIII and required a blood transfusion. She was normally treated under the care of Dr Mayne but in Dr Mayne's absence she was treated by Dr Nelson, who administered factor VIII. Prior to the tonsillectomy, the doctor conducting the procedure asked her '*if [she] was sure about the operation. He said "do you know the risks... you're going to have Factor VIII.*"' The witness states that *"this did not sink in or trigger any concerns for me because all haemophiliacs were having factor VIII at that time."* [WITN1382001 at §11]

106. In Dr Mayne's 1991 HIV Litigation report she stated that the "*possible significance of asymptomatic hepatitis became apparent by 1978 ... when structural abnormalities of the liver were described in patients*" citing the paper by Spero et al in the New England Journal of Medicine [CBLA0000072_024 at p.18]. However, in another litigation report she stated that *"the risk that non-A non B hepatitis could progress to chronic hepatitis was known in 1977 but the full significant of its effects was not appreciated, elaborated and investigated until the mid- to late-1980s"* [WITN0736011]. She also

noted in the 1991 HIV Litigation report the papers by Aledort et al in 1985, Hay et al in 1985 and Preston's paper of 1988 which, she states, found that "*the relatively benign condition of chronic persistent hepatitis could progress to the more serious condition, cirrhosis*".

107. Dr Mayne has more recently described Hepatitis C as *"the most complex virus and most insidious in its behaviour. It may lay dormant for years"* [WITN0736006 at §12]. She has also stated that "*Many of the clinicians, myself included, could not in 1995 foresee how complex, disastrous symptoms and complications of the virus would develop, sadly"* [WITN0736007 at §8]. Dr Mayne does *"not believe that in 1995 many people envisaged the magnitude of the ensuing HCV problem. To some extent I was hoist with my own petard. I mean that I had observed these abnormal liver function tests for so long without there being any apparent clinical ill effects, that I think I could have been lulled into a false sense of security. I am not at all sure."* [WITN0736007 at §13]. However, Dr Mayne has also stated that from 1991 information "*evolved*" and *"Always I had an ominous feeling about the virus"* and this is why she organised a weekend in 1995 to have a *"frank discussion with multiple experts"* [WITN0736001 at §6.2].

108. As to the relative risk between cryoprecipitate and factor concentrates, in the Litigation report, Dr Mayne notes the "*high infection rate*" that was understood, and subsequently in 1983 found, to exist amongst haemophiliacs [CBLA0000072_024 at p.19]. Dr Mayne records the involvement of single donor cryoprecipitate in hepatitis infections (referencing Lee et al's 1985 paper) and notes that this occurred "*less commonly than concentrates*".

109. On 8 March 1984 Dr Mayne informed a GP that a patient had transferred to adult care and *"To keep records straight, a mild haemophiliac of this type should be treated with cryoprecipitate or NHS factor VIII and not commercial free-dried factor VIII concentrates. This precaution is to avoid the development of non A non B hepatitis in mildly affected patients"* [WITN0198002].

110. On 1 February 1988 Dr Mayne attended the UKHCDO meeting at which Dr Craske suggested that there should be more intensive surveillance of the safety of blood

products. Dr Mayne suggested that *"two years of trying a reporting system similar to the one used by CSM ("yellow card") should be undertaken in the first instance"* [HCDO0000428 at p.4]. In her Litigation Report, Dr Mayne notes Dr Craske's recommendation to revert to cryoprecipitate and comments that *"but by that time a majority of patients were well established in self injection programmes. Unfortunately, it was impractical for home treatment"* [p. 19 of CBLA0000072_024]. She states that patients were aware of the risk of hepatitis because of the World in Action programme in 1975, but makes no reference to doctors proactively informing patients of the risks.

HIV and AIDS

111. In her witness statement, Dr Mayne records that she first came to know about HIV at an informal lunchtime discussion with Professor Bloom, Dr Craske and Dr Kernoff. She does not say when this took place [WITN0736009 at §30.1]. Dr Craske was discussing a report in the *Lancet*, which might place the discussion after 12 December 1981.[13]

112. In her HIV Litigation Report, Dr Mayne states that the early publications in 1981 and 1982 regarding unexpected outbreaks of rare disorders in homosexuals *"provoked discussion amongst Haemophilia Centre Directors as early as September 1982. At that time particular relevance to haemophilia care was not yet evident"* [CBLA0000072_024 at p. 32]. She also notes the MMWR article in July 1982 but states that *"little evidence had accumulated to suggest that haemophiliacs of themselves constituted a special risk group for AIDS"*.

113. Dr Mayne records her view that the situation had changed by the end of 1982 with haemophiliacs categorised as a separate at risk group and that *"it was thought that the syndrome might be due to an immunosuppressive virus infection... The Directors considered it possible that an infectious agent could be present in blood and present in particular in the Factor concentrates used to treat haemophiliacs"*.

114. The documents show that Dr Mayne was present at the meeting at London Airport with Immuno on 24 January 1983 at which AIDS was discussed [PRSE0002647].

[13] Letter to *the Lancet* published on 12 December 1981, 'Primary Pneumocystis carinii and cytomegalovirus infection' [PRSE0004476]

115. Dr Mayne's report states that a meeting was convened in February 1983 in which Reference Centre directors planned *"measures which might be undertaken regarding surveillance of patients and their treatment"*.[14] In her Litigation report Dr Mayne notes that at that time, in February 1983, one UK haemophiliac was suspected of having contracted AIDS and that *"...it was agreed that there was insufficient concrete evidence to warrant changing the type of concentrate used to treat severely affected patients. The decision was taken after prolonged discussion; it was felt that the immense benefits of treatment precluded change."*

116. On 22 March 1983 Drs Craske, Rizza and Bloom wrote to all Centre Directors, including Dr Mayne, circulating papers on AIDS *'so that a system for the reporting of possible cases of the Acquired Immune Deficiency Syndrome can be quickly set up to examine the problem as quickly as possible.'* [HCDO0000517_001].

117. On 13 May 1983 the Reference Centre Directors met to discuss the issue of AIDS [HCDO0000003_008]. Dr Mayne did not attend the meeting. Thereafter, recommendations were sent to all Centre Directors in June 1983.

118. Dr Mayne was present at the UKHCDO meetings on 17 October 1983 [PRSE0004440] and the meeting in Elstree in December 1984 [HCDO0000394_117], which she described as *"...certainly beneficial, if indeed somewhat depressing"* [BPLL0010480]. In her HIV Litigation Report, Dr Mayne notes the views that had been expressed in the media by some clinicians and gives her view that *"Their expression was based on the then available evidence and reflected the element of doubt which existed regarding the magnitude of the AIDS problem in haemophilia and its causation. They did not unduly underestimate or understate the position during the year 1983, a feeling which may now be construed by the aid of the retrospectoscope"* [CBLA0000072_024 at p.38].[15]

119. One infected haemophiliac recalls a conversation in 1985 where Dr Mayne told him that she suspected there was something wrong with his blood tests since about 1983:

[14] See [HCDO0000411]. Dr Mayne did not attend this meeting.
[15] Dr Mayne also wrote a letter to the Lancet which was not ultimately published expressing dismay and grave concern about the imprisonment of Professor Allain: LOTH0000080_007 and LOTH0000080_004.

"*She had noticed the same irregularities in the blood test results of my two brothers as well.*" All three siblings were infected with HIV [WITN0265001 at §12]. Both of his brothers died, in the same room of the Royal Victoria Hospital, in 1996 and 1997 having been admitted to hospital with AIDS [WITN0265001 at §48].

120. Dr Mayne has set out the figures for HIV infection in Northern Ireland as 14.5% of the haemophiliac population and noted that this was "*clearly anomalous*" compared to England and Wales [WITN0736006 at §2]. She states that when this was presented at UKHCDO in autumn 1985, "*some colleagues, not unsurprisingly were politely sceptical about the veracity of the results*". Further testing was carried out and she organised samples to be "*tested in duplicate and simultaneously*" in Belfast and Middlesex, London. The results were unchanged.

121. The lower rates of infection were considered to be because she had kept patients on one product, insofar as it was possible. Dr Mayne speculates that:

> *"repeated injections of treatment regardless of plasma source may induce a degree of immune tolerance, perhaps mediated through alteration within the Complement system? It does not seem to matter whether the treatment is Cryoprecipitate, or Concentrate sourced in Scotland, Europe or the USA.*
>
> *Figures from Scotland and NI would indicate that Cryoprecipitate may well have been the safest product available at that time. However, it was cumbersome to use, accurate dosage was impossible and HT impracticable. The advent of Factor VIII Concentrate in small vials and with accurate dosage revolutionised life for the Haemophiliac patient.*
>
> *Furthermore, an alternative explanation might have a straightforward numerical basis. Each company utilised approximately 25,000 donors. If, due to large patient numbers, financial constraints or problems relating to product availability any one patient could be treated with 2, 4 or even up to 6 different products, thus their exposure could be increased even to 125,000 donors, leading to the possibility of increased viral conversion"* [WITN0736006 at p.3].

122. On 10 May 1985, Dr Mayne was notified that the Centre had received a batch of heat treated Factorate from Armour, subsequently shown to be produced from an HTLV III positive donor [ARMO0000382].

Treatment of patients

HIV and AIDS

123. Dr Mayne has stated that of the 110 annually treated patients, 15 became HIV positive [WITN0736006 at §8]. In addition, a spouse of a patient also seroconverted. There were no positive patients in the non-HT (home treated) group and no children sero-converted [WITN0736006 at §8]. Dr Benson has stated that there were 15 patients with haemophilia A and 1 patient with haemophilia B or von Willebrand's who contracted HIV [WITN3082015 at §§56-58]. The analysis of stored sera indicated that there were 16 sero-conversions, not including a spouse of an infected patient [BHCT0000484].

124. It is unclear however what age Dr Mayne considers someone to be a child, as there is evidence that a patient then aged 14 had seroconverted, following treatment in January 1985 [BHCT0000846_004]. There is also a record titled "Surveillance of Paediatric HIV Infection and Aids Follow-up", noting manifestations of HIV infection [BHCT0000860]. It is unclear whether this relates to the same or a different patient.

125. Dr Mayne states that the 16 patients who sero-converted represented 25% of the most severely affected patients and 16.5% of all treated patients in Northern Ireland [RHSC0000067_002 at p.4]. Dr Mayne explains the difference in rate of seroconversion compared to the rest of the UK as being due to her policy of patients using one product insofar as feasible.[16]

126. However, it is not clear whether it is accurate to say that the 16 patients who sero-converted were all severely affected patients. The documents indicate that one patient (not apparently treated by Dr Mayne) who sero-converted had only received

[16] See also HCDO0000524.

treatment once on 5 May 1983, since being treated in 1974 [BHCT0000512 at p.11]. He had then received further treatment after May 1983. Moreover, a further letter from Dr Mayne, addressing the treatment in 1983 that had been given by another doctor, indicates that *"The sad and ironic aspect of the whole performance was that the patient did not need the Factor IX. He has mild Christmas disease and does not suffer from Haemarthrosis. The Doctor who saw him either forgot or did not realise these facts"* [BHCT0000612]. The patient was first tested for HTLV III on 20 August 1985 and found to have seroconverted.

127. The analysis from stored sera appears to show seroconversions taking place as early as February 1983 and as late as early 1985 [BHCT0000484].

128. Dr Mayne has stated that meetings about HIV were planned towards the end of 1984, with the meetings starting to take place in January 1985. Dr Mayne has denied that there was any HIV testing carried out prior to the 1985 meetings [WITN0736001 at §2.6].

129. In another litigation report, dated 6 November 1989, Dr Mayne stated that plans for meetings were laid in December 1984 and took several months to complete. She indicates that actual testing of samples commenced on 2 January 1985 [WITN2658002 at p.12]. It is unclear whether any patient meeting took place on 1 or 2 January 1985.

130. Two meetings took place in Ward 37, but the third could not, rather it took place in a lecture theatre. One witness describes this as an open meeting where haemophiliacs were presented with the choice of whether to find out if they were infected or not. An affected wife describes this meeting as "*bizarre*" [WITN1371001 at §26] Dr Mayne has agreed that the meeting was bizarre. She explains that the hospital was at full capacity (alternatively explained as due to a terrorist event and an outbreak of flu) and she had been up all night dealing with a patient in ICU. She goes on to state that *"the only available space for the meeting was the historic Old Surgical Extern Theatre. It was unsuitable in every respect. The space was confined; the seating was unsuitable for disabled patients and the general impression inhibitory. It was not possible to cancel the meeting as transport had been arranged for the disabled patients and others were*

coming from far afield... Professor John Bridges attended as support. He was concerned that I might pass out from fatigue." [WITN0736006 at §24].

131. In a different witness statement, Dr Mayne has referred to the location being the Sir Ian Fraser Lecture Theatre and explained, again, that it was a very uncomfortable location. One witness has described the doors being locked during the meeting; Dr Mayne has denied that the doors were locked but noted that "*it had old fashioned heavy wooden doors which clanged shut when closed*" [WITN0736001 at §5.3]. Professor Bridges has no recollection of the meeting [WITN4569001 at §34].

132. Witnesses have criticised Dr Mayne for failing to provide adequate information about HIV. Dr Mayne has stated that she gave all information that she had available at the time [WITN0736005 at §2.10.1]. In one statement, she has stated that at the 1985 meeting there was perhaps less information conveyed than at meetings with staff and it was foreshortened because of the unsuitable venue. She notes however that the situation *"was addressed as far as possible when the person was having the test carried out"* [WITN0736005 at §3.8.2]. However, in another witness statement Dr Mayne stated that *"As much time and space was given for discussion as was necessary"* [WITN0736001 at §5.3].

133. Some witnesses recall that there was no choice given about whether to be tested for HIV, only as to whether they wished to know the results. This appears to be supported by a letter from Dr Mayne to one patient simply asking them to attend for antibody testing, without giving any indication that this was a choice [WITN2658009].

134. Dr Mayne's evidence is that at the time of testing the patient was invited to give consent and could have refused [WITN0736005 at §2.9.1]. Dr Mayne's evidence that all patients had a choice to consent to testing is re-iterated in some of her other witness statements [WITN0736001 at §6.1] and [WITN0736009 at §51.1].

135. It appears that some of those who tested negative were sent letters informing them of their results. Dr Mayne has accepted this in relation to one patient stating that it was necessary because of the demands on the staff. However, in the same statement in relation to a different witness she has stated that *"If negative, at first, it was thought a*

letter might be a good idea but this was rapidly rejected. All but two families returned for results and both received a home visit" [WITN0736001 at §5.3].

136. It seems that those patients testing positive were told when they came to the Department [WITN0736005 at §3.10.1]. There is evidence of Dr Mayne attending the homes of patients who were too unwell to travel [WITN0736001 at §4.2]. In the case of one such patient, his family have raised concerns to the Inquiry about the language used by Dr Mayne in correspondence. In a letter dated 17 October 1985, Dr Mayne states that he had become positive for HIV between February 1983 and October 1983. Dr Mayne stated that he would "*be glad to know*" of the likely date of his infection [BHCT0000896]. Dr Mayne has indicated to the Inquiry that the letter followed a personal visit to the patient, where the patient had said, after being informed of his infection, that he would be glad to be told when the infection had occurred [WITN0736001 at §4.2]. Dr Mayne in her witness statement has said she '*hopes this explains the letter and the seemingly appalling use of the word "glad*"."

137. However, it is also apparent that one patient and their family were not told of their positive result at the time that Dr Mayne became aware of their positivity. Having received a positive HTLV III result on 10 July 1985, from treatment in January 1985, Dr Mayne wrote to Dr Machin at the Middlesex Hospital asking if he would care for the patient while the patient was visiting London and said *"I have not told the patient this result, nor his family, at the present time; the reasons are due to the precarious family base of the patient. I would be worried that the parents might do even less for their son should they know of this result at this time. ...I feel [the patient] is incapable of accepting the knowledge of a positive test until later this year"* [BHCT0000846_004]. It is unclear whether his school was aware of the test result [BHCT0000846_003].

138. Another patient, a severe haemophiliac who tested positive for HCV in 1995, has seen in his medical records that he was tested for HIV on 1 January 1985 and 8 June 1986. Both tests were negative but he does not recall that the tests or the results were discussed with him or his parents [WITN1546001 at §27].

139. In relation to another patient, it seems that the patient's family were told after the patient had been informed, seemingly on their own. The letter, written on 12 February 1985, states that *"I am sure that, by now, you have heard that [X's] blood sample was positive for the AIDS related virus"* and goes on to ask the whole family to attend for testing [WITN2607004]. It is unclear whether the patient had consented to that information being given.

140. One individual describes that Dr Mayne attended his family home in 1985 and told his parents that he (and his two brothers) had HIV. This was before he had himself known that he had HIV. The witness states that he then went to see Dr Mayne and told her that he had not wanted his parents to be informed "*but she said it was better from them to know*." He was aged 26 at the time of this conversation [WITN0265001 at §50]. One to one counselling was arranged for this witness when he was given his HIV diagnosis but he only attended one session [WITN0265001 at §67].

141. With regard to a further patient, Dr Mayne notes that he did not want to know his test result but in a letter to his GP she states that he will ask his wife to attend for testing. It can easily be inferred therefore that the patient had tested positive. She goes on to state that *"If [X] himself has no objection to the result being known, I will be happy to give you the information"*. It is unclear whether this relates to the wife's result or the patient's result. Dr Mayne goes on to state that the reason for this practice was *"to keep the panic situation at the minimal level throughout the Province's haemophiliac population"* [WITN2658008].[17]

142. It is clear that Dr Mayne was very aware of the considerable stigma suffered by some patients, asking staff to telephone the GP of one patient to tell them of the *"extreme need for confidentiality"* [BHCT0000981].[18] In her statement, she has said that the lack of knowledge in the community meant that she suggested to patients that they *"should not publicise their results unnecessarily"* [WITN0736009 at §53.6].

143. Following the initial testing, at the adult Centre, Dr Mayne notes that at least in relation to some patients, stored samples were tested to pinpoint the time of the infections

[17] As to avoiding panic, see similarly [BHCT0000846_003]
[18] She also raised the need for confidentiality within the hospital: RHSC0000040_050.

[WITN0736001 at §7.2]. The accuracy of those dates depended on the frequency of attendance at the Centre and for some patients, dates of seroconversion were estimated in light of *"other clinical features"* [BHCT0000978_001] and [BHCT0000512]. Testing of stored sera for some patients took place in August to October 1985 [BHCT0000158], [BHCT0000161] and [BHCT0000484].

144. It is unclear whether samples were stored of patients at the Children's Hospital. Professor Bridges states that he does not believe that samples were stored and there was therefore no discussion about the storage of samples with patients [WITN4569001 at §45].

145. Dr Mayne has claimed that with the advent of AIDS, patients were offered a return to cryoprecipitate but that was turned down and emphatically so [WITN0736009 at §43.1].

146. There is limited documentary evidence available as to how patients with HIV were treated. It appears that at least until 1994, Dr Mayne provided treatment to them herself, primarily at the Belfast Centre. This is confirmed in a paper in the Ulster Medical Journal *"Human immunodeficiency virus infection Northern Ireland 1980-1989"*, co-authored by Dr Mayne [WITN3082020]. The paper notes that all other HIV positive patients were managed by the Genitourinary Medicine Service with a designated HIV Clinic operating at the Royal Victoria Hospital. It is noted that of the haemophiliacs who had survived to that time, none of the patients had evidence of opportunist infections other than oral candidiasis affecting four patients and pityriasis versicolor affecting one. She notes that ten patients were asymptomatic in category CDC II.

147. In her witness statement, Dr Mayne has said that the Centre was provided with an additional grade E nurse and that *"Measures were taken to liaise with colleagues from other disciplines as and when necessary. A Dermatologist, a Neurologist, and an Infectious Disease expert were all briefed, and were willing to and did attend patients in the Centre"*. There were also links with the sexually transmitted disease department [WITN0736009 at §33.11]. However, in other documents there does not appear to have been any input from other specialists other than what she could glean when attending conferences or meetings [BHCT0000609].

148. It seems that Dr Mayne prescribed AZT but chose to use a reduced dosage with intermittent treatment rather than permanent prophylaxis due to its side effects [HSOC0010892 at p.3].

149. In 1991 she reported that *"visits of HIV patients for counselling by the Director of the Centre averages ten visits per month and many of these visits last up to two hours in duration"* [WITN0736010]. She noted that by 1991 three of those who were HIV positive had died, and a further person died during 1991. In a co-authored article in the Ulster Medical Journal in 1991, Dr Mayne notes that of the three patients who had died, *"one by suicide, one died from liver failure unrelated to HIV infection and one in whom HIV infection was contributory."* [WITN3082020]. Consequently, the documents suggest that Dr Mayne treated those haemophilia patients who were HIV positive, rather than either referring them to the HIV clinic or arranging for specialists to run a clinic within the Centre.

150. However, as at 2008, an HIV clinic was being run at the Centre and continues to run every 3-4 months alongside an HIV specialist [WITN3082015 at §20 and §122].

Hepatitis B and Hepatitis C

151. The Inquiry has some evidence that patients were informed of their positivity to Hepatitis B [BHCT0000766]. However, it is unclear whether this was a matter of routine within the Centre or was specific to this patient who was training to be a nurse and was subsequently advised that he could not continue in his training due to his positivity.

152. In a statement relating to one patient Dr Mayne suggests that Non-A Non-B Hepatitis was discussed [WITN0736001 at §2.4].

153. The first testing for Hepatitis C appears to have taken place in 1991. Dr Mayne records in relation to one patient that having suffered clinical jaundice in the 1970s, an aliquot of serum was retained for testing "*when other infections might be discovered or might evolve*". She states that this sample from 1976 was tested in 1991 for the HCV antibody

along with a sample taken at that time. Dr Mayne states that the 1976, 1991 and a fresh sample were all tested in 1993 when the later HCV test became available [WITN0736005 at §2.1.2].

154. Dr Mayne states that "*Present day practice would require oral or written permission to carry out viral blood tests. At the time in question, locally, nationally and internationally, expediency seemed paramount and specific consent was often not obtained. Quite unlike the situation relating to HIV testing, when no test was ever carried out without consent of the patient. Refusal to have any test was acceptable at all times*". [WITN0736005 at §2.1.3].

155. By contrast in another witness statement, Dr Mayne has stated that *"It was not my clinical practice to test patients with Hepatitis C without their consent"* [WITN0736001 at §3.2].

156. Dr Mayne's evidence is that the 1991 test results were not notified to patients. Dr Mayne has explained that this was because *"It was thought it might cause undue anxiety and worry"* in a patient who was clinically well and *"At the time, it was unclear what the future would hold for someone with such a result"* [WITN0736005 at §2.3.1].

157. As to the 1993 tests, it is unclear whether and when patients were informed about them. Although Dr Mayne has stated that *"Patients were seen as soon as possible after their results were received for consultation and discussion",* the timing of testing and informing patients is somewhat opaque:

    a. Dr Mayne has stated that one patient's *"final diagnosis of active HCV was not made until the 1993 test was in routine use, i.e.in 1996.".*

    b. In relation to another patient, Dr Mayne refers to testing in 1993 – as noted above, of a sample from 1976, 1991 and 1993 – but states that the patient's result was not established until March 1996. The patient was informed in August 1996 [WITN0736005 at §2.3.1].

c. Another patient has stated that she was told of Hepatitis C infection in 1993 but her medical notes record her as having NANB Hepatitis in 1987. Dr Mayne has indicated that *"precise laboratory testing for Hepatitis C became the norm in 1992-1993"* and states that it was not her clinical practice to discuss a patient's health in the corridor [WITN0736001 at §3.1].

d. As to a yet further patient, Dr Mayne has stated that although antibody tests were available in 1993, a patient was not informed of his infection until 1995 after the tests for RNA viral load were available. This patient was "*seen as soon as possible in rotation with his fellow patients*" [WITN0736007 at §5].

158. The Inquiry has been provided with evidence that some individuals did not receive a diagnosis with HCV until the mid to late 1990s and the early 2000s. For example:

a. One infected haemophiliac has told the Inquiry that he didn't know that he was being tested for HCV: "*I am surprised to learn through my medical notes that it was known for some time I had contracted HCV and I was not told of this until 2003.*" [WITN2570001 at §4.1].

b. An affected son describes that Dr Mayne informed his father of his diagnosis with HCV in February 1995. It is unclear why his father wasn't diagnosed in the early 1990s like some other patients. [WITN2661001 at §6.1].

159. Some witnesses describe that they were only aware of their relatives' HCV infections after those patients had died. For example, one witness describes only discussing her father's HCV with Dr Mayne after he had died. Dr Mayne explained that the witness's father had had a bleed on his brain. The witness raised the issue of HCV because Dr Mayne had made no mention of it and because she had been unable to see her father as the coffin had been sealed. She describes Dr Mayne as being "*alarmed and annoyed*" about the sealed coffin and she said she would write to the Coroner or the Haemophilia Society so another family did not have to go through this [WITN3209001].

160. Witnesses give evidence that they were not provided with sufficient information about their infections upon diagnosis. For example:

a. A female haemophiliac, who was diagnosed with HCV in 1992, describes that Dr Mayne did not tell her of any potential health issues, treatment or advice on how to manage the infection: "*she simply told me that I had it and it would do me no harm*." The witness had to conduct her own research and does not believe she was given adequate information [WITN1382003 at §18].

b. A haemophiliac, diagnosed with HCV in 2003, describes not being given any support or information upon diagnosis and being told that "*there was nothing that could be done for me*." He describes being shown "*little empathy*" when he was diagnosed. He describes being informed in "*a clinical manner*". He was not offered treatment until 2006 [WITN2569001 at §5; §6.1].

161. In a letter to a GP dated 15 April 1992, Dr Mayne said that *"Hepatitis C is an unknown quantity to some degree, between 80 and 90% of treated Haemophiliacs are known to be positive, all are clinically well. From liver biopsy specimens obtained in some centres it would appear that a small percentage of patients may ultimately develop cirrhosis or chronic active hepatitis"* [WITN2655002].[19]

162. When writing to a GP on 21 December 1992, Dr Mayne set out what she had told the patient about Hepatitis C:

> *"I have explained... that there are several viruses which cause positivity to Hepatitis C. Generally it is thought that it is very unlike Hepatitis B infection and it may not have any serious sequelae for liver function in the future."* [WITN1382003].

163. Dr Mayne has accepted that throughout the period into the early 1990s she had informed sexual partners of those infected with HCV, that there was no risk of transmission, including during unprotected sexual intercourse [WITN0736005 at §2.6.1]. By 1995, her advice had changed slightly such that she was informing patients that *"sexual transmission ... was a very low priority and very few patients' wives or*

[19] See similarly [WITN2339011].

partners had been found to be positive. In fact, no female partner has yet tested positive in Northern Ireland" [WITN2655003].

164. Dr Mayne states that she organised a residential weekend in 1995 for Centre staff and all patients to discuss Hepatitis C. For those patients who were unable to attend, it does not appear that the information from that weekend was distributed in any way [WITN0736005 at §2.7.2].

165. It does not appear that patients were advised to bring anyone with them when they were given the test results. Dr Mayne has accepted that one patient was told his HCV results without family support. She has stated that he was a mature man and appears by implication to indicate that she considered there to be no need for him to have any support. She notes that he was anxious about the episode of jaundice in the 1970s but does not appear to recognise that there was therefore any need for him to be supported when being told of the HCV diagnosis and that they were unable to predict the future course of infection [WITN0736005 at §§2.2.1-2.2.2].

166. There was no counselling available to patients diagnosed with Hepatitis C [WITN0736007 at §11]. In March 1992, Dr Mayne wrote to all relatives of haemophilia patients at the Centre to inform them *"that if at any time you would wish to have a confidential chat about any matters relating to haemophilia and its treatment"* they should contact one of the team [BHCT0000582]. Given the timing of the letter, it appears to be an attempt to address relatives' concerns about hepatitis C.

167. The number of patients who were infected has been considered by Dr Benson. In October 2010, he undertook some work to identify patients who had been diagnosed with Hepatitis C in order to enable applications to the Skipton Fund. He discovered a historic document listing patients by name, their status and, where applicable, the genotype [WITN3082023]. There were 59 patients identified as positive. He went on to identify additional patients, giving a total of 92 patients who were, or had been, hepatitis C PCR positive [WITN3082015 at §68].

168. The provision of treatment for Hepatitis C was initially undertaken by Dr Mayne, including deciding whether to give interferon [WITN1382003] and [WITN2655002].

At some stage, Dr Mayne sought to set up a joint hepatology clinic to enable clinical monitoring of patients' liver condition by a hepatologist [WITN0736007 at §11]. It is unclear when this was established but appears to have been at some point after 1995 [WITN0736001 at §6.2]. The clinic was run in conjunction with Dr M Callender, a hepatologist. However, it also appears that efforts to establish the clinic were being made in 1999 by Dr McNulty and Dr Jones [WITN0921001 at §3.16]. It is unclear therefore whether the original clinic had not in fact commenced or whether it had ceased to exist at some point after 1995.

169. By 2008 there was no joint hepatology clinic. It was Dr Benson's understanding that the clinic continued to run while treatment of interferon and ribavirin was offered, with those on a hepatoma surveillance programme or who had had a liver transplant being transferred to the regional hepatology service. However, with the advent of newer treatments, those who had not received previous therapy or were refractory to standard treatment were, as he understood it, transferred to the regional hepatology service [WITN3082015 at §21].

Record keeping

170. The general processes in relation to record keeping are presently unknown, save that a number of patients had difficulty obtaining their medical records. The Inquiry is also aware that there was a policy in place at least by 2011 for records to be destroyed after 8 years [DHNI0000334].

171. It is clear that Dr Mayne supplied data for the Oxford returns and further follow up questions regarding that data [BHCT0000850], [BHCT0000898], [HCDO0000054_005] and [HCDO0000153_008]. This included data referring to named patients and their HIV status [BHCT0000861_003].

172. Information was also shared with the SNBTS about numbers of patients who were HTLV III positive [PRSE0002200 at p.2]. It is not known whether that information was shared on a named patient or anonymous basis.

173. In addition to the Oxford returns data, it seems that Dr Mayne also provided information about patients for research purposes. For example, she provided detailed clinical information about a patient following a request from Dr Rizza to provide a copy of the patient's death certificate for a survey he was undertaking into HIV positive haemophiliacs who had died but where AIDS had not been written on the death certificate [BHCT0000831_001] and [BHCT0000831_003]. In addition, she supplied detailed clinical information about a patient enrolled in the Concorde trial [BHCT0000951].

174. Dr Mayne has stated that *"They were aware that the secretariat collected and compiled stats on an annual basis relating to their treatment and they realised the procedures were necessary in order to estimate changes in treatment product availability year by year. In those circumstances it was a matter of implied, rather than express, consent."* [WITN0736009 at §77.2] However, it is not known whether patients, or their relatives, were asked for and gave any consent to the level of data, including the named data, that was provided.

175. With regard to death certification, Dr Mayne has stated that it was *"the universal practice throughout the United Kingdom ... to omit HIV on any death certificate; however, it was important and prudent on all doctors concerned to inform the undertakers in question so that appropriate precautions could be taken"* [WITN0736001 at §4.4]. Similarly, Dr McNulty notes that Northern Ireland is a small place and that 25 years ago there was a lot of ignorance and fear associated with HIV and hepatitis. She has indicated that *"it was felt to be an act of humanity not to use those terms [of HIV and hepatitis] on the death certificate in order to protect the deceased and their relatives. Very often this was at the specific request of the patient or their family and was not done in an underhand way"* [WITN0921001 at §3.19].

Research

176. Dr Mayne undertook two years of full-time research in 1965. This research related to the role of blood platelets and the blood coagulation system in the development of vascular complications of Type One Diabetes Mellitus. By 1971 she had completed a further period of platelet research at Browne University, Rhode Island and Tufts

University, Boston. However, she has told the Inquiry that when she returned to Northern Ireland she had '*little if any time or opportunity to carry out meaningful research.*' [WITN0736009 at §73.5]. Dr Mayne later became the chair of the University Research Ethics Committee.

177. When Director of the Centre Dr Mayne took part in what she describes as '*minor*' research. This included producing two papers, published in the Ulster Medical Journal, about 20 haemophiliac patients with HIV and the issue of skin sensitivity [WITN0736013].

178. Dr Mayne was also involved in research, along with Dr McNulty, on the purity of NHS Scottish concentrates.

179. Dr Mayne has told the Inquiry that no patients were involved in research studies without their express consent. Further, she states that no patient data – whether anonymised or otherwise – was used in research without patients' express consent. [WITN0736009 at §76.1] She has told the Inquiry that all of her patients were aware of the existence of the UKHCDO and that annual returns were compiled. She describes the consent in these circumstances as '*implied, rather than express, consent.*'

180. The documents suggest that in or around 1988 Dr Mayne took part in a study on previously untreated patients ('PUPs'). She was sent the protocol of this PUP study on 23 December 1988, which had been prepared by Dr Ludlam [MACK0001300_002]. It appears the study was to test a new factor VIII product said to be 5-10 times purer than the existing product, Z8 [SBTS0000297_008]. The study was discussed during a meeting of the Scottish Factor VIII Working Party on 20 April 1989, where concerns about the lack of funding for the study were discussed [PRSE0000921 at p.3]. It is not clear from the available documents what the outcome of the study was.

181. The available documents suggest that Dr Mayne may have taken part, along with other haemophilia clinicians, in some clinical trials. For example, she is listed as attending a meeting about a Factor VIII versus Autoplex trial in February 1982 [OXUH0000451] The documents also suggest that her patients also enrolled on clinical trials, such as the HIV Concord Trial run by the MRC in 1992 [BHCT0000951 and BHCT0000948].

182. Dr Mayne, in common with other clinicians, received funding from the Haemophilia Society for research. For example, in October 1987 she was given a grant of £500 '*for a piece of work on immune response for patients with haemophilia.*' [HSOC0022966 at p.2].

183. An April 1991 memorandum from J. K. Smith refers to a practice whereby the Protein Fractionation Laboratory provided certain products, mostly free of charge to a number of clinicians, on the understanding that clinical data would be provided in return [BPLL0005964]. The available documents suggest that Drs Mayne, Bridges and Dempsey were on the list (along with many other haemophilia clinicians).

Litigation

184. As noted above, Dr Mayne provided an expert report for the Department of Health in the HIV Litigation dated May 1990 [BPLL0002573_001] and [CBLA0000072_024]. The most salient matters in the report are addressed in the relevant sections above but will be explored further during the oral presentation (as will aspects of Dr Mayne's statements to the Inquiry). It is of note that prior to writing this report, she had already been provided with the Opinion that had been obtained by the Haemophilia Society as to the likely success of any litigation [HSOC0023188].

185. When settlement discussions were ongoing, Dr Mayne was informed, as Chair of the UKHCDO, that it was hoped that a settlement would be reached and that one question was as to whether settlement would or would not prevent patients from bringing clinical negligence claims [DHSC0003658_057].[20]

[20] See also DHSC0004523_119.

vCJD

186. On 19 January 2001 the UKHCDO wrote to its members following the finding by BPL that products had been found to contain plasma from a donor who had developed vCJD [BART0000916] The letter, written by Dr Frank Hill, highlighted the varying ways that Centre Directors had chosen to inform - and not to inform - their patients about implicated batches.

187. On 22 January 2001 Dr J A M Anderson, Consultant Haematologist, wrote to the Medical Director of the Royal Group of Hospitals following the BPL notification [DHNI0000049_036]. At that stage she had identified six patients in Northern Ireland (two adults and four children) who had been treated with an implicated batch of Replenine (a factor IX product). There were also eight to nine patients identified who had received an implicated batch of anti-thrombin III.

188. From the documentation it appears that Dr Anderson and Dr Dempsey decided that the best course was to write to all affected patients "*outlining the situation and asking them to ring Dr Dempsey urgently*." The plan was for counselling to take place later that week. One of the affected adults, who had received Replenine, was described as "*a prominent member of the haemophilia society*." Dr Anderson stated:

> "*it was felt by both myself and also by Dr Mayne, with whom I discussed the situation on Saturday morning, that it was essential he was informed. The patient was counselled by myself and took the information relatively quietly, with the comment that this was probably inevitable for any patient receiving plasma derived blood products*."

189. Dr Anderson highlighted the issue about whether to inform or not inform patients who had received anti-thrombin III concentrates. She stated that it would be "*very helpful to get local Department of Health guidelines*" about the appropriate response. She further stated:

> "*I am concerned that I may be accused of with holding [sic] information from one set of patients whilst informing another set of patients. This is of concern as it*

might raise a question of professional misconduct with the GMC and again I would value your views about that. Is there a Trust lawyer who may be able to ponder me with advice about this?

At the end of the day I think this is an extremely complex situation. Dr Dempsey and I have chosen to approach the situation by considering our centre on a particularly individual basis...."

190. It appears that Dr Anderson, and others, had specific concerns about the vCJD situation in Northern Ireland due to a high usage of anti-thrombin III [BHCT0002591]. In correspondence to the Northern Irish Haematology Audit Group in February 2001 Dr Anderson highlighted that haemophiliac patients who had received affected batches of factor VIII and factor IX had been informed of this fact.

191. On 7 September 2004 Drs Dempsey and McNulty attended a Plasma Products Notification meeting at BCH. The purpose of the meeting was to propose a plan of action for notifying patients who had received plasma products potentially contaminated with vCJD [DHNI0000031_043]. It appears from the minutes of this meeting that the approach in relation to notification letters was being managed centrally by the Department of Health in London and the Northern Irish clinicians were told to wait to distribute notification letters until agreed by the Department of Health in London.

192. A further meeting took place a week later, again with Drs Dempsey and McNulty in attendance [DHNI0000031_029]. Dr Frank Jones provided an update and explained that there were two teams searching patient records to identify those that had received plasma products between 1980 and 2001. The plan remained that the Centre was to issue letters on 21 September 2004 to those patients with haemophilia (as well as other congenital bleeding disorders) who were identified as being at risk of vCJD. It was noted that the RVH had agreed the content and format of a patient information sheet to issue in addition to a plan to set up a helpline to deal with patient enquiries.

193. Evidence received by the Inquiry from infected and affected witnesses suggests that these vCJD notification letters were received by patients.

194. A statement is expected from Dr Anderson and will be addressed as appropriate as part of the oral presentation.

Other organisations

UKHCDO

195. Dr Mayne was a member of the UKHCDO from 1967-1999. She attended the inaugural meeting of the newly formed UKHCDO in Oxford in 1968 as a representative of Northern Ireland. When she became the Director of the Centre she attended in her own right [WITN0736009 at §112.2].

196. In March 1977 Professor Nelson, Dr Mayne's predecessor, wrote to Dr Rizza stating that he "*strongly support[ed]*" the establishment of UKHCDO working parties to "*tackle certain problems in the field of haemophilia management and research.*" [OXUH0000483_002] In particular, Professor Nelson supported the establishment of working parties to deal with antibodies, home treatment and quality control of specific factor assays. However, he stated that he "*would not support the topic of the investigation into the incidence of hepatitis in haemophilia, particularly because of our geographical position, and the need to collect and transport specimens.*"

197. Dr Mayne was a member of the UKHCDO Aids Group. In her sixth statement provided to the Inquiry she states that, looking back, that this group had "*reasonable success*" in achieving its aims. [WITN0736009 at §112.3].

198. In 1990 she became Chairman of the UKHCDO, taking over from Dr Rizza. She held this role until 1993.

199. During her Chairmanship, Dr Mayne was a proponent of the need for a formal constitution for the UKHCDO and the need for income generation [HCDO0000493 at p.3]. In 1991, she approached the Charity Commission seeking charitable status for the UKHCDO. This led to a reworking of the UKHCDO constitution, which was agreed at

the final meeting of her Chairmanship. Charitable status of the UKHCDO was established.

200. Dr Mayne oversaw the publication of the 1992 Recommendations on choice of therapeutic products for the treatment of patients with haemophilia A, haemophilia B and von Willebrand's Disease [BART0000877]. She also oversaw a cross regional annual audit, following a pilot scheme between Scotland and Northern Ireland.

201. In addition to the annual returns usually compiled by the UKHCDO clinicians, Dr Mayne sought more detailed information from her colleagues about HIV positive patients and their total factor usage from 1989 and 1990 [PHNT0000001_113].

202. In 1991 she developed a procedure for the reporting of adverse events from blood products [UHMB0000006_033]. During her Chairmanship she met with national providers, where issues about product purity were a central feature of discussions [BPLL0002619]. She liaised with the DHSC about purchasing policy and was not always in agreement with the government's approach: for example [DHSC0003990_059; DHSC0002574_065].

203. In 1993 Dr Mayne's term as Chair ended and she was succeeded by Dr Colvin.

Haemophilia Society

204. Dr Mayne received a number of grants from the Haemophilia Society including for coagulation equipment in September 1977 [HSOC0019918_016] and to fund a part time physiotherapist from 1982 to 1986 [HSOC0019923_003] [HSOC0019923_012][HSOC0019923_019].

205. In addition, she was a member of the Medical Advisory Panel from 1982 to 1994 [HSOC0019918_035]. In 1993 she was instrumental in seeking to change how the Medical Advisory Panel operated. By letter dated 24 February 1993, Dr Mayne noted her conversation with Dr Ludlam after an earlier meeting that *"we all felt it was unsatisfactory"* [LOTH0000069_013]. She suggested that there was a need for minutes to be taken and for discussions to be limited to one or two topics. Thereafter Dr Ludlam

indicated that he felt *"very uncomfortable about the MAP meetings. I entirely agree that minutes are really essential because I am never quite sure whether members of the Haemophilia Society have got the correct information and interpretation. Minutes would allow us to check this."* [LOTH0000069_012]. It is unclear whether this concern was conveyed to the Haemophilia Society in these terms. Nevertheless, it was agreed at the 21 May 1993 meeting that minutes would be taken and papers on one or two specific topics would be circulated in advance so that members could attend the meeting prepared to comment [HSOC0010921_010].

Trusts and schemes

206. Dr Mayne was appointed as a trustee of the Macfarlane Trust from February 1991 to 1996 [DHSC0003417_015] [DHSC0003103_010]. She was one of the Haemophilia Society trustees [DHSC0003107_006]. However, it appears that she also understood her role to be connected with her chairmanship of UKHCDO, giving a formal report to the UKHCDO about Macfarlane matters and vice versa [MACF0000017_049 at p.7] [HCDO0000495 at p.5].

207. In September 1991 she provided advice on producing a guideline for staff on when payments should be made for convalescent breaks, with Trustees wishing for this to be payable for any serious HIV related illness, not just an AIDS diagnosis. They also wished for it to cover chronic, as well as acute illnesses [HSOC0013348_002]. At the same meeting, she spoke against the funding of Haemophilia Society group events on the information available to the Trust at that time.

208. Dr Mayne's primary focus appears to have been to seek an increased sum for regular payments to recipients, rather than the frequent one off grants. In November 1991 she *"reported a request/suggestion that regular payments should be aggregated into a periodic lump sum which would create a more 'usable' sum. The Administrator said that this would be possible, though a not particularly welcome complication"* [MACF0000002_032 at p.6]. Concerns were also raised whether such sums would be charitable payments if people saved the money as it would not then be concerned with the extra cost of living with HIV. This suggestion appears to have been followed up with a paper on the issue in November 1992 which Dr Mayne and Ms Harrington, from

St Thomas' hospital, produced. The paper set out a general and qualitative assessment of needs and costings information. The recommendation to increase regular payments was rejected because they had been increased four months earlier. It was agreed that *"further thought should be given to the viability of a health-related supplement to the regular payment compared with current use of single grants for health-related needs"* [MACF0000002_036 at p.6]. The matter arose again in November 1993 when it was agreed that the regular payments at that time were *"still reasonable"* for those in reasonable health but *"less adequate for those in advanced stages of illness"*. Dr Mayne and Ms Harrington were asked to make proposals on a system of assessment for a "sickness premium" *"which could be objective and fair and could reasonably be presented to people registered without alarming those to whom it was offered or offending those to whom it was not"* [MACF0000013_004 at p.7].

209. Dr Mayne also had some involvement in seeking the opinion of Haemophilia Centre Directors about the provision of funding for IVF and other fertility treatments [MACF0000017_049] [DHSC0003186_009] [HCDO0000495]. It is unclear, however, from the documents what her own view of the issues was.

210. Dr Mayne was also appointed as a trustee of the Eileen Trust from March 1993 to 1996 [DHSC0002757_016].

Relationship with pharmaceutical companies

211. The documents suggest that Dr Mayne was in regular contact with pharmaceutical companies about their products, including providing the results of studies of different products [IPSN0000332_002] and [IPSN0000332_001]. She also provided to them detailed information about the clinical course of individual patients:

    a. In 1972 providing a full account of a patient requiring Haemofil following dental surgery [BHCT0000775].

    b. In 1987 there appear to have been detailed discussions about a patient's adverse reaction to Hyate:C [IPSN0000037_001].

c. Dr Mayne corresponded with pharmaceutical companies, such as Speywood, about the efficacy of factor product following her own testing of it, for example, in July 1980 [IPSN0000332_001] and [IPSN0000332_002]

212. As noted above, Dr Mayne seemingly had strong loyalty to Baxter products because of their *"considerable financial help in the early days"* [IPSN0000332_021]. Other than this, the support provided by pharmaceutical companies appears to have been focused on the provision of hospitality, including at meetings and international get-togethers [IPSN0000332_013]. Speywood sponsored Dr Agnaf's attendance at a conference in 1987 and sponsored Dr Mayne to attend a conference, both of which were to present papers on porcine factor [IPSN0000037_001] [IPSN0000263]. Dr Agnaf was also provided with financial support to visit Speywood for an open day of the laboratories in 1987 [IPSN0000138_009]. In December 1987, Dr Mayne was also given *"a small present, only given to our very best friends, a guaranteed non-leaking Speywood pen"* [IPSN0000037_001].

213. Dr Mayne met with other pharmaceutical companies about their products, including Speywood [IPSN0000332_020] [IPSN0000332_019] IPSN0000332_003]. Dr Mayne describes the relationship between the Centre and pharmaceutical companies as "*business-like and professional*" [WITN0736009 at §11.1].

214. In 1992, there was an outbreak of Hepatitis A, raising concerns about the fractionation processes at Octapharma. Consequently, and seemingly in her role as Chair of UKHCDO, Dr Mayne went to the Octapharma plant in Vienna together with Drs Lee and Jones and Professors Peake and Preston *"to obtain detailed information on the fractionation procedures and to discuss the HAV problem"*. At a meeting of the UKHCDO on 10 December 1992, Dr Mayne reported that she *"had been favourably impressed by the visit to Octapharma"* subject to it being a short visit, and Dr Jones *"agreed with Dr Mayne that it was unlikely that any batch of plasma had been topped up by a different country's input"*. By contrast, Professor Preston was *"less reassured"* by the visit and noted that *"it was unrealistic to expect the company to be completely frank"* [HCDO0000447][LOTH0000051_052].[21] Following the meeting, guidelines

[21] See also HCDO0000446, DHSC0002543_217 and NHBT0000079_085.

were produced recommending that all recipients of pooled plasma should be tested, and where required, vaccinated for hepatitis A, and any case of hepatitis A that was identified should be reported [PRSE0000510] [BAYP0000033_046].

215. In relation to UKHCDO meetings, it appears that at the meeting on 5 September 1994, when Dr Colvin was Chair, Dr Mayne introduced a paper that set out a process of directors making declarations of interest. This paper was agreed [HCDO0000452]. It does not appear that there was any such requirement prior to this meeting.

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